

Poster presentations

Oesophageal, gastric and duodenal disorders

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P0001

LOCAL INFLAMMATORY RESPONSE TO GASTROESOPHAGEAL REFLUX: ASSOCIATION OF GENE EXPRESSION OF INFLAMMATORY CYTOKINES WITH MULTICHANNEL INTRALUMINAL PH-IMPEDANCE DATA

S. Morozov¹, I. Vorozhko², T. Sentsova³

¹Federal Research Center of Nutrition and Biotechnology, Gastroenterology, Hepatology and Nutrition, Moscow, Russian Federation, ²Federal Research Center of Nutrition and Biotechnology, Laboratory of Clinical Biochemistry and Immunology, Moscow, Russian Federation, ³Russian National Research Medical University named after N.I. Pirogov, Department of Hospital Pediatrics No. 2, Moscow, Russian Federation

Contact E-Mail Address: morosoffsv@mail.ru

Introduction: Expression of inflammatory cytokines' genes may take part in pathophysiology of different forms of gastroesophageal reflux disease (GERD). However, its role in local inflammatory response and association with types and number of gastroesophageal refluxes is poorly studied yet¹.

Aims & Methods: To explore the expression of inflammatory cytokines' genes in esophageal mucosa in patients with erosive esophagitis and non-erosive forms of gastroesophageal reflux disease and its association with data of esophageal multichannel intraluminal pH-impedance measurements.

This was a single-center prospective study. Esophageal mucosa samples were taken from lower part of the esophagus during endoscopy. Expression of IL-1 β , IL-10, IL-18, TNFA, TLR4, GATA3, CD68 and beta-2 macroglobulin genes in esophageal mucosa was assessed with ImmunoQuantex assays.

Multichannel intraluminal esophageal pH-impedance (MII-pH) studies were performed to all the participants.

Diagnosis of GERD was confirmed by the results of MII-pH data. Based on the endoscopy, patients were allocated to the group of erosive esophagitis (EE) and non-erosive GERD (NERD).

The control group consisted of non-symptomatic subjects with normal endoscopy and MII-pH results. We used non-parametric statistics to compare the differences between the groups. Association of expression of the mentioned genes and the results of MII-pH data was assessed with Spearman rank method.

Results: Data of 60 patients with GERD and 10 subjects of the control group were available for the analysis. Higher expression of IL-18 (5.89 $\pm$ 0.4 vs 5.28 $\pm$ 1.1, p=0.04) and GATA3 (2.92 $\pm$ 0.86 vs 2.23 $\pm$ 0.96, p=0.03) genes was found in EE group compared to NERD.

Expression of IL-1 β , IL-18, TNFA, and TLR4 genes was lower (P<0.05) in the control group compared to EE and NERD. Esophageal acid exposure correlated with the expression of IL-1 β (Spearman rank R = 0.29), IL-18 (R=0.31), TNFA (R=0.35), GATA3 (R=0.34), TLR4 (R=0.29), CD68 (R=0.37) genes.

Mean esophageal pH correlated inversely with the expressions of IL-18, TNFA, GATA3, TLR4, CD68 genes. No association between genes expression and number of gastroesophageal refluxes was found (Table 1).

	Number of GERs	Acid GERs	Weak-acid GERs	Non-acid GERs	High GERs	Mean pH	AET
IL-1 β	-0.02	0.14	-0.11	0.04	-0.03	-0.24	0.29 ^a
IL-10	-0.15	-0.02	-0.16	0.02	0.01	-0.21	0.18
IL-18	0.01	0.06	-0.02	0.01	0.01	-0.28 ^a	0.31 ^a
TNFA	-0.03	0.08	-0.12	0.01	-0.12	-0.33 ^a	0.35 ^a
GATA3	0.04	0.15	-0.13	-0.1	0.02	-0.28 ^a	0.34 ^a
TLR4	-0.05	0.04	-0.15	0.06	-0.04	-0.28 ^a	0.29 ^a
CD68	0.01	0.05	-0.03	-0.01	-0.08	-0.39 ^a	0.37 ^a
B2M	0.04	0.10	-0.04	0.17	0.09	-0.26	0.34 ^a

Notes: ^a - marked values are statistically significant (P<0.05); GERs – gastroesophageal refluxes; AET – acid exposure time (proportion of time with pH<4 per 24 hours at 5 cm above upper border of lower esophageal sphincter); mean pH – mean values of pH at 5 cm above upper border of lower esophageal sphincter.

Table 1. Correlation coefficients (by Spearman rank R) between the results of between the data of 24-hours multichannel intraluminal pH-impedance records and local expression of inflammatory cytokines.

Conclusion: In patients with erosive esophagitis, local expression of interleukin 18 and GATA3 transcription factor genes was higher compared to subjects with non-erosive form of gastroesophageal reflux disease. Esophageal acid exposure correlated directly with expression of IL-1 β , IL-18, TNFA, TLR4, CD68 and B2M genes. Inverse correlation revealed between expression of IL-18, TNFA, GATA3, TLR4 CD68 genes and mean esophageal pH.

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P0002

RNA SEQUENCING REVEALS FEW MOLECULAR DIFFERENCES IN OESOPHAGEAL MUCOSA BETWEEN PATIENTS WITH EROSIVE AND NON-EROSIVE REFLUX DISEASE

A. Ustaoglu¹, M. Peiris¹, D. Sifrim¹, P. Woodland¹

¹Blizard Institute, Queen Mary University of London, Wingate Institute of Neurogastroenterology, London, United Kingdom

Contact E-Mail Address: a.ustaoglu@qmul.ac.uk

Introduction: Molecular signature of the oesophageal mucosa of patients with gastro-oesophageal reflux disease (GORD) is yet to be clearly established. We recently identified expression of transient receptor potential vanilloid subfamily member-1 on superficial sensory nerves in patients with non-erosive reflux disease (NERD), alongside increased epithelial cell expression of acid-sensing ion channel-3 in erosive esophagitis and NERD, collectively highlighting mucosal mechanisms for heartburn sensation in different reflux phenotypes.

However, acid reflux-induced alterations to epithelial barrier integrity, mucosal inflammation and sensitivity are likely to have an overlapping role in heartburn pathogenesis in GORD.

Aims & Methods: We sought to better understand why some patients with heartburn symptoms develop oesophagitis while others develop NERD, using a bulk RNA sequencing approach.

19 patients with heartburn symptoms were phenotyped endoscopically and with objective reflux studies into erosive oesophagitis (N=10) and NERD (N=9) groups. Erosive oesophagitis patient biopsies were collected from a non-macroscopically inflamed segment of the distal oesophagus. RNA extracted from distal oesophageal mucosal biopsies taken at endoscopy from 19 GORD patients and 8 healthy volunteers were sequenced using NEBNext Ultra II Directional RNA Kit. Differential expression analysis and downstream functional enrichment analysis were performed with DESeq2 and goseq R packages, respectively.

Results: Compared with the oesophageal mucosa of healthy controls, erosive oesophagitis patients had 1665 significantly differentially expressed (DE) genes which were highlighted in 147 molecular pathways including, an enriched immune response, cytokine-mediated signalling, and leukocyte migration, as statistically significant ($p < 0.01$). NERD patients had 945 significantly differentially expressed (DE) genes compared to healthy controls, enriched in 84 molecular pathways including increased neutrophil degranulation, regulation of axon regeneration, and keratinocyte differentiation in NERD.

Interestingly, DESeq2 analysis between oesophageal mucosa of patients with erosive oesophagitis and NERD revealed only 10 significantly DE genes which were implicated in enriched extracellular matrix organisation, cell proliferation, and nerve growth factor signalling in erosive oesophagitis compared to NERD. None of the 10 DE genes identified were critically involved in barrier function.

Conclusion: Although the oesophageal mucosal gene expression signature is heterogeneous between healthy controls and heartburn patients, in erosive and non-erosive reflux disease it is strikingly similar at a molecular level. This suggests it is more likely that mucosal differences between erosive oesophagitis and NERD result from differences in severity of reflux or the chemical composition of refluxate damaging the oesophageal mucosa in these patients.

Disclosure: Nothing to disclose.

P0003

THE ACTIVITY OF THE JAK/ STAT PATHWAY IS DECREASED IN PATIENTS WITH ACHALASIA

S. Kipcak^{1,2}, P. Ergun^{2,3}, N. Selvi Gunel¹, S. Bor²,
Ege Reflux Study Group

¹Ege University, School of Medicine, Department of Medical Biology, Izmir, Turkey, ²Ege University, School of Medicine, Department of Gastroenterology, Izmir, Turkey, ³Ege University, School of Medicine, Department of Medical Biochemistry, Izmir, Turkey

Contact E-Mail Address: kipcaksezgi@gmail.com

Introduction: The pathogenesis of achalasia is not well characterized. The disease is localized in the muscle and effects neurons however data is limited at the esophageal epithelium (EE). EE is particularly important because therapeutic procedures such as POEM increases the risk of gastroesophageal reflux disease (GERD).

It is not known that long-term stasis and other effects predispose the EE to GERD. Jak/STAT is the main signaling mechanism for various cytokines and growth factors and its role within the EE.

Aims & Methods: The aim of the study is to determine the activation states of JAK/STAT pathway in achalasia. 37 (23 female) achalasia patients and 15 (6 female) healthy volunteers (HV) were included in the study. Epithelial esophageal biopsies taken by endoscopy were used to determine the

expression levels of JAK STAT-related genes and phosphorylated proteins. Gene expression levels were determined by the qRT-PCR method, protein levels were examined by Multiplex ELISA method.

Results: In our results, JAK1, JAK2, STAT1, STAT2 (-3.02, -2.43, -5.72, -4.31 fold, respectively) gene expression levels, which are important genes of the JAK/STAT pathway, expressed at lower levels in achalasia patients compared to HVs. The SOCS family activated by cytokines, is a negative regulator of the JAK-STAT pathway (1).

We determined that the SOCS1 and SOCS3 (8.15, 2.99 fold, respectively) genes are expressed at higher levels in achalasia patients compared to HVs. MAPK/ERK pathway is involved in the downstream regulation of the JAK-STAT pathway (2).

We also studied the levels of important proteins involved in MAPK/ERK pathway. Erk1/2 (Th202/Tyr204), MEK1 (Ser217/Ser221), c-Jun (Ser63) were low expressed in achalasia compared to HVs.

Conclusion: The low expression of the important genes of the JAK-STAT pathway and the high expression of the genes of the SOCs family, which is the negative regulator of this pathway, are important evidence of the low activity of the JAK-STAT pathway in achalasia patients. In addition, low expression of the proteins which are downstream of the JAK/STAT pathway supported the gene expression data. Long-term stasis and other effects in the achalasia EE do not cause activation of inflammation pathways like JAK/STAT, therefore achalasia EE may not be predisposed to GERD before the achalasia treatment.

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Disclosure: Nothing to disclose.

P0004

CALORIC RESTRICTION CONDITIONS AS A MODULATOR SIGNAL FOR SIRTUINS (SIRT) EXPRESSION - A NOVEL VIEW OF GASTRIC CANCER METASTASIS? (IN VITRO STUDY)

A. Poniewierska-Baran¹, P. Warias¹, K. Zgutka²

¹University of Szczecin, Institute of Biology, Szczecin, Poland,

²Pomeranian Medical University of Szczecin, Department of Physiology, Szczecin, Poland

Contact E-Mail Address: agata.poniewierska@gmail.com

Introduction: Gastric cancer is a major health burden worldwide. It is the second cause of cancer deaths after lung cancer. The literature is reviewed for evidence concerning the relation between calorie intake or body weight and cancer formation. Yet, various forms of reduced calorie intake such as caloric restriction or fasting demonstrate a wide range of beneficial effects able to help prevent malignancies and increase the efficacy of cancer therapies. It is known that Sirtuins (SIRT), are NAD(+)-dependent histone deacetylases regulating important metabolic pathways. The seven members of this family of enzymes play also fundamental roles in carcinogenesis.

They are key factors in maintenance of the malignant phenotype, mainly participating in cancer cell viability, apoptosis, metastasis, and tumorigenesis. So far, there are no data describing the impact of caloric restriction on the production of the entire SIRT family in gastric cancer cells.

Aims & Methods: The aim of our study was to perform SIRT's expression profiles in an established gastric cancer line CRL-1739 under caloric restriction.

We used AGS (ATCC®, CRL-1739™) adenocarcinoma cell line. The cells were cultured in two types of caloric restriction models:

1. RPMI +10% FBS (fetal bovine serum) with glucose limitation (0 mg/mL; 1mg/mL; 4,5mg/mL and 10mg/mL) and
2. RPMI without any glucose (0 mg/mL) and with different concentration of FBS (0%, 10%), to see if glucose or nutrients restriction are more shocking for cancer cells. Profile of SIRT's expression was assessed in 6 time points between 0-96h of incubation, using qRT-PCR method.

Results: For the first time, all sirtuins family expression analysis was performed in gastric cancer cell line. The results showed: 1. Large production of SIRT's (especially 1 and 7) during the caloric restriction period. The highest increase in SIRT's expression was noticed at the first time points (1h and 24h). After 48h the level of SIRT's expression returned to the values recorded in non-conditioned cells (without limitation of FBS or glucose).

Conclusion: These results prove a strong impact of caloric restriction in the production of SIRT in gastric cancer cells. We also noticed correlations in SIRT expression, caloric restriction and gastric cancer cell proliferation.

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Disclosure: Nothing to disclose.

P0005

HEPATITIS B REPLICATION MARKERS ALONG WITH ENTRY RECEPTOR ON PLACENTA INDICATE: ANOTHER HOME FOR THE VIRUS

G. Garg¹, K. Patel¹, S. Purwar¹, S. Mukhopadhyay², N. Mishra³, D. Biswas¹, A. Singh¹, A.K. Vyas¹

¹All India Institute of Medical Sciences, Microbiology, Bhopal, India,

²All India Institute of Medical Sciences, Pathology, Bhopal, India,

³Gandhi Medical College, Microbiology, Bhopal, India

Contact E-Mail Address: a88_ashish@yahoo.co.in

Introduction: Hepatitis B chronic infection due to mother-baby vertical transmission of HBV is one of the major causes of HCC worldwide 1,2,3. The role of sodium taurocholate co-transporting polypeptide (NTCP), in facilitating the binding of the virus on the surface of hepatocytes is well documented 4.

Expression of NTCP in extrahepatic cells may make these cells susceptible to HBV infection and support cellular proliferation akin to hepatocytes. *Placental replication of HBV is not well explored/studied*.

Aims & Methods: In this study, our aim is to investigate the role of the placenta in HBV mother-to-baby vertical transmission. We have assessed the expression of NTCP and HBV replication markers (HBeAg, HBcAg, and HBV DNA) in placental cells, to investigate if these cells act as host/reservoir for HBV and which could be one of the causes of HCC in the pediatric population.

Results: Twenty HBsAg+ve pregnant women along with 10 healthy controls were enrolled after obtaining informed consent. The HBV DNA in the placenta was detected by qPCR using primers for X and core ORF. The expression of NTCP in the placenta was analyzed by qRT-PCR and was further investigated by immunohistochemistry (IHC) along with HBV replication biomarkers, HBsAg, HBeAg, and HBcAg.

HBV-infected females showed increased expression of NTCP in trophoblasts of the placenta compared to the control group (3.62±0.96 Vs 1.44±0.81). Furthermore, a significant difference in NTCP expression was also observed between HVL and LVL groups (3.62±0.96 Vs 2.06±1.3) and it was correlated with the maternal HBV DNA load. Membranous and/or Cytoplasmic immunostaining of NTCP, and cytoplasmic staining of HBeAg and HBcAg in trophoblasts along with the presence of HBV DNA indicated that trophoblasts are not only susceptible to HBV infection but may also be a probable site for viral replication.

Conclusion: This is the pioneer study, which demonstrates the expression of NTCP on the placenta which may facilitate the entry of HBV. Furthermore, the study establishes the presence of HBeAg in trophoblasts indicating these cells may act as replication host/reservoirs. The correlation of NTCP expression with maternal viral load and the presence of HBeAg in the placenta indicates its probable role in the vertical transmission of HBV and which could be one of the causes of HCC in a pediatric population. Our preliminary findings suggest that NTCP blocking strategy may be used for therapeutic intervention of vertical transmission.

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Disclosure: Nothing to disclose.

P0006

MODERN STUDY ABOUT THE ROLE OF MACROPHAGES AND TRANSFORMING FACTOR B1 IN THE PATHOGENESIS OF PRIMARY SCLEROSING CHOLANGITIS AND ITS ASSOCIATION WITH INFLAMMATORY INTESTINAL DISEASES

G. Goyibova¹, A. Umarov², F. Alyaviya²

¹Tashkent Pediatric Medical Institute, Department of Gastroenterology, Tashkent, Uzbekistan, ²Tashkent Medical Academy, Department of Gastroenterology, Tashkent, Uzbekistan

Contact E-Mail Address: miss_gulinoza@mail.ru

Introduction: Macrophages are cells capable of absorbing and digesting foreign or harmful particles for the body: bacteria, the remains of destroyed cells, etc. It is important to investigate their new features.

Aims & Methods: To study the role of macrophages (CD68+) and transforming factor β1 (TGF-β1) in the pathogenesis of primary sclerosing cholangitis (PSC) and its association with inflammatory bowel diseases (IBD) in the interests of searching for new differential diagnostic markers of isolated and combined PSC and IBD. Immunohistochemical study of samples

(4 biopsies each) of the lamina propria (SO) of the ileum, the colon was carried out in 18 patients with PSC, of which 11 had active IBD. The control group consisted of 24 patients with moderate and severe isolated IBD (14 and 10 patients with ulcerative colitis (UC) and Crohn's disease (CD), respectively).

When evaluating liver biopsies (17 patients with PSC, of which 9 people with IBD/PSC), the counting was carried out in 3 sections of the hepatic lobule. Quantification of CD68+ and TGF- β 1 expression (absolute number of cells) was performed in 5 fields of view for each marker in 1 mm².

Results: Expression of CD68+ and TGF- β 1 in intestinal mucosa was high in all patients with PSC, regardless of the presence of active inflammation. The presence of CD68+ and TGF- β 1 in the intact intestinal mucosa is most likely due to their involvement in maintaining homeostasis. It is possible that we observed preclinical manifestations of IBD or predictors of their development. Expression of macrophages CD68+ and TGF- β 1 was higher ($p < 0.05$) in intestinal mucosa with active inflammation than in PSC without endoscopic and morphological signs of colitis. This is consistent with literature data and indicates that hyperproduction of CD68+ and TGF- β 1 inactive IBD. The expression of CD68+ in our study was higher in patients with isolated UC than in IBD/PSC, and the expression of TGF- β 1 did not differ statistically.

These changes may be explained by the higher morphological activity of UC in our work. High expression of CD68+ and TGF- β 1 in nonparenchymal liver cells confirms their key role in the pathogenesis of PSC. According to our data, increased expression of CD68+ occurred in all parts of the hepatic lobule, however, we recorded the predominance of CD68+ expression in the periportal zone, which is explained by the localization of inflammation in PSC. This may be of great practical importance in differential diagnosis with others, including autoimmune, liver diseases.

Conclusion: CD68+ and TGF- β 1 play an important role in the pathogenesis of PSC and its association with IBD. A promising diagnostic marker of PSC may be an increased expression of TGF- β 1 in the periportal zone of the hepatic lobule. CD68+ is probably important for the diagnosis of isolated and associated IBD. Further research is required.

Disclosure: Nothing to disclose

P0007

FERULIC ACID TREATS GASTRIC ULCER VIA SUPPRESSING OXIDATIVE STRESS AND INFLAMMATION

A. Ermis¹, G. Aritici Colak², M. Acikel Elmas³, S. Arbak³, M. Kolgazi⁴

¹Acibadem Mehmet Ali Aydinlar University, Institute of Health Sciences, Department of Nutrition and Dietetics, Istanbul, Turkey,

²Acibadem Mehmet Ali Aydinlar University, Faculty of Health Sciences, Department of Nutrition and Dietetics, Istanbul, Turkey,

³Acibadem Mehmet Ali Aydinlar University, School of Medicine, Department of Histology and Embryology, Istanbul, Turkey,

⁴Acibadem Mehmet Ali Aydinlar University, School of Medicine, Department of Physiology, Istanbul, Turkey

Contact E-Mail Address: aleya.ermis@acibadem.edu.tr

Introduction: Gastric ulcer is one of the most common gastrointestinal system diseases, affecting approximately 10% of the world population. It mainly develops due to an imbalance between aggressive and protective factors. For years, the main targets of the treatment have been accepted as gastric acid secretion and H2RA blockers, PPIs are used to treat stomach ulcer cases.

However, there are adverse effects such as hypersensitivity, arrhythmia, hypomagnesemia, gynecomastia, and gastric cancer that restrict the clinical usage of most medications, in addition to a lack of complete recovery

in the treatment of gastric ulcers. It has become a research target to determine a new treatment that is safe, effective, and non-toxic derived from vegetables and fruits with gastric protective effects.

Aims & Methods: The present study aimed to evaluate the gastroprotective potential of ferulic acid on indomethacin-induced gastric ulcers in rats. Adult male Sprague-Dawley rats (200–250 g) were randomly divided into five groups: the control group, the ulcer group, and the FA groups (100, 250, and 500 mg/kg, respectively). After 24-h starvation, all the groups received subcutaneous indomethacin at a dose of 25 mg/kg dissolved in 5% NaHCO₃, except for the control group. Fifteen minutes later, the rats in the control and ulcer groups were given vehicle (10% tween 80) with oral gavage, and the rats in the FA groups were treated with 100, 250, and 500 mg/kg FA (suspended in 1 mL of 10% tween 80). On the 4th hour, rats were euthanized by exsanguination under isoflurane anesthesia.

Gastric samples were collected for macroscopic and microscopic examination. To assess the oxidative and inflammatory state, stomach samples were also analyzed for malondialdehyde (MDA), glutathione (GSH), and superoxide dismutase (SOD), myeloperoxidase (MPO), tumor necrosis factor (TNF)- α , interleukin (IL)-1 β , IL-6, and nuclear factor kappa-B-p65 (NF- κ B-p65) levels.

Results: In the ulcer group, indomethacin injection significantly increased the macroscopic and microscopic damage scores, gastric levels of the MDA, MPO, TNF- α , IL-1 β , IL-6, and NF- κ B p65 levels, but reduced the SOD and GSH content of gastric tissues. Treatment with FA significantly improved gastric injury both macroscopically and microscopically. FA displayed a marked decrease in the gastric levels of MDA, MPO, TNF- α , IL-1 β , IL-6, and NF- κ B p65 and a significant increase in the gastric levels of SOD and GSH when compared to the indomethacin group. While the 100 mg/kg dose had no significant effect, 250 mg/kg FA was the most effective dose.

Conclusion: This study showed that FA has considerable anti-ulcer activity. Our results revealed that the gastroprotective effect of FA against indomethacin-induced gastric ulcers in rats might be attributed to its antioxidant and anti-inflammatory properties. In conclusion, FA is a potential treatment choice for indomethacin-induced gastric ulcers.

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P0008

SEVERE GASTRITIS AND DUODENITIS IN PATIENTS TREATED WITH IMMUNE CHECKPOINT INHIBITORS: A MULTICENTER STUDY

C. Breteau¹, P. Bonnet², C. Robert³, P. Saiag², B. Buecher⁴, C. Lebbe⁵, M. Allez⁶, R. Benamouzig⁷, H. Hagège⁸, H. Bécheur⁹, A. Meyer¹, F. Carbonnel¹

¹Bicêtre Hospital, Paris Saclay University, Gastroenterology, Le Kremlin-Bicêtre, France, ²Ambroise Pare Hospital, Université Versailles Saint-Quentin-en-Yvelines, Dermatology, Boulogne-Billancourt, France, ³Institut Gustave Roussy, Paris Saclay University, Medicine, Villejuif, France, ⁴Institut Curie, PSL Research University, Genetics and Medical Oncology, Paris, France, ⁵Saint Louis Hospital, Paris University, Dermatology, Paris, France, ⁶Saint Louis Hospital, Paris University, Gastroenterology, Paris, France, ⁷Avicenne Hospital, Sorbonne Paris Nord University, Gastroenterology, Bobigny, France, ⁸Hôpital Intercommunal de Créteil, Gastroenterology, Créteil, France, ⁹Bichat-Claude Bernard Hospital, Paris University, Gastroenterology, Paris, France

Contact E-Mail Address: breteau49@msn.com

Introduction: Immune checkpoint inhibitors (ICI; anti-PD1 and/or anti-CTLA-4) can induce immune-related adverse events (irAEs). Upper gastrointestinal (GI) irAEs have been reported but data are scarce.

Aims & Methods: We aimed to describe upper GI irAEs in patients treated with ICI. In this retrospective study we included patients with upper GI symptoms and endoscopic erosions or ulcerations of the esophagus, stomach or duodenum during or up to 6 months after ICI discontinuation, in hospitals of the Paris area.

We excluded patients who had upper gastrointestinal symptoms unrelated to ICI (gastroesophageal reflux disease, *Helicobacter pylori* infection, Crohn's disease, amyloidosis, metastasis).

Results: Between January, 2013 and December, 2021, 35 patients were included. Twenty-three (66 %) were men, their median age was 63 years (range 27-89). Patients were treated with anti-PD1 (n=19, 54%), anti-CTLA-4 (n=4, 11%) or both (n=12, 34%). Twenty-eight patients had a melanoma (80.0%), 4 had a Non-Small Cell Lung Cancer (11.4%), 3 (8.6%) had another cancer. Symptoms occurred 3.3 months (0.10-23.80) after the initiation of ICI. These were epigastric pain (n=25, 71%), nausea (n=22, 63%), weight loss (n=23, 66%), diarrhoea (n=20, 57%), and early satiety (n=12, 34%). Twenty-six (74%) had others irAEs including 18 (51%) with gastrointestinal irAEs (ileitis or colitis).

Twenty-eight (80%) patients had a severe gastritis. Main endoscopic findings were erosions in 8 (23%), ulcerations in 9 (26%), hemorrhage in 9 (26%), and necrotic gastritis in 2 (6%) patients. Endoscopic biopsies showed chronic gastritis in 3 (11%) patients (lymphoplasmacytic infiltrate without activity), and active gastritis in 25 (89%) patients (periglandular inflammation, lymphoplasmacytic infiltrate and neutrophils).

Fourteen patients (40%) had a severe duodenitis. Eight (23%) patients had erosions, 5 (14%) had ulcers, and 1 (3%) had a hemorrhagic duodenitis. Endoscopic biopsies showed active duodenitis (lymphoplasmacytic infiltrate and neutrophils in the lamina propria and in the epithelium), with (n=2, 17%) or without (n=10, 83%) villus atrophy.

Three patients (9%) had an esophagitis associated with gastritis or duodenitis: 1 patient had superficial erosive lesions of the esophagus, 2 patients had ulcerated lesions of the esophagus.

The median follow-up was 15 months (1-80). Thirty-one patients (89%) were treated with corticosteroids. Among them, 26 patients (84%) responded and 18 (58%) reached clinical remission. Fourteen patients had a new upper gastro-intestinal endoscopy after corticosteroids; 12 (86%) had an endoscopic response; including two patients (14%) with mucosal

healing. Seven patients were treated with infliximab, 5 responded (71%), including 2 (29%) who reached clinical remission. One patient was treated with vedolizumab and had clinical response without remission.

Conclusion: ICI can induce severe esophagitis, gastritis and duodenitis. Corticosteroids and infliximab induce clinical response in the majority of patients.

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P0009

A SINGLE-CELL TRANSCRIPTIONAL LANDSCAPE OF IMMUNE CELLS REVEALS A DISEASE-SPECIFIC COMPOSITION AND TRANSCRIPTIONAL PHENOTYPE IN HUMAN ACHALASIA

Z.-Q. Liu¹, X.-Q. Li¹, H. Dai², L. Yao¹, L.-N. Chen², P.-H. Zhou², Q.-L. Li¹

¹Zhongshan Hospital, Endoscopy Center and Endoscopy Research Institute, Shanghai, China, ²Shanghai Institute of Biochemistry and Cell Biology, Center for Excellence in Molecular Cell Science, Chinese Academy of Sciences, Key Laboratory of Systems Biology, Shanghai, China

Contact E-Mail Address: li.quanlin@zs-hospital.sh.cn

Introduction: Achalasia is a rare motility disorder of the esophagus caused by the gradual degeneration of myenteric neurons. Immune-mediated ganglionitis has been proposed to underlie the loss of myenteric neurons. We aimed to map the immune cell transcriptional landscape and identify disease-associated transcriptional changes in achalasia using single-cell RNA sequencing (scRNA-seq).

Aims & Methods: Nine achalasia patients and 4 controls with paired tissue and blood samples, and 2 achalasia patients with only peripheral blood samples were included in this study. Patients with benign leiomyomas originating from LES served as controls. Immune cells in tissue were dissociated from smooth muscle in LES. Transcripts of 137,346 cells were determined using scRNA-seq and coupled T cell receptor and B cell receptor sequencing. Results were confirmed by multicolor immunohistochemistry.

Results: In achalasia, we identified a pattern of expanded immune cells and a unique transcriptional phenotype, especially in LES tissue. The C1QC⁺ macrophages, ZNF683⁺ CD8⁺ tissue-resident memory T (Trm), and XCL1⁺ CD4⁺ Trm clusters were significantly expanded and localized surrounding the myenteric plexus in LES tissue of achalasia. C1QC⁺ macrophages were functionally similar to microglia of the central nervous system and exhibited a neurodegenerative dysfunctional phenotype in achalasia. ZNF683⁺ CD8⁺ Trm and XCL1⁺ CD4⁺ Trm clusters also expressed transcripts of an inflammatory phenotype in achalasia. Moreover, inflammation increased with disease progression since immune cells were more activated in type I compared with type II achalasia.

Conclusion: We identified the C1QC⁺ macrophages, ZNF683⁺ CD8⁺ Trms, and XCL1⁺ CD4⁺ Trms as distinct immune cell clusters that underlie the mechanism of the inflammatory process in achalasia.

Disclosure: Nothing to disclose.

P0010

TISSUE ADHESIVE POLYACRYLAMIDE HYDROGEL INCORPORATING TRIAMCINOLONE ACETONIDE IS EFFECTIVE FOR PREVENTION OF FIBROSIS IN RATS' ESOPHAGUS

N. Nakajima^{1,2}, S. Mitragotri², S. Terai¹

¹Graduate School of Medical and Dental Sciences, Niigata University, Division of Gastroenterology and Hepatology, Niigata, Japan, ²Harvard John A. Paulson School of Engineering and Applied Sciences, Allston, United States

Contact E-Mail Address: naon_funky1@yahoo.co.jp

Introduction: Esophageal stricture formation is known as a very challenging complication of endoscopic submucosal dissection (ESD) for wide spread superficial esophageal cancer. It is caused by hyper fibrosis on the esophageal epithelium. Topical triamcinolone acetonide (TCA) injection to the ulcer base after ESD is partly effective for the stricture. However, it still has limitations to manage the disease completely. Tissue adhesive

materials to wet and dynamic surfaces such as gastrointestinal tract have great benefits for sustained release of drug. Based on these stories, we hypothesized that tissue adhesive material which has stability to the esophagus and controlled-releases TCA could be helpful to manage the disease. Here, we designed highly adhesive polyacrylamide hydrogel with controlled-releasing TCA and predicted that the local administration of the hydrogel could effectively prevent fibrosis in the esophagus.

Aims & Methods: The objective of this study is to examine the efficacy of the tissue adhesive polyacrylamide hydrogel incorporating TCA for preventing fibrosis in rats' esophagus.

Methods (1) Making the tissue adhesive polyacrylamide hydrogel : Solution of acrylamide, ammonium persulfate, tannic acid, TCA drug crystal, and N,N'-methylene bisacrylamide were mixed with tetramethylethylenediamine to synthesize the hydrogel. The hydrogel was characterized by FT-IR, scanning electron microscope, and tensile test. (2) Controlled-release of TCA from the hydrogel : The hydrogel was placed in 2 mL of PBS containing collagenase D. The release test was carried out at 37°C and the PBS was exchanged at different time points. The amount of TCA in the supernatant was determined by High Performance Liquid Chromatography. (3) In vivo stability test in rats' esophagus : 647 ovalbumin solution was added while making the hydrogel for this stability study. 200 µL of PTA hydrogel was applied to the rats' esophagus. After that, rats were restricted water and food intake. 24 hours later, rats were euthanized and extracted esophagus was observed by fluorescent imaging. (4) In vivo rat esophageal fibrosis model : Rats were performed a median laparotomy and 1 cm segment of the distal esophagus was exposed. The isolated segment was distended by administering 0.1 mL of 30% NaOH for 90 secs. The rats were euthanized in three weeks and the histology of the esophagus was evaluated by Masson's trichrome staining.

Results: 1. Making the tissue adhesive polyacrylamide hydrogel : The hydrogel was obtained in 30 minutes and characterizations showed its high adhesiveness.

2. Controlled-release of TCA from the hydrogel : The amount of released TA increased gradually over time. $85.3 \pm 3.4\%$ of TCA in the PTA hydrogel was released in 24 h and 100% of TCA was released in 48h.

3. In vivo stability test in rat's esophagus : 24 hours after the PTA hydrogel administration, the fluorescent imaging showed that the hydrogel remained in the rat's esophagus.

4. In vivo rat esophageal fibrosis model : In histological analysis, Masson's trichrome staining positive area/whole area (Fibrosis area rate) with the hydrogel group was significantly smaller than that with the disease group ($9.04 \pm 0.62\%$ vs $18.91 \pm 1.82\%$, $p = 0.004$).

Conclusion: We developed tissue adhesive hydrogel incorporating TCA. It had stability in the rats' esophagus and its efficacy in preventing fibrosis was observed. This study implicates the potential of the hydrogel as a topical TCA treatment for the stricture formation after the ESD.

Disclosure: Nothing to disclose.

P0011

FUNCTIONAL DYSPEPSIA DUODEUM MUCOSAL ASSOCIATED MICROBIOTA: COMPARISON BETWEEN FRESH BIOPSY AND HISTORICAL FORMALIN-FIXED PARAFFIN-EMBEDDED BIOPSIES IS VIABLE

E. Hoedt¹, K. Fan¹, G. Burns¹, S. Kang², M. Morrison³, N.J. Talley³, S. Keely⁴

¹University of Newcastle, Centre for Research Excellence in Digestive Health, Newcastle, Australia, ²University of Queensland, Diamantina Institute, Brisbane, Australia, ³University of Newcastle, Faculty of Health & Medicine, New Lambton Heights, Australia, ⁴University of Newcastle, New Lambton Heights, Australia

Contact E-Mail Address: Emily.Hoedt@newcastle.edu.au

Introduction: Emerging evidence suggests there is a specific duodenal mucosal associated microbiota (MAM) signature for functional dyspepsia (FD), although study numbers are low and consensus on biomarkers have not been reached. Additionally, we now know that FD is associated with high duodenal eosinophil counts and this site-specific immune response is likely interacting or responding to the MAM.

Aims & Methods: As duodenal biopsies for research can be difficult to obtain, we aimed to investigate formalin-fixed paraffin-embedded (FFPE) biopsies, routinely collected for pathology, sequence the MAM and compare them to the MAM profiles of matched RNAlater preserved biopsies. Duodenal biopsies (n=4) stored in RNAlater were homogenized for 3 mins at 5,000 rpm using the Precellys 24 homogenizer after removal from RNAlater solution. The total DNA was then extracted and purified with the Promega Maxwell automated DNA recovery system following manufacturer's instructions. DNA from matched FFPE sections (40 µm) were extracted with Qiagen deparaffinization solution and FFPE DNA extraction kit following manufacturer's instructions. 16S amplicon sequencing was completed targeting the V6-V8 region. Reads were processed with QIIME2/DADA2 and referenced against the SILVA SSU r138 database. Analysis of microbiota diversity was performed in R packages and Calypso. Data was transformed using Cumulative Sum Scaling + log2.

Results: The mean sequencing depth of RNAlater biopsies was 4115 and FFPE was 20170. The alpha diversity was significantly greater for FFPE sequenced samples when compared to whole biopsies (Chao1 P=0.029). Additionally, RDA multivariate analysis demonstrated significant clustering (P=0.024) of FFPE communities compared to the patient matched whole biopsy extracts. Permutational multivariate analysis of variance (adonis function) and ANOSIM Bray-Curtis were also both significant when comparing the MAM of each extraction type (P=0.0297 and 0.023 (R =1), respectively). There were also fewer "unknown" taxonomic assignments for FFPE samples compared to the matched biopsies.

Conclusion: Here we have shown that MAM 16S sequencing from FFPE tissue sections (tested 2-4yrs old) is a viable option and means that single biopsies can be multi-functional (histopathology and viable DNA recovery). The viability of MAM sequence amplification from FFPE provides a tantalising opportunity as the historical catalogue of samples where there were previously no specific biopsies collected for microbial analysis is extensive and would substantially contribute to the integration of FD associated MAM profiles.

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P0012

CIRCULATING PLASMA MICROBIOME AND GASTRIC CANCER

D. Nikitina¹, J. Kupcinskas², L. Kupcinskas³, J. Skieceviciene¹

¹Institute for Digestive Research, Lithuanian University of Health Science, Laboratory of Clinical and Molecular Gastroenterology, Kaunas, Lithuania, ²Lithuanian University of Health Sciences, Department of Gastroenterology, Kaunas, Lithuania, ³Lithuanian University of Health Sciences Inst. for Digestive Research, Gastroenterology Department, Kaunas, Lithuania

Contact E-Mail Address: darijanik@gmail.com

Introduction: Previous studies have shown that microbiome plays an important role in maintaining a healthy state, and their imbalance is associated with various diseases. Recently microbial DNA was detected in the circulated blood. It has been shown that bacterial DNA corresponds to various states of human health as well.

Aims & Methods: The aim of the current study was to perform a microbiome analysis and identify possible circulating biomarkers for GC. Plasma DNA samples from 35 GC patients and 43 controls were used. V1-V2 region of bacterial 16S rRNA gene was 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 the groups, PERMANOVA and Mann-Whitney test followed by false-discovery rate test were used. ROC curve analysis was performed to predicting outcome of study disease status.

Results: Analysis revealed Actinobacteriota, Proteobacteria, Firmicutes, Bacteroidota, and Patescibacteria as most abundant bacterial at phylum level in GC and control group. The depth of GC samples reads was statistically lower than control group samples. Analysis of alpha-diversity revealed differences by Simpson's diversity and Pielou evenness indices, GC group was statistically less diverse than control group. Abundance of *Escherichia-Shigella* at 4 taxonomic levels (order, family, genus, ASV) was increased and abundance of *Collinsella aerofaciens* decreased in GC patients' blood plasma.

The combination of *Escherichia-Shigella* and *C. aerofaciens* yielded AUC 0.833, while using these bacteria separately AUC was 0.803 and 0.633, respectively. No significant differences were identified between blood plasma microbiome and gastric cancer clinical data.

Conclusion: The global circulating microbiome profile of GC patients differs from that of the control group. GC patients' blood microbiome are less diverse than controls. *Escherichia-Shigella* and *Collinsella aerofaciens* could presumably be used as clinical biomarkers of GC.

Disclosure: Nothing to disclose.

P0013

THE EFFECTS OF VARIABLE DOSES OF HERBAL FORMULATIONS ON THE DUODENAL MUCOSA-ASSOCIATED MICROBIOTA FROM SUBJECTS WITH AND WITHOUT FUNCTIONAL DYSPESIA AND SELECT ISOLATES OF DUODENAL BACTERIA

L. Schooth¹, T. Fairlie^{2,3}, Y. Lim¹, J. Jimenez Loayza¹, E. Noon^{2,3}, A. Shah^{2,3}, N.A. Koloski^{2,4}, G.J. Holtmann^{2,3,5}, M. Morrison¹

¹The University of Queensland, Diamantina Institute, Faculty of Medicine, Brisbane, Australia, ²Princess Alexandra Hospital, Department of Gastroenterology and Hepatology, Brisbane, Australia, ³The University of Queensland, Faculty of Medicine, Brisbane, Australia, ⁴University of Newcastle, School of Medicine and Public Health, Newcastle, Australia, ⁵The University of Queensland, Faculty of Health and Behavioural Sciences, Brisbane, Australia

Contact E-Mail Address: l.schooth@uq.edu.au

Introduction: Functional gastrointestinal disorders such as functional dyspepsia (FD) are disorders of gut-brain interactions, characterized by unexplained, chronic and relapsing gastrointestinal symptoms. Low grade mucosal inflammation, altered gut motility and sensory function, and the microbiota of the proximal small intestine may be important to the onset and recurrence of these conditions.

While diet and herbal medicines have been shown to positively affect FD symptoms, the impact of these treatments on the duodenal microbiota is largely unknown.

Aims & Methods: Here, we have assessed how two formulations of herbal extracts (STW5 and STW5-II) affect the growth and inflammatory tenor of the secretomes produced by mixed cultures and individual isolates of duodenal bacteria. The microbial communities resident on duodenal biopsy tissue from 6 FD and 6 non-FD (healthy control) subjects were cultured using a habitat-simulating medium with no additions or supplemented with 2, 4, or 8 µL/mL of either STW5 or STW5-II for 24 hours.

Cell biomass from these microbial communities was harvested and characterized by 16S rRNA gene amplicon sequencing. The secretomes produced by these mixed cultures were also recovered by harvesting the spent culture fluids via centrifugation, followed by their filter-sterilization and storage at -80°C. The immunomodulatory potential of these secretomes was evaluated *in vitro*, by challenging a human monocyte-derived NF-κB reporter cell line (THP1-luciferase).

Here, the secretomes (or uninoculated bacterial medium as a control) were diluted 1:4 with cell culture medium and 0.1 vol added to the THP1-luciferase cultures. In parallel, heat-killed *Listeria monocytogenes*, or lipopolysaccharide as stimulators of a TLR2 or TLR4 response, respectively, were used alone or in combination with the secretomes. The magnitude of NF-κB signalling was measured via luciferase output using standard methods.

Separately, axenic isolates of duodenal bacteria affiliated with *Escherichia*, *Streptococcus*, and *Veillonella* were also cultured using brain heart infusion broth supplemented with hemin and vitamin K, with no additions or supplemented with STW5 or STW5-II, as described above. The growth of these axenic cultures was monitored by measurement of optical density at 600nm.

Results: The profiles of bacterial communities recovered from duodenal tissue were separable according to subject phenotype (i.e., FD and non-FD). In general terms, the within sample (alpha) diversity was greater for the FD group. However, neither STW5 nor STW5-II at concentrations tested appear to exert gross, condition-specific alterations to these microbial communities. Similarly, immunomodulatory effects of the secretomes prepared from these cultures as tested on the THP1-luciferase cultures were not significantly different from control mixed cultures (i.e., no ad-

dition of STW5 or STW5-II). Interestingly, the growth rates of some of the axenic isolates were affected by either or both formulations and effects varied both within and between genera.

Conclusion: Both STW5 and STW5-II can affect the growth of select duodenal bacteria. However, at the concentrations tested these effects were not readily observed in more complex communities of duodenal bacteria from either FD or non-FD subjects. The inflammatory tenor of the secretomes from these consortia also appear to be unaffected. As such, neither STW5 or STW5-II resulted in dramatic shifts in the microbial communities suggesting – when compared to numerous other medications – both are tolerated by the duodenal microbiota.

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P0014

THE SAFETY AND EFFICACY OF DIRECT ORAL ANTICOAGULANT RESUMPTION FOLLOWING A GASTROINTESTINAL BLEEDING EPISODE: A SYSTEMATIC REVIEW AND META-ANALYSIS

D. Palinkas^{1,2}, B. Teutsch^{1,3}, E.B. Gagyi¹, M.A. Engh¹, D.S. Veres^{1,4}, N. Hosszúfalusi⁵, L. Herszényi⁶, P. Hegyi^{7,1,8}, B. Erőss^{1,8,3}

¹Semmelweis University, Centre for Translational Medicine, Budapest, Hungary, ²Military Hospital – State Health Centre, Budapest, Hungary, ³Department of Gastroenterology, Budapest, Hungary, ⁴University of Pécs, Pécs, Hungary, ⁵Institute for Translational Medicine, Pécs, Hungary, ⁶Semmelweis University, Department of Biophysics and Radiation Biology, Budapest, Hungary, ⁷Semmelweis University, 3rd Department of Internal Medicine, Budapest, Hungary, ⁸Medical Centre, Hungarian Defence Forces, Scientific Institute, Budapest, Hungary, ⁹University of Pecs, Centre for Translational Medicine, Pecs, Hungary, ¹⁰Semmelweis University, Division of Pancreatic Diseases, Heart and Vascular Center, Budapest, Hungary

Contact E-Mail Address: dr.d.palinkas@gmail.com

Introduction: The number of patients treated with direct oral anticoagulants (DOACs) has rapidly elevated in the last decade. Compared to Vitamin-K antagonists (VKA), DOACs were reported to have a better safety profile, except for gastrointestinal bleeding (GIB). After successfully managing GIB, a decision of therapy reintroduction has to be made carefully, although data addressing this topic is lacking.

Aims & Methods: We aim to determine the safety and efficacy of DOACs resumption after a GIB event.

Our protocol was registered in advance in PROSPERO (CRD42021284314). We performed our study according to the Cochrane Handbook's recommendations for Systematic Reviews of Interventions. Studies that reported rebleeding, thromboembolic events, and mortality after restarting DOACs or withholding therapy were selected as eligible articles.

The systematic research was conducted in five databases (MEDLINE, EMBASE, CENTRAL, Web of Science, and Scopus) without any restriction. Random effect model was implemented to calculate pooled odds ratio (OR) with 95% confidence interval (CI). ROBINS-I tool was used for risk of bias assessment, certainty of the evidence was evaluated with the GRADE approach.

Results: From 8577 articles, 3 retrospective cohort studies were included in the meta-analysis. We did not find a significant increase in the risk of rebleeding in patients restarting DOACs after index GIB (OR=1.09; CI: 0.72–1.64). The outcomes of thromboembolic events and mortality data were not suitable for meta-analytic calculations. Single studies comparing DOAC resumption and withdrawal did not show statistically significant

differences in these outcomes (OR=1.21, CI: 0.61–2.42; OR=2.36, CI: 0.52–10.78 respectively). Data quality assessment showed a serious overall risk of bias and very low quality of evidence (GRADE D).

Conclusion: Based on our results, DOAC resumption after a GIB episode may not elevate the risk of rebleeding. However, the need for high-quality randomized clinical trials focusing on this clinically relevant question is crucial.

References:

Based on our results, DOAC resumption after a GIB episode may not elevate the risk of rebleeding. However, the need for high-quality randomized clinical trials focusing on this clinically relevant question is crucial.

Disclosure: Nothing to disclose.

P0015

PREDICTIVE ABILITY OF AVAILABLE SCORES IN MASSIVE UPPER GASTROINTESTINAL BLEEDING

R. Jiménez-Rosales¹, M. López-Vico¹, J.M. López-Tobaruela¹, E.J. Ortega-Suazo¹, J.G. Martínez-Cara¹, E. Redondo-Cerezo¹

¹Hospital Universitario Virgen de Las Nieves, Gastroenterology, Granada, Spain

Contact E-Mail Address: ritajimenezrosales@gmail.com

Introduction: Massive Gastrointestinal Bleeding (MGIB) refers to patients with severe bleeding who require emergency intervention in order to prevent mortality and limit morbidity(1).

Aims & Methods: The aim of our study was to describe patients with Upper MGIB (UMGIB) and to analyze the predictive ability of available scores in these patients.

Although no consensus definition exists, for the purpose of this study we have used D'Amore and Swaminathan (1) definition of MGIB (gastrointestinal bleeding that results in hemodynamic instability, signs of poor perfusion, transfusion of >2 packed red blood cells during the initial resuscitation or significant hematemesis/hematochezia) supported by that offered by Nagata et al. (2) (who accept two transfused units both during the initial resuscitation and during the hospital stay and/or shock).

Ours was a prospective study on consecutive and unselected patients admitted to the emergency room of Virgen de las Nieves University Hospital with upper gastrointestinal bleeding (2013-2020). We only considered for the analysis patients who fulfill UMGIB criteria as described in the previous definition. Information regarding clinical, biochemical data and procedures was collected. The discriminative ability of risk scores was evaluated by the AUROC curve. Comparison of the scores was performed by the deLong test.

Results: A total of 1179 patients were recruited, 92 (7.8%) presented UMGIB, with a median age of 62.17±13.55, 41.3% were female.

The most common causes of UMGIB were duodenal ulcers (26.1%), esophageal varices (18.5%) and gastric ulcer (17.4%).

Patients with UMGIB presented higher rates of endoscopic (76.1% vs. 42.6%; p=0.000), radiological (8.7% vs. 0.9%; p=0.000) and surgical (9.8% vs. 3.3%; p=0.006) intervention. Furthermore, they had higher rates of rebleeding (23.9% vs. 9.1%; p=0.000), in hospital deaths (21.3% vs. 9.4%; p=0.002) and delayed hemorrhagic events within the ensuing 6 months (23.7% vs.14.7%; p=0.047).

No differences were found in sex, comorbidity, NSAIDs, anticoagulants and antiaggregant previous use, underlying etiology and 6 month-delayed mortality.

Using the threshold for a low risk of adverse events previously defined for MAP(AHS) and Glasgow-Blatchford (GB), no patient presented UMGIB (0% vs. 100%; p=0.000 and p=0.043, respectively). For those low-risk patients identified through ABC score, 11 presented UMGIB (13.8% vs. 86.3%; p=0.000).

Scores' ability for UMGIB prediction is shown in Figure 1, with MAP(ASH) performing better than ABC (difference 0.247; 95% CI 0.196-0.298; p<0.001) and GB (difference 0.088; 95% CI 0.051-0.124; p<0.001).

	AUROC	95% CI
MAP(ASH) score	0.951	0.936 – 0.964
ABC score	0.704	0.674 – 0.733
GB score	0.864	0.840 – 0.885

Conclusion: Being UMGIB uncommon, it has gloomy outcomes in terms of need for intervention, rebleeding and in-hospital mortality. Hence, it is especially important to identify patients with a potential risk of developing this event in order to treat earlier.

Although none of the scores has been constructed or validated to predict this event, the MAP(ASH) score, a simple calculated pre-endoscopy risk score created from a Spanish cohort, performs accurately. Indeed, it performed better when predicting UMGIB than the other available scores.

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Disclosure: Nothing to disclose.

P0016

USEFULNESS OF THE MODIFIED PREENDOSCOPIC ROCKALL INDEX TO PREDICT OUTCOMES IN UPPER GASTROINTESTINAL BLEEDING DUE TO PEPTIC ULCER

L.P. Llovet Soto¹, E. Brunet Mas¹, P. Pedregal¹, F. Junquera¹, L. Melcarne¹, X. Calvet Calvo¹, E. Frisanchi¹, V. Puig-Divi¹, P. García-Iglesias¹, E. Martínez-Bauer¹

¹Hospital Parc Tauli, Gastroenterology, Sabadell, Spain

Contact E-Mail Address: lpllovet@tauli.cat

Introduction: The main prognostic indices for the study of upper gastrointestinal bleeding (UGB) have hemoglobin value as a common variable. The Rockall pre-endoscopic score (PreRock) does not include hemoglobin (Hb). We hypothesized that a modification of this score to include hemoglobin levels might perform as well as other current scoring systems in predicting outcomes in UGB.

Aims & Methods: The objective of the study was to determine: 1:The PreRock score plus Hb value (Modified PreRockall score -PreRockMod) can predict the outcome of peptic ulcer bleeding (PUB) and 2:To compare PreRockMod score with 2 other validated scores for PUB: Glasgow-Blatchford score (GBS) and PreRock score.

Prospective unicenter study conducted for 5 years in a university tertiary care. Patients with PUB were defined by:

1. Presence of hematemesis, maelenas, hematochezia;
2. Confirmed by endoscopy<24 horas after the onset of bleeding.

The adverse outcomes considered were:

1. Rebleeding,
2. Red blood cell transfusión,
3. Endoscopic treatment,
4. Mortality, and;
5. Clinical intervention (transfusion, endoscopic treatment, embolization and/or surgery, rebleeding and death).

Area under the receiver operating characteristic (AUROC) curve and its IC95% were calculated for the PreRockMod score and compared for each

adverse outcome with the others scores (GBS and PreRockall). AUROCs were compared with the DeLong method using Stata 14.1 Software (Stata Corp.2015).

Results: A total of 230 patients were identified consecutively. The mean age was 63.8 years, standard deviation (SD±18.2), 152 (51%) were men. Mean hemoglobin was 9.5 g/dL (SD±2.4); 93 (40.4%) patients with gastric ulcer. Forrest classification was: Forrest I 51 (22.2%), Forrest IIa 59 (25.7%);Forrest IIb 30 (13%);Forrest IIc 36 (15.6%) and Forrest III 54 (23.5%) patients. Twenty-six (11.3%) patients rebleeding 7 (3%) died, 101 (43.9%) required transfusion, 140 (60.9%) received endoscopic treatment, 9 (3.9%) received arterial embolization.

When comparing ROC curves, we found no differences between the 3 scores for the outcomes considered. The only difference found is for the need for transfusion*. PreRockMod and GBS have similar AUROCs for transfusion requirement and more accurate than PreRock (Table 1. AUROC and IC95% for PreRockMod an Ris Scores).

SCORE	REBLEEDING	TRANSFUSION *	ENDOSCOPIC TREATMENT	MORTALITY	CLINICAL INTERVENTION
PreRockMod	0.73 (0.64-0.81)	0.90 (0.85-0.94)	0.72 (0.65-0.79)	0.85 (0.66-1.00)	0.73 (0.64-0.81)
PreRock	0.72 (0.64-0.81)	0.78 (0.72-0.84)	0.71 (0.64-0.78)	0.82 (0.66-0.99)	0.72 (0.64-0.81)
GBS	0.68 (0.58-0.79)	0.88 (0.83-0.92)	0.65 (0.58-0.72)	0.77 (0.61-0.93)	0.68 (0.58-0.79)

Table.

Conclusion: The PreRockMod score is better at predicting transfusion than PreRock score, and equivalent to GBS. They are similar for the rest of the outcomes.

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-Comparison of risk scoring systems for patients presenting with upper gastrointestinal bleeding: international multicentre prospective study. Stanley AJ, et al. BMJ. 2017

Disclosure: Nothing to disclose.

P0017

AN AUDIT OF LOCAL MANAGEMENT OF UPPER GASTROINTESTINAL BLEEDS IN A UNITED KINGDOM DISTRICT GENERAL HOSPITAL

A. Patel¹, K. Simpson¹, N. Duffy¹, W.K. Tan^{1,2}, R. Kassam¹

¹North West Anglia NHS Foundation Trust, Department of Gastroenterology, Huntingdon, United Kingdom, ²University of Cambridge, Early Cancer Institute, Cambridge, United Kingdom

Contact E-Mail Address: aamie.patel1@nhs.net

Introduction: Acute upper gastrointestinal bleed (AUGIB) is associated with a 10% in-patient mortality and this outcome has not significantly improved over the past 50 years (1).

The UK's National Institute for Health and Care Excellence (NICE) has developed guidance for the management of patients presenting with AUGIB, which highlights several priorities that should be addressed such as:

- risk assessment using the Blatchford and Rockall scores,
- the optimal timing of endoscopy,
- management of non-variceal bleeds,
- management of variceal bleeds, and;
- guidance on controlling bleeding and preventing re-bleeding in patients on NSAIDs, aspirin or clopidogrel (1).

Aims & Methods: This study aimed to assess the compliance of AUGIB management in a district general hospital against the NICE quality standards. In the first cycle, we retrospectively reviewed case notes from 52 patients who presented with AUGIB and were admitted between September 1 and December 31, 2019. A re-audit was performed between December 1, 2020 to March 31, 2021 where we reviewed the case notes of 22 patients. We allowed for a 1-year interval between the first and second cycle where we educated doctors about the NICE quality standards of AUGIB management. The primary outcome of the study was the compliance of local management of AUGIB in a district hospital compared to NICE quality standards.

Results: The indications for intervention in the first cycle of patients were haematemesis in 26.9% (14/52), melaena in 50% (26/52), and both haematemesis and melaena in 23.1% (12/52); indications for the second cycle were haematemesis in 64% (14/22), melaena in 18% (4/22), and both haematemesis and melaena in 8% (4/22). The compliance for the discontinuation of aspirin during an AUGIB was 60% (3/5) in the first cycle, increasing to 80% (4/5) in the second cycle. When we assessed the use of risk score in the risk stratification of AUGIB, Blatchford score was calculated in 12.5% (5/40) in the first cycle, increasing to 50% (11/22) in the second cycle. When we assessed the time to endoscopy among patients with haemodynamic instability at presentation, endoscopy was performed immediately after resuscitation in 100% of patients in both the first (4/4) and second (3/3) cycle. Among haemodynamically stable patients, 91.4% (32/35) had endoscopy within 24 hours in the first cycle, but only 53% (10/19) in the second cycle.

Parameter	Audit (Sept 1, 2019 - Dec 31, 2019)	Re-audit (Dec 1, 2020 - Mar 31, 2021)
Number of patients	52	22
Use of non-steroidal anti-inflammatory drugs (NSAIDs), aspirin, clopidogrel		
- Continue low dose aspirin once haemostasis achieved	60% (3/5)	80% (4/5)
- Stop NSAIDs/COX2 inhibitor during acute phase	100% (4/4)	100% (3/3)
- Specialist advice regarding clopidogrel	100% (1/1)	100% (2/2)
Resuscitation and initial management		
- Platelet transfusion if platelet count <50 x 10 ⁹ /L	N/A	100% (2/2)
- Fresh frozen plasma transfusion if prothrombin time/international normalized ratio/activated partial thromboplastin time >1.5 times normal	N/A	N/A
- Cryoprecipitate use	N/A	N/A
- Prothrombin complex use	100% (1/1)	100% (2/2)
Risk assessment		
- Blatchford score at first assessment	12.5% (5/40)	50% (11/22)
- Full Rockall score post-endoscopy	0% (0/40)	14% (3/22)
Timing of endoscopy		
- Post-resuscitation	100% (4/4)	100% (3/3)
- Within 24 hours	91.4% (32/35)	53% (10/19)
Management of non-variceal bleed		
- PPI use before endoscopy	74/4% (29/39)	77% (17/22)
- Endoscopic management: clips with or without adrenaline	100% (2/2)	100% (2/2)
- Endoscopic management: thermal coagulation with adrenaline	100% (1/1)	0% (0)
- Endoscopic management: fibrin or thrombin with adrenaline	N/A	0% (0)
- Treatment after first or failed endoscopy: endoscopy for re-bleed	N/A	100% (2/2)
- Treatment after first or failed endoscopy: endoscopy for re-bleed	100% (1/1)	100% (1/1)
Varices management		
- Terlipressin	100% (4/4)	100% (5/5)
- Antibiotics	100% (4/4)	100% (5/5)
- Band ligation	100% (4/4)	100% (5/5)
- Referral for transjugular intrahepatic portosystemic shunts (TIPS)	N/A	N/A

Table.

Among patients with non-variceal bleed, proton pump inhibitors (PPI) were used in 74.4% (29/39) in the first cycle and 77% (17/22) in the second cycle. Regarding endoscopic management for non-variceal bleed, we achieved 100% compliance for the use of clips with or without adrenaline in both the first and second cycles. Dual therapy of thermal coagulation with adrenaline was performed in 100% (1/1) of patients in the first cycle, and none in the second cycle. For variceal bleeds, 100% of patients in the first (4/4) and second (5/5) cycle were given terlipressin antibiotics, with band ligation.

Conclusion: In our district hospital, pre-endoscopic management of AUGIB such as PPI use, and time to endoscopy were adequate, but did not fully meet the quality standards stipulated by NICE. Endoscopic management for AUGIB, however, was fully compliant with NICE standards.

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Disclosure: Nothing to disclose.

P0018

COMPARISON OF RISK SCORING SYSTEMS FOR PATIENTS PRESENTING WITH ACUTE UPPER GASTRO-INTESTINAL BLEEDING

S. Nacer¹, S. Bouamama¹, F.Z. Elrhaoussi¹, M. Tahiri Joutei Hassani¹, F. Haddad¹, W. Hliwa¹, A. Bellabach¹, W. Badre¹

¹CHU Ibn Rochd, Casablanca, Morocco

Contact E-Mail Address: saramedstudies@gmail.com

Introduction: Acute Upper gastrointestinal bleeding (UGIB) remains a common medical emergency in gastroenterology with significant mortality. The early use of risk stratification scores is recommended for follow up and treatment selection in patients with UGIB. The most widely used risk scoring systems are the Glasgow–Blatchford (GBS), the Rockall score (RS) and AIMS65.

Aims & Methods: We aimed to compare the performance of the Scoring Systems in predicting the need for blood transfusion, short-term mortality, and re-bleeding among Moroccan population with UGIB. This was a retrospective study conducted at university hospital between January 2020 and December 2021 including all patients hospitalized for acute UGIB. The diagnosis was based on patient presentations, including hematemesis, melena or both. Variables including demographic information, physical examination, laboratory values, medical treatment and endoscopic findings were recorded. GBS, RS and AIMS65 were calculated for all patients. The area under the receiver operating characteristic (AUROC) curve was determined to compare the predictive power of each scoring system.

Results: A total of 410 patients were included. The mean age was 55,6 years and 63,8% were males. Major comorbidities, including liver, heart and renal diseases and diabetes mellitus were present in 49,9% of patients. Blood transfusion was indicated in 40,6% of patients with a median transfusion requirement of 2 units.

The endoscopic findings included peptic ulcer in 33,5%, esophageal varices in 37,9%, gastric varices in 8,31% and upper gastrointestinal tumors in 5,6%. In 11 patients no evident cause of UGIB was identified. Endoscopic therapy was required in 36,7% in order to achieve haemostasis and 3,9% proceeded to surgery.

Short-term mortality occurred in 3,42% of the patients, and rebleeding was noted in 3.7% of the patients. The median risk scores were as follows: GBS: 11.4 (range 2–19); RS: 3,64 (range 1–11) and AIMS65: 1.08 (range 0–4). The scoring systems showed comparable results in predicting blood transfusion (GBS: AUC = 0.55, RS: AUC = 0.52, AIMS65: AUC = 0.51, p=0.05)

The RS (AUC = 0.67) was superior to GBS and AIMS65 for predicting endoscopic treatment (p = 0.016, p = 0.023; respectively) and the need of surgery (AUC = 0.60, p = 0.02, p = 0.013). RS was also significantly better in predicting rebleeding (AUC = 0.63) comparing with GBS (p < 0.001) and AIMS65 (p < 0.001).

The GBS (AUC=0.49), RS (AUC=0.50) and AIMS65 (AUC=0.58) were predictors of in-hospital mortality. No significant differences were noted (p=0,24) between the three scores in this outcome.

Conclusion: Finding from this study suggested that these three scoring systems might be acceptable to predict outcomes of patient with UGIB. However, The RS was superior to the GBS and AIMS65 for predicting endoscopic therapy, surgery and rebleeding while the three scoring system showed comparable results in predicting blood transfusion and in hospital mortality.

Disclosure: Nothing to disclose.

P0019 WITHDRAWN

P0020

HEDONIC AND SOMATIC RESPONSES TO MEAL INGESTION IN FUNCTIONAL DYSPEPSIA

D.M. Livovsky^{1,2}, C. Barber Caselles², F. Azpiroz²

¹Shaare Zedek Medical Center, Digestive Diseases Institute, Jerusalem, Israel, ²University Hospital Vall d'Hebron, Centro de Investigación Biomédica en Red de Enfermedades Hepáticas y Digestivas (Ciberehd), Universitat Autònoma de Barcelona, Digestive System Research Unit, Bellaterra (Cerdanyola del Vallès), Spain

Contact E-Mail Address: danlivo@yahoo.com

Introduction: Introduction. In healthy subjects, ingestion of a comfort meal induces homeostatic sensations (satiety, fullness) and satisfaction (sensation of digestive well-being). Patients with functional dyspepsia and postprandial distress syndrome complain of early satiety and excessive fullness in response to meal ingestion, but their hedonic experience (whether and to what extent they enjoy the meal and experience satisfaction) has not been characterized.

Aims & Methods: Aim. To determine whether the hedonic response to meal ingestion is affected in patients with postprandial dyspepsia.

Methods. Randomized parallel trial in patients fulfilling Rome IV criteria of postprandial distress syndrome (n = 24) and age-and-gender-matched healthy controls (n = 18) comparing the responses to stepwise ingestion of a comfort meal up to full satiation. Homeostatic and hedonic sensations were measured (by 10-score scales) before, during and after meal ingestion; changes in girth (using adaptable belts) and diaphragmatic position (position of the hepatic border by ultrasonography) from pre- to post-ingestion were also measured.

Results: Results. Healthy subjects enjoyed the comfort meal and experienced sensation of digestive well-being (peak of 3.6± 0.2 score) up to a meal load of 856± 90 Kcal; well-being decreased at full satiation (0.2± 0.7 score with 1287± 54 Kcal), without abdominal discomfort (0.4± 0.2 score). As compared to healthy subjects, patients tolerated smaller meal loads and experienced early satiety (full satiation at 666± 57Kcal; p < 0.001), postprandial bloating (6.5± 0.4 score; p=0.052) and discomfort (5.9± 0.5 score; p<0.001).

Based on their hedonic response, two distinct categories of dyspepsia were recognized: a subpopulation of dyspeptic patients (n = 9) enjoyed the meal and experienced satisfaction during eating (3.0± 0.3 maximal well-being score at 450 ± 79 Kcal; p < 0.001), while the other subgroup (n

= 15) did not and experienced an aversive sensation (-0.6 ± 0.3 maximal well-being score at 187 ± 30 Kcal); to note, both subgroups exhibited similar levels of meal tolerance and postprandial discomfort. Interestingly, the group that enjoyed the meal (enjoyers) developed an abnormal somatic response (abdominophrenic dyssynergia with increase in girth by 3.9 ± 0.5 cm and diaphragmatic descent by 1.1 ± 0.3 cm; $p < 0.05$ vs. healthy subjects for both), but the others (non-enjoyers) did not (no significant differences vs. healthy subjects).

Conclusion: Conclusions. Differences in hedonic and somatic responses to meal ingestion in subgroups of functional dyspepsia indicate that their pathophysiology is heterogeneous. Postprandial bloating in some patients may be related to a somatic, rather than visceral dysfunction, without impairment of their capability to enjoy the meal.

Disclosure: Nothing to disclose.

P0021

PRECISION MEDICINE IN DYSPEPSIA. DEVELOPMENT AND INTERNAL VALIDATION OF A PREDICTIVE PROGNOSIS MODEL OF RESPONSE TO PROTON-PUMP INHIBITOR IN ADULT PATIENTS WITH FUNCTIONAL DYSPEPSIA

L. Osorio¹, S.F. Niño Ramirez², M. Santisteban¹, L.F. Roldan^{3,2}, A.L. Leon⁴, L.G. Guevara¹

¹CES University, Gastroenterology, Medellín, Colombia,

²Gastroclinic Institute, Gastroenterology, Medellín, Colombia,

³Gastroclinic Institute, Medellín, Colombia, ⁴Hector Abad Gómez National Faculty of Public Health, Universidad de Antioquia, Medellín, Colombia

Contact E-Mail Address: sfnesp@gmail.com

Introduction: The expected prognosis, to the first-line management of functional dyspepsia can personalize the need for interventions and establish individualized management in the context of precision medicine (1,2).

Aims & Methods: Development and internal validation of a multivariable prognostic predictive model to establish the probability of symptomatic response to proton pump inhibitor (PPI) management in adult patients with functional dyspepsia.

A cross-sectional study was carried out in adults with functional dyspepsia consulting a gastroenterology center in Medellín, Colombia, between August 2021 and March 2022. Adults with functional dyspepsia according to ROME IV criteria (3) were included; biliary, pancreatic neoplastic disease, peptic ulcer or pregnancy were excluded.

A pilot study was conducted to identify the variables most related to treatment response: nausea, bloating, anxiety (defined as excessive worry) or depression symptoms (defined as permanent sad mood), fibromyalgia (according to criteria of the American College of Rheumatology), age, sex, sleep disorder (4).

The 6 variables with the highest association were selected to be evaluated in the model, the outcome was defined as complete resolution of dyspeptic symptoms after 8 weeks treatment with esomeprazole, partial resolution or no resolution of symptoms was defined as poor response. Sample size was established according to Freeman's formula (5), random missing values <5% were resolved with multiple imputation.

A multivariable logistic regression model was developed using the best subset for the number and selection of variables, internal validation was performed by splitting the sample, 70% for development and 30% for validation. Variables with a value of $p < 0.1$ in the bivariate analysis were included to be tested in the model.

The final model was transformed into a scoring rule. The scores assigned to each variable were obtained by dividing each regression coefficient by

half the smaller coefficient and rounding to the nearest integer (6). Predictive ability was evaluated with AUC (area under the curve) and Hosmer lemeshow statistic.

Results: 192 patients were included (134 development, 58 validation), the best subset method identified 4 variables, as the best performing variables in terms of Akaike information criteria. The logistic model demonstrated adequate calibration and discrimination with AUC of 0.89 and a Hosmer-Lemshow chi-square test result with $p=1$. The final scoring system assigned a score to each variable; for anxiety 3 points, fibromyalgia 2 points, depression 1, female sex subtracted 1 point. The sum of scores lower than 4 points was related to favorable response to PPI with a sensitivity of 96,5%, confidence interval (CI) 88,1% to 100%, specificity of 56,6%, CI 37,2% to 76%, positive predictive value of 68,2%, CI 52,8% to 83,7%, and negative predictive value of 94,4%, CI 81% to 100%.

Variable	Coefficient*	P-value	Score**
Intercept	3.13	0.000	
Sex	1.05	0.124	-1
Anxiety	-3.56	0.001	3
Fibromyalgia	-2.65	0.000	2
Depression	-1.40	0.01	1

*Logistic regression coefficient. **Scores <4 are selected with favorable response to PPI.

Table 1. Logistic model of the score in the validation sample.

Conclusion: This model represents an easy-to-use and novel tool which allows early identification of patients with better therapeutic response to first-line management of functional dyspepsia.

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P0022

PREVALENCE AND IMPACT OF MIGRAINE HEADACHES IN ROME IV-BASED FUNCTIONAL DYSPESPSIA

F. Wuestenberghs^{1,2}, C. Melchior³, C. Desprez¹, H. Soliman^{1,4}, A.-M. Leroi⁵, G. Gourcerol¹

¹Rouen University Hospital, INSERM Unit 1073, UNIROUEN, Normandie University, Physiology, Rouen, France, ²CHU UCL Namur, Godinne University Hospital, UCLouvain, Gastroenterology and Hepatology, Yvoir, Belgium, ³Rouen University Hospital, INSERM Unit 1073, CIC-CRB-1404, UNIROUEN, Normandie University, Gastroenterology, Rouen, France, ⁴Hôpital Louis Mourier, DMU ESPRIT - GHU (AP-HP), Paris Diderot University, Gastroenterology, Colombes, France, ⁵INSERM CIC-CRB 1404, Rouen University Hospital, INSERM Unit 1073, UNIROUEN, Normandie University, Physiology, Rouen, France

Contact E-Mail Address: fabien.wuestenberghs@uclouvain.be

Introduction: Migraine headaches are associated with functional dyspepsia (FD) according to Rome IV criteria in the general population (prevalence of 43.6% vs. 20.0% in controls, OR 3.1 [95% CI = 2.2-4.3], $p < 0.005$) (1).

Indeed, common pathophysiological mechanisms have been reported in both disorders, especially alterations of the gut-brain axis (2).

Furthermore, patients with uninvestigated dyspepsia referred for an upper gastrointestinal endoscopy frequently have migraine headaches (3).

Aims & Methods: Our aim was therefore to assess the impact of the overlap with migraine in patients with FD. Consecutive patients with investigated dyspepsia were assessed with self-administered questionnaires. FD, its subtypes postprandial distress syndrome (PDS) and epigastric pain syndrome (EPS), and irritable bowel syndrome (IBS) were diagnosed according to Rome IV criteria.

Self-reported migraine was assessed by questioning patients for migraine headaches. Patients were also asked if they had fibromyalgia. Quality of life (QoL) was assessed by the *Gastrointestinal Quality of Life Index* (GIQLI).

Anxiety and depression levels were evaluated using the *Hospital Anxiety and Depression* (HAD) scale. Sleep was assessed using both the *Pittsburgh Sleep Quality Index* (PSQI) and the *Insomnia Severity Index* (ISI). Gastric half-emptying time was assessed using octanoic acid breath testing.

Results: 355 patients with Rome IV-based FD were identified. Overlap with migraine was present in 134 of the patients (37.7%). In univariate analysis, this comorbidity was associated with better QoL (GIQLI: 74.1 ± 18.6 vs. 80.9 ± 18.9 points, $p = 0.0011$), increased overlaps with IBS (52.2% vs. 40.3%, $p = 0.036$), fibromyalgia (12.7% vs. 5.9%, $p = 0.031$) and insomnia (70.9% vs. 54.3%, $p = 0.0024$), and a longer duration of FD (98.0 ± 109.8 vs. 62.9 ± 90.9 months, $p = 0.0011$).

On the contrary, age, body mass index, sex distribution, gastric half-emptying time, HADS score, FD subtypes distribution, and sleep quality ($p > 0.05$ for all). In multivariate analysis, independent predictors of the overlap with migraine in FD patients were FD duration (OR 1.003 [95% CI = 1.001-1.006]; $p = 0.0044$) and the presence of insomnia (OR 1.66 [95% CI = 1.01-2.76]; $p = 0.047$).

Conclusion: Migraine headaches affect more than one third of patients suffering from functional dyspepsia. Overlap with migraine is independently associated with a longer duration of the disorder and with the presence of insomnia.

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P0023

INTRAVENOUS FERRIC CARBOXYMALTOSIDE TREATMENT IS SAFE, EFFECTIVE, AND LONG-LASTING IN PATIENTS WITH CORPUS ATROPHIC GASTRITIS

L. Dottori¹, D. Corleone Tsar'kov¹, E. Dilaghi¹, G. Pivetta¹, G. Esposito¹, B. Annibale¹, E. Lahner¹

¹Sapienza University of Rome, Department of Medical-Surgical Sciences and Translational Medicine, Sant'Andrea Hospital, Rome, Italy

Contact E-Mail Address: ludovica.dottori@uniroma1.it

Introduction: Corpus Atrophic Gastritis (CAG) is characterized by chronic inflammation of gastric mucosa leading to destruction of typical gastric glands which are replaced by intestinal metaplasia, pseudo-pyloric metaplasia or fibrosis. Oxyntic mucosa involvement leads to impairment of hydrochloric acid and intrinsic factor secretion, resulting in iron and cobalamin deficiency. Iron deficiency anemia (IDA) is one of the most common manifestations of CAG and, with iron deficiency (ID), affects more than 50% of the CAG patients (1).

Oral iron therapy is poorly effective and poorly tolerated. Ferric carboxymaltose (FCM) is an intravenous (iv) preparation shown to be safe and effective in many GI diseases, but its efficacy in CAG patients has not been investigated so far.

Aims & Methods: The aim of this study is to assess the safety and efficacy of iv FCM in treating IDA in patients with CAG.

CAG patients with IDA, irrespective of concomitant cobalamin deficiency, were included. Other not-CAG-related causes of IDA were accurately excluded. Since availability of FCM in our centre (March 2015) until July 2021, 100 patients were treated, 31 patients with incomplete follow-up were excluded. Three patients who interrupted FCM infusion due to mild side effects not requiring further treatment, were excluded too. The remaining 66 patients (77.7% females; mean age 58.6 ± 2.2 years) were included and evaluated for clinical characteristics, anemia and iron status, previous oral iron therapy, FCM dosage, timing of FCM therapy, efficacy at 4 and 12 weeks for ID and IDA, timing for required FCM retreatment.

Paired sample t-tests were used to compare Hb and ferritin at baseline (T0), 4 weeks (T4) and 12 weeks (T12). IDA was defined as Hb < 13 g/dl for men and Hb < 12 g/dl for women associated with ferritin < 45 ng/dl. Moderate and severe anemia were defined as Hb 8-10 g/dl and Hb < 8 g/dl, respectively. ID was defined as ferritin < 45 ng/dl in presence of normal Hb values. Cobalamin deficiency was defined as serum levels < 220 pg/ml.

Results: At T0, mean Hb was 10.7 ± 0.3 g/dl, 36.4% had moderate and 6% severe anemia. Mean time from CAG diagnosis to FCM treatment was 20 ± 3.5 months, with 59% of patients receiving FCM within 9 months from diagnosis. FCM dosage was 1000 mg in 58.2%, 700 mg in 18.2% and 500 mg in 23.6% of patients, based on Hb levels. Two patients reported mild side effects not requiring FCM interruption. At 4 and 12 weeks, 68% and 77.5% of patients, respectively, recovered from IDA; T4 Hb significantly increased compared to T0 (12.6 ± 0.2 g/dl vs 10.7 ± 0.3 g/dl; $p < 0.0001$). At T12 a further

increase of mean Hb was observed (13.1 ± 0.2 g/dl vs 12.6 ± 0.2 g/dl; $p < 0.05$). At T4, ferritin levels significantly increased with respect to T0, but significantly decreased at T12.

After a mean time of 23.7 ± 2.9 months, 56% of patients were retreated with iv FCM: in 4.5% IDA relapsed due to new causes unrelated to CAG, in the remaining ones IDA was due to CAG only. At multivariate analysis, female gender (OR, 95%CI: 6.2, 1.2–32.1) and mild-moderate atrophy (OR, 95%CI: 4.3, 1.2–15.3) were associated with IDA relapse, while other factors (age, NSAIDs, baseline severe anemia, cobalamin supplementation) had no role.

Conclusion: Iv FCM is effective and safe in CAG patients, recovering IDA in nearly 80% of cases at 12 months after treatment. Two years after FCM treatment about half of patients remained non-anemic, while IDA relapsed more frequently in females and in those with mild-moderate atrophy. These data show that FCM treatment in CAG patients should be considered as first line treatment to recover from IDA promptly and safely.

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P0024

MECHANISMS OF ACTION OF AN HERBAL MULTI-COMPONENT PREPARATION IN FUNCTIONAL DYSPEPSIA: EFFECTS ON GASTRIC MOTILITY

M.-R. Piqué-Borràs¹, J. Röhl¹, M. Jaklin¹, A. Ammendola¹, G. Künstle¹

¹Weleda AG, Arlesheim, Switzerland

Contact E-Mail Address: mpiqueborras@weleda.ch

Introduction: Functional dyspepsia (FD) is amongst the most common functional gastrointestinal disorders. FD is mostly characterized by an impaired gastric accommodation and upper gastrointestinal symptoms such as epigastric pain, heartburn, bloating and vomiting.

However, the origin of these symptoms remains poorly understood and effective treatment options are limited. Therapeutic efficacy studies of phytotherapeutic combinations of herbal extracts such as STW-5 (Iberogast®) have demonstrated to improve dyspeptic symptoms in FD patients.

In this study, we investigated another herbal multi-component preparation (MCP): Weleda Amara oral drops (Amara-Tropfen). MCP is traditionally used to treat disturbances of gastrointestinal motility and contains nine bitter hydroethanolic herbal extracts (*Artemisia abstinthium*, *Centaurium erythraea*, *Cichorium intybus*, *Gentiana lutea*, *Juniperus communis*, *Millefolium herba*, *Peucedanum ostruthium*, *Salvia officinalis* and *Taraxacum*).

Aims & Methods: Our studies aimed to investigate the mode of action of MCP on gastric motility *ex vivo* / *in vitro*. The MCP dry extract was prepared from the commercial medicinal product Weleda Amara oral drops. Muscle strips from guinea-pig gastric fundus, corpus and antrum were set up in organ baths in circular orientation. Upon stabilization of the baseline tone, the muscle strips were exposed to ethanol-free MCP in a concentration-dependent manner ($3.5 - 1,000 \mu\text{g/mL}$).

Each concentration was applied for a minimum of 20 minutes or until plateau of response was reached. To understand the underlying mechanism of the effects of MCP on the muscle strips, we studied different G-protein-

coupled receptors (GPCRs) known to play a central role in the pathogenesis of gastrointestinal disorders: muscarinic M₃ receptor, serotonin 5-HT₄ receptor, opioid δ and opioid μ receptors. MCP was studied *in vitro* for binding affinities to muscarinic M₃ receptor and for agonist and antagonist activity on serotonin 5-HT₄, opioid δ and μ receptors. All assays were performed in CHO-K1 cell line.

Results: Addition of ethanol-free MCP caused relaxation of guinea-pig fundus circular muscle strips which was found to be significantly different compared to the vehicle group at the highest concentration tested ($850 \mu\text{g/mL}$). MCP also caused concentration-dependent relaxation of corpus and antrum circular muscle strips. This relaxation effect was significantly different compared to the vehicle group at concentrations ranging from 450 to 1,000 $\mu\text{g/mL}$ and 650 to 1,000 $\mu\text{g/mL}$, respectively.

To understand the relaxation mechanism, we investigated MCP activity on muscarinic M₃, opioid δ and μ and serotonin 5-HT₄ receptors. MCP inhibited the binding of 3H-4-DAMP to muscarinic M₃ receptors (IC₅₀: 380 $\mu\text{g/mL}$). In addition, MCP potentially inhibited the activity of opioid δ and μ receptors, shown by inhibition of intracellular cAMP release (IC₅₀: 304 & 256 $\mu\text{g/mL}$, respectively). However, MCP did not affect serotonin 5-HT₄ receptor activity.

Conclusion: This data demonstrates that the multi-component hydroethanolic extract MCP alters gastric motility by relaxing the three different parts of the stomach, most likely by inhibiting three motility-related receptors: muscarinic M₃ receptor, opioid δ and opioid μ receptors.

These findings suggest that MCP / Weleda Amara oral drops could be an efficient treatment for FD patients suffering from motility disorders with impaired gastric accommodation. However, additional studies are required to further characterize potential therapeutic advantages of Weleda Amara oral drops herbal preparations.

Disclosure: All authors are employees of Weleda AG.

P0025

OVERLAP OF FUNCTIONAL GASTROINTESTINAL DISORDERS REFLECTING BRAIN-GUT INTERACTIONS: A SYSTEMATIC REVIEW AND META-ANALYSIS

T. Fairlie^{1,2}, A. Shah^{1,2}, N.A. Koloski^{1,3,2}, M. Jones⁴, G.J. Holtmann^{1,2}

¹Princess Alexandra Hospital, Gastroenterology & Hepatology, Brisbane, Australia, ²University of Queensland, Faculty of Medicine and Faculty of Health and Behavioural Sciences, Brisbane, Australia, ³University of Newcastle, School of Medicine and Public Health and Hunter Medical Research Institute, Newcastle, Australia, ⁴Macquarie University, Department of Psychology, Sydney, Australia

Contact E-Mail Address: thomas.fairlie@uqconnect.edu.au

Introduction: Functional gastrointestinal disorders (FGIDs) are defined as distinct combinations of chronic or recurrent gastrointestinal symptoms, with no obvious structural or biochemical abnormalities offering explanation^{1,2}. While attributed to altered gastrointestinal motility, abnormal visceral sensory function, epithelial barrier disturbances, mucosal immune activation or alterations of gastrointestinal microbiota function, there is increasingly the notion of altered brain-gut-interactions in these patients². It has been suggested that overlap of FGIDs such as functional dyspepsia and irritable bowel syndrome (occurring simultaneously in a given subject) is linked to increased symptom burden, impaired quality of life, and increased healthcare utilisation^{3,4}.

Aims & Methods: We conducted a systematic review and meta-analysis to explore the prevalence of an overlap of FGIDs, the relationship with symptom severity, impaired quality of life and psychological comorbidities. MEDLINE(PubMed) and Embase electronic databases were searched until

Feb 2022 for studies reporting prevalence of overlapping FGIDs. Pooled prevalence (PP) reported as a proportion, pooled standardised mean difference (SMD), Odds Ratio (OR) and 95% confidence intervals (CI) of FGID overlapping patients and singular FGID patients were calculated, utilising a random effects model.

Results: 32 studies reporting 124,776 adult subjects and 47,160 patients with FGID diagnosis (PP: 0.3779, 95%CI:0.3753 – 0.3807) were identified. An increased number of females (PP: 0.5755, 95%CI: 0.5728 – 0.5783) were included in these studies.

Overall, the majority of subjects had one FGID diagnosed (PP: 0.6740, 95%CI:0.6698 – 0.6782), while smaller numbers of patients had two (PP: 0.2854, 95%CI:0.2764 – 0.2946), three PP: 0.1818, 95%CI:0.1726 – 0.1913), four (PP: 0.1145, 95%CI:0.1068 – 0.1225), five (PP: 0.1046, 95%CI:0.0949 – 0.1150), and six (PP: 0.0464, 95%CI:0.0374 – 0.0567) FGIDs. Quality of life was significantly reduced in patients with overlapping FGIDs as compared to patients with a single FGID in both mental (SMD: -0.250, 95%CI:-0.467, -0.033, $p=0.024$) and physical component scores (SMD:-0.634, 95%CI:-0.634, -0.335, $p=0.0001$). Patients with an overlap of FGIDs had both increased prevalence of anxiety (SMD:0.501, 95%CI:0.347-0.654, $p=0.0001$) and depression (SMD:0.532, 95%CI:0.366, 0.698, $p=0.0001$).

Conclusion: Based upon this meta-analysis a substantial proportion of patients have more than one FGID as defined by the Rome criteria. Patients with an overlap have more severe impairment of quality of life and are characterised by a significantly higher rate of anxiety or depression. All this points towards the possibility that disturbances of brain-gut interactions are in particular relevant for patients presenting with an overlap of different FGID.

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P0026

ENRICHMENT OF PATIENTS WITH EHLERS DANLOS SYNDROME IN IDIOPATHIC GASTROPARESIS – A GENE SET ENRICHMENT ANALYSIS

S. Smieszek¹

¹Vanda Pharmaceuticals, Genetics, DC, United States

Contact E-Mail Address: sandra.smieszek@vandapharma.com

Introduction: Ehlers Danlos Syndrome (EDS) is a heritable disorder of the connective tissue. It is usually inherited as an autosomal dominant trait; however, recessive mode of inheritance has been documented¹. EDS comprises a genetically heterogeneous group of connective tissue disorders of which the main clinical features are joint hypermobility, skin hyperextensibility, delayed wound healing with atrophic scarring, and generalized connective tissue fragility^{2,3}.

The genetic etiology is not well explained and there are 100s of variants within the core genes. In the current gastroparesis study, we report 16 cases of EDS (confirmed by electronic medical records), specifically enriched in the cohort of idiopathic gastroparesis.

Aims & Methods: Assuming incidence rate of 1 in 5000 the enrichment is 160-fold ($p= 8.18743E-26$). In order to explore the genetic surrogates of EDS we have done gene set enrichment analysis. We focused our analysis on core genes: COL1A1,COL1A2,COL3A1,COL5A1, andCOL5A2 and ADAMTS2,FKBP14,PLOD1, andTNXB, as reported in LOVD⁵.

Results: All EDS cases are of Caucasian ancestry, females with idiopathic gastroparesis. All self-reported ancestry was verified by principal component analysis. We report all coding/splicing variants in the core genes with a minor allele frequency (MAF)<0.05. Most of our EDS cases for which we have whole genome sequencing available (n=13) with exception of 1, have at least one such nonsynonymous variant/or splicing variant within the core gene set. We report 2 duplicate variants across this set.

The first variant is COL5A1:NM_000093:exon13:c.G1588A:p.G530S (rs61735045). It has a global MAF in gnomAD of 0.03 (ranging from 0.04 NFE to 0.0009 amongst East Asian). The variant is reported in ClinVar as pathogenic and associated with EDS, classic type and has a high CADD score of 24.9. This variant has been previously reported in literature in association with EDS¹.

These findings suggested that heterozygosity for the Gly530Ser substitution is associated with mild ultrastructural abnormalities and variably subtle clinical signs and is disease modifying, while homozygosity for this mutation is associated with classical EDS¹. Furthermore, the variant is significant in association analysis of idiopathic versus diabetic gastroparesis patients. We report 5/128 diabetic versus 27/238 idiopathic, p -value<0.007 (EDS gene set). The other variant duplicated in our cohort is the TNXB:NM_019105:exon26:c.A9044G:p.K3015R, with a high CADD score of 23.3. Amongst the 19 variants (total 21) reported in the 13 EDS patients, 9 have been reported in association with EDS confirmed in ClinVar⁶.

Additionally, a gene enrichment analysis was performed on core genes, $MAF<5$, idiopathic versus diabetic gastroparesis, and led to a significant result, specifically enrichment of variants in COL5A1, COL5A2, TNXB and ADAMTS2.

Conclusion: These results suggest a statistically significant enrichment of EDS patients in this gastroparesis study, with confirmed known and novel variants in the EDS gene set. Furthermore, these results suggest an enrichment of such gene variants in the entire idiopathic cohort of patients with idiopathic gastroparesis.

Disclosure: The authors are employees of Vanda Pharmaceuticals Inc.

P0027

THE EFFECT OF SINGLE AND REPEATED DOSES OF RIVASTIGMINE ON GASTRIC MYOELECTRIC ACTIVITY IN EXPERIMENTAL PIGS

J. Bures¹, C.C. Tsianou¹, J. Kvetina¹, I. Tachecí², V. Radochova³, D. Kohoutova⁴, S. Rejchrt², V. Knoblochova¹, M. Valis⁵, J. Zdarova Karasova⁶, O. Soukup¹

¹University Hospital, Biomedical Research Centre, Hradec Kralove, Czech Republic, ²University Hospital, 2nd Department of Internal Medicine - Gastroenterology, Hradec Kralove, Czech Republic,

³University of Defence, Faculty of Military Health Sciences, Animal Laboratory, Hradec Kralove, Czech Republic, ⁴Royal Marsden Hospital NHS Foundation Trust, London, United Kingdom,

⁵Charles University Faculty of Medicine and University Hospital, Hradec Kralove, Department of Neurology, Hradec Kralove, Czech Republic,

⁶University of Defence, Faculty of Military Health Sciences, Department of Toxicology and Military Pharmacy, Hradec Kralove, Czech Republic

Contact E-Mail Address: bures.jan@uvn.cz

Introduction: Rivastigmine is a pseudo-irreversible cholinesterase inhibitor used for therapy of Alzheimer's disease and non-Alzheimer dementia syndromes (including vascular and Parkinson disease dementia) [1]. Rivastigmine is a relatively weak, but long-lasting, cholinesterase inhibitor (IC₅₀ = 4.5 µM) that inhibits the action of both acetylcholinesterase and butyrylcholinesterase by reversible binding to them. In humans, rivastigmine can cause significant gastrointestinal side effects that can limit its clinical use.

Aims & Methods: The aim of this study was to assess the impact of rivastigmine on gastric motor function by means of electrogastrography (EGG) in experimental pigs.

Six experimental adult female pigs (*Sus scrofa* f. *domestica*, hybrids of Czech White and Landrace breeds; 3-month-old; mean weight 30.7 ± 1.2 kg) were enrolled into the study twice and created two experimental groups. In group A, a single intragastric dose of 6 mg rivastigmine hydrogen tartrate was administered in the morning to fasting pigs before EGG recording. In group B, rivastigmine was administered to overnight fasting animals in a dietary bolus in the morning for 7 days (6 mg per day).

On day 8, an intragastric dose of 12 mg rivastigmine was given in the morning to fasting pigs before EGG. EGG recording was accomplished by means of an EGG standalone system. Recordings from both groups were evaluated in dominant frequency and EGG power (areas of amplitudes).

Results: In total, 1,980 one-minute EGG intervals were evaluated. In group A, basal EGG power (median 1290.5; interquartile range 736.5 - 2330 µV²) was significantly higher in comparison with the power of intervals T6 (882; 577 - 1375; p = 0.001) and T10 (992.5; 385 - 2859; p = 0.032). In group B, the dominant frequency increased significantly from basal values (1.97 ± 1.57 cycles per minute) to intervals T9 (3.26 ± 2.16; p < 0.001) and T10 (2.14 ± 1.16; p = 0.012), respectively.

In group B, basal EGG power (median 1030.5; inter-quartile range 549 - 5093) was significantly higher in comparison with the power of intervals T7 (692.5; 434 - 1476; p = 0.002) and T8 (799; 435 - 1463 µV²; p = 0.004).

Conclusion: Both single as well as repeated intragastric administration of rivastigmine hydrogen tartrate caused a significant decrease of EGG power (areas of amplitudes) in experimental pigs. EGG power may serve as an indirect indicator of gastric motor competence. These findings provide a possible explanation of rivastigmine-associated dyspepsia in humans.

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Disclosure: Nothing to disclose.

P0028

LONG-TERM OUTCOMES OF PER-ORAL ENDOSCOPIC MYOTOMY IN ESOPHAGEAL MOTILITY DISORDERS: A SYSTEMATIC REVIEW AND META-ANALYSIS

Z. Nabi¹, H. Mandavdhare², R. Talukdar¹, D.N. Reddy¹

¹Asian Institute of Gastroenterology, Gastroenterology, Hyderabad, India, ²Post Graduate Institute of Medical Education and Research, Gastroenterology, Chandigarh, India

Contact E-Mail Address: zaheernabi1978@gmail.com

Introduction: Per-oral endoscopic myotomy (POEM) is an established treatment for achalasia with emerging data on long-term outcomes. In this systematic review and meta-analysis we aim to analyse the long-term outcomes of POEM in esophageal motility disorders.

Aims & Methods: In this systematic review and meta-analysis we aim to analyse the long-term outcomes of POEM in esophageal motility disorders.

Literature search was performed in the databases including PubMed, Embase, Cochrane databases and Google scholar from Jan 2010 to May 2021. The primary objective of the study was clinical success (Eckardt score ≤ 3 or < 4) after POEM at mean follow-up of more than 30 months. Secondary objectives included post POEM gastroesophageal reflux (GER) as evaluated by symptoms, increased esophageal acid exposure and reflux esophagitis.

Results: Seventeen studies with 3,591 patients were included in the review. The sub-types of motility disorders were type I in 952 (27%), type II in 1,926 (54.5%), type III in 378 (10.7%), DES/JHE 71 (2%), EGJOO 62 (17.5%). Pooled mean follow-up duration from nine studies was 48.9 months (95% CI 40.02 to 57.75).

Pooled rate of clinical success at 30-60 months follow-up was 87% (95% CI 81% to 91%; I²86%) and ≥ 60 months was 84% (95% CI 76% to 89%; I²47%). Pooled rate of clinical success in type I achalasia was 87% (95% CI 80%-92%; I²28%), type II achalasia 88% (95% CI 83%-91%; I²23%) and type III achalasia 76% (95% CI 64%-84%; I²10%).

In non-achalasia esophageal motility disorders (EGJOO, DES and JHE), the pooled rate of clinical success was 77% (95% CI 65% - 85%; I²0%). GER as estimated by symptoms was 23% (95% CI 19%-27%; I²74%), erosive esophagitis was 27% (95% CI 18%-38%; I²91%), and increased esophageal acid exposure was 41% (95% CI 30%-52%; I²88%).

Symptomatic reflux at short term (< 6 months) was 19% (95% CI 14 to 24; I² 77%), mid-term (1-2 years) was 16% (95% CI 9 to 27; I² 70%) and long-term (> 2 years) was 23% (95% CI 15% to 32%; I² 77%). Pooled rate of erosive esophagitis at short-term (< 6 months) from ten studies was 28% (95% CI 17%-41%; I² 91%) and long-term (≥ 2 years, five studies) was 13% (95% CI 6%-25%; I² 77%).

Conclusion: POEM is a durable treatment option in cases with achalasia. One-fourth patients suffer from erosive GER in long-term and success rates are lower in non-achalasia esophageal motility disorders.

Disclosure: Nothing to disclose.

P0029

CHICAGO CLASSIFICATION VERSION 3 VERSUS VERSION 4: WHAT ARE THE DIAGNOSTIC IMPLICATIONS?

M. Freitas^{1,2,3}, V. Macedo Silva^{1,2,3}, C. Arieira^{1,2,3}, J. Cotter^{1,2,3}

¹Hospital da Senhora da Oliveira, Gastroenterology Department, Guimarães, Portugal, ²Life and Health Sciences Research Institute (ICVS), School of Medicine, University of Minho, Braga, Portugal, ³ICVS/3B's, PT Government Associate Laboratory, Braga/Guimarães, Portugal

Contact E-Mail Address: martasfreitas@gmail.com

Introduction: The Chicago classification (CC) categorizes esophageal motility disorders according to the parameters obtained in esophageal high-resolution manometry (HRM). Recently, a new version of CC, CCv4.0, was published.

Aims & Methods: We aimed to compare esophageal motility disorders diagnosed according to the last two versions of CC (CCv3.0 vs CCv4.0). We performed a retrospective study that included consecutive patients undergoing esophageal HRM with 10 swallows in the supine position and 5 swallows in the upright position between February 2021 and February 2022. The manometric studies were reviewed, and motility disorders classified according to CCv3.0 and CCv4.0 by two operators.

Results: Fifty-nine patients were included, 50.8% were male, with mean age of 58±15 years. According to CCv3.0, 8 (13.6%) patients were diagnosed with esophagogastric junction (EGJ) relaxation disorders, 23 (39.0%) with peristalsis disorders: 8 (13.6%) major, 15 (25.4%) minor, and 28 (47.5%) were normal. According to CCv4.0, 7 (11.9%) patients were diagnosed with EGJ relaxation disorders, 19 (32.2%) with peristalsis disorders, and 33 (55.9%) were normal.

The diagnosis of motility disorders changed in 5 (8.5%) patients: 2 with EGJ outflow obstruction in CCv3.0 became normal in CCv4.0 because they had normal integrated relaxation pressure (IRP) in the upright position; 1 absence of contractility changed to achalasia in CCv4.0 by increased IRP in the upright position; 2 with ineffective esophageal motility in CCv3.0 became normal in CCv4.0.

Conclusion: EGJ relaxation disorders and peristalsis disorders were less frequently diagnosed with CCv4.0 comparing to CCv3.0. Ineffective esophageal motility and EGJ outflow obstruction had the greatest diagnostic variation between the two classifications. Future studies should assess the clinical implications of the new CC.

Disclosure: Nothing to disclose.

P0030

AUTONOMIC AUTOANTIBODIES IN ACHALASIA

D. Ben-Ami Shor¹, Y. Ron², N. Bar³, O. Shibolet¹, G. Halpert⁴, H. Heidecke⁵, Y. Shoenfeld⁶

¹Tel Aviv Medical Center, Gastroenterology, Tel Aviv, Israel, ²Tel Aviv Medical Center, Tel Aviv, Israel, ³Tel Aviv Sourasky Medical Center, Gastroenterology and Hepatology, Tel Aviv, Israel, ⁴Sheba Medical Center, Ramat Gan, Israel, ⁵CellTrend GmbH, Luckenwalde, Germany, ⁶Zabludowicz Center for Autoimmune Diseases, Ramat Gan, Israel

Contact E-Mail Address: benamidana@gmail.com

Introduction: Idiopathic achalasia is an esophageal motor disorder, characterized by loss of enteric neurons leading to absence of peristalsis and impaired relaxation of the lower esophageal sphincter (LES). The pathophysiology of achalasia is still unknown, although an autoimmune etiology is suspected.

Aims & Methods: We aimed to determine whether autoantibodies against the autonomic nervous system receptors can explain the enigmatic pathogenesis of achalasia.

This is an observational cross-sectional study using an ELISA method designed to identify the level of circulating autoantibodies against G protein-coupled receptors of the autonomic nervous system (adrenergic, muscarinic, endothelin and angiotensin receptors). Peripheral blood was obtained from forty achalasia patients diagnosed by an expert gastroenterologist based on esophageal manometry and upper endoscopy findings. The medical records of each patient was reviewed. Peripheral blood was also obtained from forty matched healthy donors (HDs) with no history of achalasia, no history of an autoimmune disease, as well as no symptoms suggestive for upper motility disorder.

Results: We herein report a significant reduction in the sera level of anti-muscarinic 2 receptor (anti-M2R) autoantibodies among achalasia patients as compared with aged matched HDs ($p < 0.009$).

Conclusion: Anti-M2R autoantibodies could be involved in the pathophysiological mechanism of achalasia. Further studies are needed in order to evaluate whether a higher expression of M2 receptor in the tissues among achalasia patients may lead to a high binding of the anti-M2R autoantibodies to these receptors and therefore a decreased level of these antibodies in the circulation.

Disclosure: Nothing to disclose.

P0031

PREVALENCE OF DELAYED GASTRIC EMPTYING IN DIABETIC PATIENTS WITH GASTROPARESIS-LIKE SYMPTOMS

I.-H. Huang^{1,2}, F. Carbone¹, L. Van Aelst¹, J. Schol¹, Y. Chen³, L. Michaja Balsiger¹, B. Broeders¹, T. Vanuytsel¹, J. Tack¹

¹Translational Research Center for Gastrointestinal Disorders, University of Leuven, Leuven, Belgium, ²Tri-Service General Hospital, National Defense Medical Center, Department of Gastroenterology and Hepatology, Taipei, Taiwan, ³Takeda Pharmaceuticals, GI TAU, Cambridge, United States

Contact E-Mail Address: alberttsggh@gmail.com

Introduction: Diabetes mellitus (DM) is a highly prevalent metabolic condition which is often associated with bothersome upper gastrointestinal symptoms. In some patients the dyspeptic symptoms are attributed to delayed gastric emptying, i.e. diabetic gastroparesis (GP). However, the distinction between patients with diabetic GP from those with dyspepsia is challenging because of large overlap.

The recent European consensus defined GP as a condition characterized by delayed gastric emptying in the absence of mechanical obstruction, with a symptom pattern of predominant nausea and/or vomiting and overlapping postprandial distress syndrome (PDS) (Schol, UEGJ 2021). So far, there is a paucity of data on the relationship between the symptom pattern and delayed gastric emptying in DM patients.

Aims & Methods: **Aim:** To investigate to what extent the symptom pattern may differentiate diabetic GP from dyspepsia in DM patients.

Methods: This retrospective study included 55 DM patients from the Leuven University Hospital, who underwent a ¹³C-octanoic acid gastric emptying breath test (GEBT) for clinical reasons and had no organic gastrointestinal disease, a history of abdominal surgery or medications that delay gastric emptying.

The severity of 6 epigastric symptoms (postprandial fullness, epigastric pain and burning, bloating, nausea, and belching) scored on a 5-point Likert scale, 0=Absent, 1=Very mild, 2=Mild, 3=Moderate, 4=Severe, was assessed every 15 minutes, before and 4h after the test meal (250 kCal), during the GEBT.

Included patients were defined as having gastroparesis-like symptoms (GPLS, i.e. total score of nausea ≥ 1 combined with total score of postprandial fullness ≥ 1), or dyspeptic symptoms (not fitting GPLS). We compared demographic and clinical variables as well as GEBT results in GPLS vs. dyspepsia patients by Mann-Whitney U and Pearson's chi-square tests. To investigate to what extent the symptom pattern may differentiate diabetic GP from dyspepsia in DM patients.

Results: Among 55 DM patients (median age of 50 years), 21 reported GPLS and 34 were DM with dyspepsia. The characteristics of the patients in both groups are shown in Table 1.

The prevalence of delayed gastric emptying (half gastric emptying time ($T_{1/2}$) > 109 min) in GPLS was significantly higher than in the dyspepsia group (33.2% (27.2-39.69) vs 8.8% (1.9-23.7), $p=0.02$). The $T_{1/2}$ was 73.0 (45.0-123.0) min in GPLS, compared to 63.0 (40.8-85.3) min in DM with dyspepsia ($p=0.19$). In the GPLS group, patients with type 2 DM (median age, 52 years) had a significantly higher prevalence of delayed gastric emptying than patients with type 1 DM (median age, 46 years) (71.4% (29.0-96.3) vs 14.3% (1.8-42.8), $p<0.01$).

When subgrouping GPLS patients into delayed ($n=7$) and normal ($n=14$) gastric emptying, we found no significant difference in age and body mass index (52 (36-55) vs 46 (27-55) years; 25.2 (22.5-30.8) vs 26.1 (20.0-29.0) kg/m^2 , respectively). There was no significant difference in severity of 6 epigastric symptoms and overall dyspepsia symptom severity (all $p>0.4$).

	Overall ($n=55$)	Dyspepsia ($n=34$)	GPLS ($n=21$)	P value
Female	38 (70.4%)	19 (55.9%)	19 (90.5%)	<0.01
Age (years)	50 (37.0-29.0)	51 (42.5-65.0)	46.0 (28.0-55.0)	0.09
BMI	25.9 (22.5-29.0)	25.8 (23.7-28.8)	25.9 (20.6-29.0)	0.69
Type 1 DM	37 (67.3%)	23 (67.6%)	14 (66.7%)	0.93
OSS	28.0 (6-57)	16.0 (0.8-35.0)	61.0 (30.0-119.0)	<0.01
$T_{1/2}$ (min)	68.0 (43-94)	63.0 (40.8-85.3)	73.0 (45.0-123.0)	0.19
Delayed gastric emptying	10 (29.4)	3 (8.8%)	7 (33.3%)	0.02

* Results expressed as median (interquartile range) for a continuous variable or count (%) for a categorical variable.

Table 1. Characteristics of diabetic patients indyspepsia and gastroparesis-like symptom group

Conclusion: In DM patients reporting upper gastrointestinal symptoms, the prevalence of delayed gastric emptying is associated with GPLS as defined by the recent European consensus. These findings are in favor of the symptom pattern proposed by the European consensus.

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P0032

G-POEM FOR REFRACTORY GASTROPARSIS: BASAL SYMPTOM SEVERITY AND INTRAGASTRIC MEAL DISTRIBUTION DURING GASTRIC EMPTYING SCINTIGRAPHY MAY BE PREDICTORS OF 12-MONTH CLINICAL OUTCOME

S.G.G. Testoni¹, F.V. Mandarino¹, A. Barchi¹, G. Pepe², D. Esposito¹, E. Viale¹, L. Fanti¹, P. Biamonte¹, S. Danese¹, F. Azzolini¹

¹IRCCS San Raffaele Scientific Institute, Vita-Salute San Raffaele University, Division of Gastroenterology and Gastrointestinal Endoscopy, Department of Experimental Oncology, Milano, Italy,

²IRCCS San Raffaele Scientific Institute, Vita-Salute San Raffaele University, Division of Nuclear Medicine, IRCCS San Raffaele Scientific Institute, Vita-Salute San Raffaele University Milan, Milano, Italy

Contact E-Mail Address: barchi.alberto@hsr.it

Introduction: Gastroparesis is a chronic disorder characterized by multiple different pathophysiological mechanisms beyond delayed gastric emptying, in the absence of mechanical obstruction. Gastric peroral endoscopic myotomy (G-POEM) represents a proven technique for treating refractory gastroparesis, with modest clinical effectiveness at 12-month [1,2]. Localized measurements at gastric emptying scintigraphy (GES) may represent a patient selection criterion for G-POEM. The Intra-gastric Meal Distribution (IMD), as measure of impaired fundic accommodation, has never been evaluated in patients treated with G-POEM

Aims & Methods: Patients with refractory gastroparesis prospectively treated with G-POEM from March 2019 to October 2020 (NCT04349670) were investigated regarding clinical and functional response up to 12-month follow-up. Inclusion criteria were: gastroparesis diagnosis through gastric emptying half time ($T_{1/2}$) ≥ 180 min and/or Percent Gastric Retention (PGR) after 2 hours $\geq 60\%$ at GES and Gastroparesis Cardinal Symptom Index (GCSI) [3] ≥ 1.5 ; GCSI < 1.5 with GES parameters below the abovementioned average after a good response to botulin injection (100UI); age ≥ 18 years; no response to medical therapy with symptoms from more than 6 months.

Main outcome was clinical success, defined as at least 1-score decrease in the total GCSI with decrease $> 25\%$ in at least 2 out of 3 symptomatic subscales (post-prandial fullness, nausea/vomiting, bloating) at 3-, 6-, and 12-month assessments. Secondary outcomes were: a) functional response, assessed with $T_{1/2}$, 2-hour PGR, IMD, and retention index (RI) at 3-month GES, defining functional success as decrease $\geq 30\%$ of 2-hour PGR [4]; b) identification of any baseline predictive factors of 3-month functional success and 12-month clinical success; c) G-POEM technical success and safety

Results: Eighteen patients with refractory gastroparesis (11 idiopathic, 6 post-surgical and 1 diabetic) were treated with G-POEM. Technical success was achieved in all procedures (100%). Clinical success was 66.7%, 52.9% and 62.5% at 3-, 6- and 12-month follow-up. Compared with baseline, the median total GCSI score reduced significantly up to 12-month ($p<0.0001$ at 3- and 6-month, $p=0.0013$ at 12-month), as well as all three median symptomatic GCSI subscales.

At 3-month GES, no significant changes compared with baseline were observed for the median $T_{1/2}$, and the mean 2-hour PGR, IMD and RI. At ROC analysis a significant predictive yield for functional success at 3-month GES was found for basal total GCSI and IMD ($p<0.0001$ and $p=0.045$), with sensitivity of 100% and 100% and specificity of 88.9% and 77.8% at the best cut-off values of ≤ 1.86 and ≤ 84 , respectively.

The basal total GCSI and IMD confirmed a significant predictive yield for the 12-month clinical success ($p=0.0297$ and $p=0.0152$). A significant decrease of the total GCSI up to 12-month was observed in patients with basal total GCSI > 2.7 and IMD ≤ 96.78 ($p=0.0156$ and $p=0.0126$), as the best

cut-off values with sensitivity of 54.55% and 87.51% and specificity of 100% and 75%, respectively. Whilst patients with basal GCSI ≤ 2.7 and IMD > 96.78 experienced a non-significant decrease of total GCSI.

Conclusion: G-POEM is an effective procedure for refractory gastroparesis-related symptoms. The pre-procedural symptom severity and IMD at GES might predict the long-term clinical response to G-POEM. Further studies on large samples are required to confirm these results and understand the correlation between symptoms and gastric motility localized patterns in gastroparesis.

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P0033

GASTROESOPHAGEAL REFLUX DISEASE AFTER PERORAL ENDOSCOPIC MYOTOMY

R. Muñoz González¹, A. Ezquerro Durán¹, S. Casabona-Francés¹, T. Pérez Fernández¹, C. Santander¹, P. Miranda¹

¹Hospital Universitario de La Princesa, Gastroenterology, Madrid, Spain

Contact E-Mail Address: pmpablomiranda@gmail.com

Introduction: Concern about gastroesophageal reflux disease (GERD) after peroral endoscopic myotomy (POEM) exists since high rates of pathological acid exposure time (AET) in pHmetry have been described. However, in treated achalasia patients, most cases of esophageal acidification are not related to reflux but are due to acid fermentation or stasis induced by acidic foods (1). Few studies have evaluated the relevance of fermentation or stasis after POEM.

Aims & Methods: The aim of our study was to evaluate the clinical, endoscopic, manometric and pHmetric characteristics of GERD in patients undergoing POEM.

From June 2018 to April 2022, we prospectively evaluated GERD in patients undergoing POEM at Hospital Universitario La Princesa (Spain) at months 3 and 12 after myotomy.

Clinical GERD was defined as GerdQ ≥ 8 , erosive esophagitis was reported according to Los Angeles classification, and an AET $> 6\%$ was considered pathological in 24h pHmetry registry (off acid suppression). In patients with a pathological AET, manual analysis of the pHmetric records was performed by an experienced physician who classified patterns in acidic reflux, fermentation or stasis, as previously described (1).

Results: 45 patients (20-86 years) underwent POEM. The main indication was achalasia type II (75%). Clinical success rate was 95% (Eckardt score < 3).

At follow-up (4-46 months), only 3 patients presented clinical GERD. Esophagitis was present in 9/32 (28%) and the vast majority were mild. Normalization of IRP4 occurred in 26/29 patients (89%) and pathological AET in 15/28 (53%). Of these (n=15), 10 (66%) had "real" GERD with prolonged clearance, while 4 (26%) presented acid fermentation and one (6%) was due to distal esophageal stasis.

Conclusion: Post-POEM GERD is usually asymptomatic. Objective tests such as endoscopy and pH-metry are needed to rule out GERD.

Manual interpretation of pathological AET is recommended to distinguish real acid reflux from fermentation or stasis, which has management implications.

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Disclosure: Nothing to disclose.

P0034 WITHDRAWN

P0035

ASSOCIATION BETWEEN GASTRIC EMPTYING AND SYMPTOMS IN A LARGE COHORT OF PATIENTS WITH DYSPESIA

J. Keller¹, A. Buchholtz¹, V. Andresen¹, P. Layer¹

¹Israelitisches Krankenhaus Hamburg, Department of Medicine, Hamburg, Germany

Contact E-Mail Address: j.keller@ik-h.de

Introduction: The current European consensus postulates that nausea and vomiting are the cardinal symptoms of gastroparesis (Schol et al. UEG J 2021). However, the association between gastric emptying and dyspeptic symptoms remains controversial, and a recent study by Carbone et al. (Clin Gastroenterol Hepatol 2022) showed no correlation between gastric emptying rate and simultaneously assessed dyspeptic symptoms in functional dyspepsia. However, the test meal used in this study was small (250 kcal) and may have elicited less symptoms than the patients' regular meals.

Aims & Methods: To investigate the association between gastric emptying and dyspeptic symptoms in a large cohort of patients, consecutive patients undergoing a ¹³C-octanoic acid breath test (¹³C-OAT, Ghos et al. 1993) at our institution were asked to also rate symptom severity using the Gastroparesis Cardinal Symptom Index (GCSI, Revicki et al. Qual Life Res 2004) while performing the gastric emptying test. The index reflects symptoms during the past 2 weeks. It requires graduation of severity of 9 symptoms from 0 (absent) to 5 (very severe), which are summarized in subscales for nausea/vomiting (N/V), postprandial fullness/early satiety (F/ES) and bloating (B). The GCSI is constructed as the average of these subscales. Normal gastric emptying half time (T_{1/2}) as established at our institution ranges from 50 to 150 min (Keller et al. UEG J 2021).

Results: We included 643 patients (447 females) with a median age of 50 [IQR 33-63] years. 13.5% of these patients had accelerated, 9.0% had delayed gastric emptying. Women had a higher GCSI than men (2.22[1.44-2.88] vs. 1.78[1.44-2.22], $p < 0.001$) with similar T_{1/2} (81[61-107] vs. 78[60-105] min, $p = 0.38$). In the total group and independent of sex, accelerated, normal or delayed GE, symptom severity for B was always significantly higher than severity of F/ES and N/V, respectively (tab). For the total group, there was no significant association between GCSI and T_{1/2} ($p = 0.468$). By contrast, in patients with delayed gastric emptying, T_{1/2} was a significant predictor of symptom severity, independent of age and sex ($R = 0.326$, $p = 0.020$). With regard to individual symptoms, vomiting ($R = 0.232$, $p = 0.039$)

and stomach fullness ($R=0.353$, $p=0.003$) were significantly associated with $T\frac{1}{2}$. The subscale, which correlated best with gastric emptying velocity, was F/ES ($R=0.255$, $p=0.027$).

	Total group (N=643)	Males (N=196)	Females (N=447)	$T\frac{1}{2}<50$ min (N=87)	$T\frac{1}{2} 50-150$ min (N=498)	$T\frac{1}{2}>150$ min (N=58)
<i>N/V</i>	1.0[0.0-1.7]	0.7[0.0-1.7]	1.0[0.3-1.7]	1.0[0.0-2.0]	1.0[0.0-2.0]	0.7[0.0-1.7]
<i>F/ES</i>	2.3[1.3-3.5]*	2.0[1.0-3.0]*	2.3[1.5-3.8]*	2.3[1.5-3.8]*	2.0[1.3-3.8]*	2.5[1.0-3.8]*
<i>B</i>	3.5[1.5-4.5]§	2.5[1.0-4.0]§	3.5[2.0-4.5]§	3.5[2.0-4.5]§	3.5[1.5-5.0]§	3.0[1.5-4.5]§

Data given as median with IQR, * $p<0.001$ vs *N/V*, § $p<0.015$ vs *N/V* and *F/ES*

Table.

Conclusion: In a large cohort of patients, who underwent a ^{13}C -OAT because of dyspeptic symptoms, more than 20% showed gastric emptying disturbances, about 10% had gastroparesis. When asked for symptom severity during the past 2 weeks, women recorded more severe symptoms than men despite similar gastric emptying.

Bloating was always the most bothersome symptom, independent of sex and gastric emptying velocity. In patients with gastroparesis (but not in patients with normal or accelerated gastric emptying), the degree of gastric emptying disturbance was an independent predictor of symptom severity. However, *F/ES* - and not *N/V* as postulated by the European consensus - correlated best with GE velocity in gastroparesis.

Disclosure: Nothing to disclose.

P0036

A RANDOMIZED CONTROLLED TRIAL TO COMPARE TRANSVERSE VERSUS LONGITUDINAL INCISION FOR ENTRY INTO THE SUBMUCOSAL SPACE DURING PER ORAL ENDOSCOPIC MYOTOMY FOR ESOPHAGEAL MOTILITY DISORDERS

H. Mandavdhare¹, J. Samanta¹, J. Shukla¹, J. Shah¹, A.K. Singh¹, A. Jafra², H. Singh³, P. Gupta⁴, U. Dutta¹

¹Post Graduate Institute of Medical Education and Research, Gastroenterology, Chandigarh, India, ²Post Graduate Institute of Medical Education and Research, Anaesthesiology, Chandigarh, India, ³Post Graduate Institute of Medical Education and Research, Surgery, Chandigarh, India, ⁴Post Graduate Institute of Medical Education and Research, Radiodiagnosis, Chandigarh, India

Contact E-Mail Address: hmandavdhare760@gmail.com

Introduction: Per oral endoscopic myotomy (POEM) has been established as the modality of choice for treatment of esophageal motility disorders (EMD). Longitudinal incision is the commonly used incision for entry into the submucosal space during POEM. Transverse incision is another alternative for entry, however, it is less commonly used. Retrospective data suggests that transverse incision has less chance of gas related events. However, a randomized controlled trial comparing the 2 types of incisions is lacking.

Aims & Methods: We performed a randomized controlled trial comparing the transverse and longitudinal incision for entry into the submucosal space during POEM for EMD. The primary objective was to compare the time for entry into the submucosal space.

The secondary objectives were to compare the time needed to close the incision, number of clips required to close the incision and gas related events in the form of capnoperitoneum needing needle aspiration under water seal and capnotherax needing intercostal drain placement.

Diagnosed cases of EMD (achalasia cardia (AC) type I, II, III, esophagogastric junction outflow obstruction (EGJO) and other spastic motility disorder like distal esophageal spasm (DES) and jackhammer esophagus (JE) as per the Chicago V 3.0 classification were enrolled.

The patients who were willing to undergo POEM after written informed consent were randomized to group A (longitudinal incision) and group B (transverse incision). Two experts and 2 trainees performed the POEM procedures. The opaque sealed envelope for randomization was opened after creation of the mucosal bleb.

The longitudinal incision was taken in a linear fashion along the long axis of esophagus starting proximally over the bleb and extending 2-3 cm aborally. The transverse incision was taken perpendicular to the long axis of the esophagus on the proximal aspect of the bleb in a right to left direction extending upto 2-3 cm.

Time taken for entry into the submucosal space, tunneling time, myotomy time, tunnel length and myotomy length, incision closure time and number clips needed for closure were noted during the procedure. Intraoperative events in the form of bleeding, mucosal injury (type I/II), capnoperitoneum/capnotherax needing aspiration were also noted. The technical success was defined as successful entry in to the submucosal space along with completion of all steps of POEM including myotomy.

Results: Between September 2021 and March 2022, 60 patients were randomized (30 each in the longitudinal and the transverse incision group). The median age was 39 (30,47.8) and 33 (55%) were males. Types of EMD were AC-I-33, II-16, III-2, DES-2, EGJO-2 and unclassified 5.

On comparing the 2 types of incisions there was no difference in entry time [3 (2, 5) min vs 2 (1.75, 5) min, $p=0.39$], closure time [7 (4, 13.5) min vs 9 (6.75, 19) min, $p=0.15$] and number clips needed for closure [4 (4, 6) vs 5 (4,7) min, $p=0.15$]. Also, the gas related events were comparable between the 2 groups (capnoperitoneum needing needle aspiration-5 vs 2, $p=0.22$).

On subgroup analysis, experts (n=42) needed more time to close the transverse incision as compared to longitudinal incision [7 (5,12) vs 11 (7,19), $p=0.04$]. This comparison was not feasible among trainees due to small sample size.

Conclusion: On comparison of the longitudinal and transverse incisions in POEM, entry time, number clips needed to close and gas related events were comparable while closure time was more for transverse incision.

Disclosure: Nothing to disclose.

P0037

A BASELINE SEVERITY INFLATION ANALYSIS IN STUDY VP-VLY-686-3301 OF TRADIPITANT IN GASTROPARESIS

J.L. Carlin¹, C. Polymeropoulos¹, C. Xiao¹, G. Birznies¹, M.H. Polymeropoulos¹

¹Vanda Pharmaceuticals, Inc., Washington, United States

Contact E-Mail Address: Jesse.Carlin@vandapharma.com

Introduction: Tradipitant is a novel NK-1 receptor antagonist that has previously showed efficacy in improving nausea, vomiting and overall gastroparesis symptoms in a phase 2 study (VP-VLY-686-2301) in patients with diabetic and idiopathic gastroparesis. The efficacy of tradipitant in gastroparesis was further evaluated in a phase 3 randomized, double-blind, placebo-controlled study (VP-VLY-686-3301).

A large placebo effect was observed which may have masked the true size of tradipitant benefit. Large placebo responses can be driven by Baseline Severity Inflation (BSI) especially on parameters which patients are selected for inclusion into the study. Here we present such a BSI analysis at the prespecified endpoint of change of nausea severity in VP-VLY-686-3301.

Aims & Methods: Idiopathic and diabetic gastroparesis patients with delayed gastric emptying, moderate to severe nausea, and at least 1 vomiting episode in screening were randomized to 85mg tradipitant BID or placebo for 12 weeks. Nausea was assessed using the 5-point Gastroparesis Core Symptom Daily Diary (GCSDD).

Overall gastroparesis symptom improvement was evaluated using the Patient Global Impression of Change (PGI-C) and the Overall Patient Benefit (OPB) scales. The BSI analysis subgroup included ITT (Intent-to-Treat) subjects with at least 1 but less than 7 average vomiting episodes and similarly excluded subjects whose vomiting severity was zero or highest severity category at baseline. This baseline threshold allows for censoring of patients with minimal or very high frequency of vomiting.

This method uses a symptom scale for censoring other than the scale used for the primary endpoint, is an accepted strategy to minimize placebo effect, and allows for a less biased estimation of true treatment effect.

Results: A patient responder analysis of PGI-C and OPB Score in the BSI subgroup showed a larger proportion of tradipitant treated patients improved versus placebo at start (Week 2) and end (Week 12) of the study. Similarly, at the same timepoints nausea was improved.

For the primary endpoint of change in nausea from baseline at week 12, tradipitant treated patients reported a greater reduction in nausea than placebo treated patients (-1.98 v. -1.28, $p=.028$). Improvement in tradipitant treated patients versus placebo was also seen at week 2 (-.99 v. -.50, $p=.013$). In the PGI-C scale more tradipitant treated patients demonstrated improvement as compared to placebo at week 2 (86% v. 53%, $p=.002$) and at week 12 (84% v. 65%, $p=0.056$). For the OPB scale, more tradipitant treated patients demonstrated benefit compared to placebo at week 2 (95% v. 68%, $p=.003$) and week 12 (92% v. 68%, $p=.009$).

Conclusion: Tradipitant treatment in the Baseline Severity Inflation Analysis subpopulation resulted in improvements in Nausea, PGI-C, and Overall Patient Benefit Score both the earliest (Week 2) and last (Week 12) timepoints.

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P0038

QUANTITATIVE ASSESSMENT OF ESOPHAGEAL BOLUS RETENTION WITH HIGH-RESOLUTION IMPEDANCE MANOMETRY

K. Oura¹, J. Akiyama¹, M. Hamada¹, S. Shinohara¹, E. Yamada¹, K. Suzuki¹, Y. Hisada¹, Y. Otake¹, Y. Yanai¹, N. Akazawa¹, C. Yokoi¹

¹National Center for Global Health and Medicine, Department of Gastroenterology, Tokyo, Japan

Contact E-Mail Address: koura@hosp.ncgm.go.jp

Introduction: High-resolution impedance manometry (HRIM) allows evaluation of esophageal bolus retention in conjunction with assessment of esophageal motor phenomena.

Aims & Methods: The aim of this study was to evaluate the relationship between esophageal bolus retention metrics and peristaltic integrity using HRIM. We retrospectively reviewed HRIM studies performed between Dec 2015 to Jan 2021, using an Unisensor catheter with 36 pressure sensors and 18 impedance segments with dedicated software (Starlet, Star Medical).

After excluding patients with achalasia, esophagogastric junction outflow obstruction, distal esophageal spasm, and Jackhammer esophagus, 119 patients (age: 63.2±15.5, female 52%) were included in this study. HRIM data were analyzed to assess Chicago Classification (CC) metrics, the esophageal impedance integral (EII) ratio (estimated as the summated EII in post-swallow domain/EII in swallow domain), and impedance ratio (IR) (calculated as nadir impedance/peak pressure impedance).

Contractility of each swallow was evaluated according to CCv4.0, but the normal contraction was further divided into two categories with or without a small break: normal contraction, normal contraction with a small break (2-5cm break with DCI>450), fragmented swallow (>5cm break with DCI>450), weak contraction (100≤DCI≤450), and failed peristalsis

(DCI<100). Dysphagia symptom was graded using a 4-point graded Likert scale from no discomfort to very severe.

Results: A total of 1217 swallows in 119 patients were analyzed. A) Per-patient analysis. Esophageal motility diagnoses included normal (n=103), ineffective esophageal motility (n=11) and absent contractility (n=5) according to CCv4.0. There were significant correlations between the values of esophageal bolus retention metrics and the severity of esophageal motility diagnoses (Spearman's rho: EII ratio 0.44; IR 0.20).

The median values of these metrics were higher in dysphagia patients than in non-dysphagia patients (EII ratio: 0.16 vs. 0.09, $p=0.006$; IR: 0.69 vs. 0.64, $p=0.006$). The EII ratio and IR values significantly correlated with the dysphagia symptom severity (Spearman's rho: EII ratio 0.31; IR 0.30). B) Per-swallow analysis. Contractility in the esophageal body included normal (n=749), normal with a small break (n=179), fragmented (n=80), weak (n=125) and failed (n=84).

There were significant correlations between the values of esophageal bolus retention metrics and the severity of esophageal peristaltic dysfunction (Spearman's rho: EII ratio 0.58; IR 0.24). ROC curve analysis revealed that the EII ratio was a better marker for quantifying bolus retention associated with ineffective swallow than IR (AUC: EII ratio 0.849, IR 0.655), with a sensitivity of 60% and a specificity of 89% at a cut-off value of 0.25.

Conclusion: The EII ratio and IR showed a consistent trend of increased values with increasing degrees of peristaltic dysfunction. The EII ratio appears to be a useful metric for the quantitative assessment of esophageal bolus retention.

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P0039

THE EFFECT OF BODY POSITION ON HIGH RESOLUTION ESOPHAGEAL MANOMETRY METRICS AND DIAGNOSIS IN ASIAN PATIENTS UNDERGOING ESOPHAGEAL MOTILITY TESTING

J. Kuang¹, K.B. Chuah¹, C. Chia¹

¹Tan Tock Seng Hospital, Gastroenterology & Hepatology, Singapore, Singapore

Contact E-Mail Address: ziyang_kuang@ttsh.com.sg

Introduction: The performance of upright wet swallows as a secondary position has been incorporated into the Chicago Classification (CC) 4.0 for the diagnosis of esophageal motility disorders. There is little data on the comparison of manometric diagnosis when comparing supine and upright swallows in Asian patients undergoing High Resolution Esophageal Manometry (HREM) testing.

Aims & Methods: This study aims to assess the effect of position on key HREM metrics and diagnosis based on CC 4.0, comparing testing performed in the conventional supine position with the upright position. The latter is generally favoured by patients as this represents the physiological posture during meals. A retrospective review of patients undergoing HREM at Tan Tock Seng Hospital, Singapore from January 2019 to January 2022 was carried out. HREM was performed using the Manoscan ESO high resolution manometry (Medtronic) software and solid-state catheter. Only patients who had at least 10 supine wet swallows and 5 upright wet swallows were included. Information on demographics, HREM metrics and manometric diagnosis was collected. SPSS version 15 was used to perform statistical analysis.

Results: A total of 104 patients were included in this study. The median age was 56 years old and 53.8% of patients were female. The median BMI was 24 kg/m². The indication for HREM in 64.4% of patients was for esophageal motility testing prior to 24-hour pH ambulatory testing. 31.7% of patients had dysphagia and 3.8% of patients had a dilated esophagus on computed tomography scans requiring HREM. Using 2-tailed paired sample T-test, comparison across all cases showed a consistently lower median Integrated Relaxation Pressure (IRP) [6.0 mmHg vs 8.7 mmHg; $p < 0.01$] and lower mean Distal Contractile Integral (DCI) [1463 mmHg/cm/sec vs 1864 mmHg/cm/sec; $p = 0.014$] in the upright position compared to supine position. The difference in the mean Distal Latency (DL) between these two positions was not significant [6.21 secs vs 6.27 secs; $p = 0.491$].

During upright position and supine position comparison respectively, subgroup analysis on subjects with normal HREM diagnosis showed an even lower median IRP [4.9 mmHg vs 7.5 mmHg; $p < 0.01$] and lower mean DCI [1436 mmHg/cm/sec vs 1695 mmHg/cm/sec; $p < 0.01$] with mean DL in this subgroup showing no significant difference [6.29 secs vs 6.38 secs; $p = 0.545$].

The final HREM diagnosis in the upright position is concordant with the conventional supine position in 81.7% of patients and showed an even higher concordance in terms of management similarity in 98.1% of patients. Only 2 patients had a significant discordance between supine and upright HREM diagnosis [normal HREM vs esophagogastric junction-outflow obstruction (EGJ-OO), and hypercontractile esophagus vs normal HREM]. Minor diagnostic discordance [normal HREM vs ineffective esophageal motility (IEM)] was noted in 16.3% of cases but this had no major clinical impact on patients and could be overcome by adopting a lower cut-off for mean DCI for the upright position group.

Conclusion: In conclusion, our study shows significantly lower median IRP and lower mean DCI values in the upright position as compared to the supine position. In addition, majority of patients had a final HREM diagnosis in the upright position that is concordant with that in the supine position. In patients who are unable to perform HREM in the supine position or in those who may be at high risk of aspiration when lying down, adopting the upright position shows a high clinical concordance and may be considered a more physiological approach in future HREM protocols.

Disclosure: Nothing to disclose.

P0040

IMPACT OF REFLUX BURDEN IN PATIENTS WITH INEFFECTIVE ESOPHAGEAL MOTILITY ACCORDING TO THE CRITERIA PROPOSED BY CCv4.0 COMPARED TO CCv3.0

P. Visaggi¹, L. Mariani¹, D. Stefani Donati¹, F. Baiano Svizzero¹, A. De Bernardi¹, S. Russo², R. Penagini³, M. Bellini¹, E.V. Savarino⁴, N. de Bortoli¹

¹Gastroenterology Unit, University of Pisa, Translational Research and New Technologies in Medicine and Surgery, Pisa, Italy,

²Digestive Endoscopy Unit, Azienda Ospedaliero-Universitaria di Modena Ospedale Civile di Baggiovara, Modena, Italy,

³Università degli Studi di Milano, Department of Pathophysiology and Transplantation, Milan, Italy, ⁴University of Padua, Division of Gastroenterology, Department Of Surgery, Oncology And Gastroenterology, Padua, Italy

Contact E-Mail Address: pierfrancesco.visaggi@gmail.com

Introduction: Ineffective esophageal motility (IEM) could be a manifestation of GERD. Recently, Chicago Classification (CC) v4.0 updated the criteria for IEM compared to CCv3.0, with CCv4.0 requiring $>70\%$ ineffective or $\geq 50\%$ failed swallows for a diagnosis of IEM, compared to $\geq 50\%$ ineffective swallows of CCv3.0.

Aims & Methods: The primary aim of this study was to investigate the prevalence of IEM according to CCv4.0 among those who had been diagnosed according to CCv3.0. The secondary aim was to compare acid exposure time (AET) and the other pH-impedance (MII-pH) parameters in patients with IEM as per CCv4.0 vs IEM as per CCv3.0. We extracted HRM tracings, endoscopy, and clinical data of patients diagnosed with IEM as per CCv3.0 between 2019-2020. We re-analyzed the tracings applying CCv4.0 criteria and grouped patients as follows: group A (IEM according to CCv4.0) and group B (No-IEM according to CCv4.0). Voluptuary habits, treatment with PPI, esophageal symptoms (heartburn, regurgitation, non-cardiac chest pain, dysphagia) were retrieved for all patients.

All patients had undergone upper endoscopy prior to HRM. During HRM, all patients underwent standard protocol and three multiple rapid swallows (MRS). After manometry, all patients underwent MII-pH. Vigor of contraction (DCI), prevalence of failed peristalsis and MRS/SS ratio were evaluated at HRM. Total and recumbent AET, number of reflux events and mean nocturnal baseline impedance (MNBI) and post-reflux swallowed induced peristaltic wave (PSPW)-index were calculated at MII-pH. The prevalence of GERD was calculated based on Lyon consensus criteria.

Results: Of 879 esophageal HRM performed, 134 (58F, mean age 51.9 $\pm$ 16.9 yrs) met the criteria for IEM as per CCv3.0 (15.2%). The prevalence changed to 86/879 (9.8%) applying CCv4.0 criteria. Group A, 86 patients (35F, mean age 51.5 $\pm$ 17.1 yrs), and Group B, 48 patients (23F, mean age 52.6 $\pm$ 16.2 yrs) did not show differences in epidemiological characteristics, voluptuary habits (alcohol, smoking, coffee) and clinical presentation (heartburn, regurgitation, dysphagia) ($p = \text{NS}$). Erosive esophagitis was more frequent in Group A (44/86 vs 15/48; $p = 0.03$). At HRM there were no differences in esophagogastric junction (EGJ) mean pressure, type III, integrated relaxation pressure, and distal latency ($p = \text{NS}$).

With regards to HRM results, DCI was lower, the number of failed swallows was higher, and MRS/SS ratio >1 was less frequent in group A compared to group B ($p < 0.001$). Reflux burden was higher in patients from group A: AET $>6\%$ was more frequent, number of total reflux events was higher, and PSPW index and MNBI were lower in group A compared to group B ($p < 0.001$). Table 1 reports the most relevant data.

	Group A (IEM CCv4.0)	Group B (No-IEM CCv4.0)	P value
Erosive Esophagitis	44/86 (51.2%)	15/48 (31.3%)	0.0303
AET $>6\%$	63/86	22/48	0.0026
AET tot	7.7 $\pm$ 2.7	6.3 $\pm$ 1.7	0.0015
Reflux numb	62.3 $\pm$ 31.8	51.5 $\pm$ 20.2	0.0355
PSPW-index	37.3 $\pm$ 11.4	41.6 $\pm$ 10.4	0.0327
MNBI	1367.3 $\pm$ 411	1524.7 $\pm$ 457.4	0.0433

Conclusion: Patients with IEM diagnosed with CCv4.0 criteria showed higher reflux burden in terms of erosive esophagitis, acid exposure, number of reflux events, and the novel MII-pH parameters (MNBI and PSPW-index) compared to those with IEM as per CCv3.0 who would be reclassified as no-IEM applying CCv4.0 criteria. These findings stress the tight relationship between GERD and IEM.

Disclosure: Nothing to disclose.

P0041

DOES BODY MASS INDEX INFLUENCE THE PARAMETERS OF HIGH-RESOLUTION ESOPHAGEAL MANOMETRY?

T. Surdea-Blaga¹, L.-E. David¹, C. Sabo¹, R.-L. Caragut¹, S. Grad¹, D.L. Dumitrascu¹

¹University of Medicine and Pharmacy "Iuliu Hatieganu" Cluj-Napoca, 2nd Medical Department, Cluj-Napoca, Romania

Contact E-Mail Address: dora_bлага@yahoo.com

Introduction: In one of our previous studies (1), we reported that overweight patients with achalasia had the resting pressure of the lower esophageal sphincter (LES) lower compared to lean subjects. Integrated relaxation pressure (IRP) was also lower, while the length of the esophago-gastric junction was longer. The aim of this study was to see whether the body mass index influenced the manometric parameters of patients with normal esophageal high-resolution manometry (HRM).

Aims & Methods: This was a retrospective study, based on esophageal HRM recordings from our department, from November 2015 to November 2021. All the manometries were performed with the patients in the supine position, using the same system and solid-state catheter, with 36 sensors (Unisensor®). All patients, irrespective of their complaints, without major or minor esophageal motility disorder were included.

We compared the following parameters: esophago-gastric junction (EGJ) morphology, LES resting pressure, IRP, esophageal length, EGJ length and the vigour of contraction (distal contractile integral – DCI).

Results: We identified 52 patients with normal esophageal HRM, and 2 were excluded for incomplete data. In the end we analyzed 50 patients, 23 females. Twenty-seven patients were overweight (BMI ≥ 25kg/m²).

We compared the manometry parameters in lean vs. overweight subjects. The morphology of esophago-gastric junction did not differ between the two groups (chi-square test = 1.09, p=0.30). There was no difference between the resting LES pressure (36.8±12.0 mmHg, vs. 35.2±11.6 mmHg, p = 0.64), the mean IRP (18.1±6.5 mmHg vs. 16.7±4.4 mmHg, p=0.37), the esophageal length (22.9±2.4 cm vs. 22.0±2.9 cm, p=0.27) in lean patients compared to overweight patients.

We separated patients based on BMI in obese (n=10, 4 males, 58.6±10.5 years), lean (n=23, 12 males, 46.8±14.0 years), and slightly obese (BMI between 25-29.9 kg/m², n=17, 11 males, 55.2±11.0 years), and we compared the subgroups. The presenting symptoms were similar in the 3 subgroups, with almost half of the subjects with reflux symptoms and/or dysphagia. Obese subjects were significantly older compared to lean subjects (p=0.02). Eight out of 10 obese patients, had type II EGJ morphology, and one had type III morphology. Among the lean subjects, 12 (54.2%) had type II EGJ morphology, and the remaining had type I morphology. In overweight subjects, 50% had type I EGJ morphology, and none had type III. Consequently, a clear demarcation between LES and crural diaphragm was observed in 8/10 obese subjects, 7/23 lean subjects, and 5/17 overweight subjects. The morphology of esophago-gastric junction differed between obese and lean subgroups (chi-square test = 4.3, p=0.04).

Obese patients had higher EGJ length, but the difference was not significant (4.3±2.0 vs. 3.4±1.0, p=0.11). The resting pressure of the LES (34.1 ±6.5 mmHg vs. 35.8±12.5 mmHg, p=0.67), the mean IRP (16.8±3.0 mmHg vs. 17.6±6.6 mmHg, p=0.69), the esophageal length (21.3±3.8 cm vs. 22.9±2.4 cm, p=0.15), and the DCI (1225±513 vs. 1487±809, p=0.35) were lower in obese compared to lean subjects, but the differences were not significant.

Conclusion: Obese subjects were more likely to have a clear separation between LES and crural diaphragm, and a type II or III EGJ morphology. With the limitation induced by the small number of subjects, our study did not find significant changes in the manometry parameters in obese versus lean subjects.

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Disclosure: Nothing to disclose

P0042

ANXIETY, DEPRESSION AND QUALITY OF LIFE PATIENTS WITH FUNCTIONAL DYSPEPSIA: A CROSS-SECTIONAL STUDY

T. Kugler¹

¹Donetsk National Medical University named M.Gorky, Internal Medicine, Donetsk, Ukraine

Contact E-Mail Address: kugler2@mail.ru

Introduction: Functional gastrointestinal disorders are often associated with changes in the psycho-emotional sphere [1,2]. However, data on the contribution of anxiety and depression in the patient's quality of life (QOL) are insufficient. The urgency of the problem is determined by the fact that functional diseases mainly affect young people of working age. This makes the problem not only medical but also social.

Aims & Methods: The aim of this study was to evaluate the clinical characteristics of anxiety and depression in different subtypes of functional dyspepsia (FD) group in comparison with control group and to establish the presence of a possible correlation between anxiety/depression and QOL. 125 patients with FD (Rome criteria IV) and 70 healthy volunteers were included in cross-sectional study. All participants filled out a HADS scale to identify anxiety/depression, SF-8 questionnaire (standard 4-week form) to assessment of the quality of life, Leuven postprandial distress scale (LPDS) to rate the severity of epigastric pain (burning) or abdominal discomfort. Data were evaluated with MedStat and NCSS (PASS 11). Linear regression analysis was performed in the case of functional relationships between two groups of random variables. Results obtained with p<0.05 and 95% CI were considered statistically significant.

Results: Anxiety and depression were observed in 50.4% and 42.4% of FD patients, respectively, and in 13.3% and 6.66% of healthy volunteers (p<0.001). The average anxiety score in FD patients was higher than in control (7.93 vs. 4.17; p<0.001), with max 17. The average score of depression in FD patients was also higher (6.94 vs. 3.4; p<0.001), with a max of 15. All patients with FD had a low level of QOL, both due to physical health (PCS) and emotional and psychological components (MCS) compared to controls (p<0.001).

		FD group		Control group	
Factors		Anxiety	Depression	Anxiety	Depression
Sex	Male	6,54±3,55†	5,86±3,57*	4,96±2,76	3,17±2,79
	Female	8,54±3,70†	7,47±3,80*	3,56±2,13	4,20±3,31
Subtype	PDS	7,43±3,56*	6,90±3,71*		
	EPS	8,18±3,57*	6,45±3,80		
	Overlap	8,5±4,06*	7,16±3,96*		
Severity of symptoms	Moderate	7,92±3,74†	6,94±3,78†		
	Severe	7,96±3,80†	7,06±3,80†		
Duration	< 3 years	7,45±3,67*	6,54±3,76*		
	3-5 years	7,12±3,88*	6,96±3,89*		
	> 5 years	8,01±3,47*	7,34±3,23*		

Table 1. HADS indicators of FD and control groups (note: * - p < 0,05 in comparison with the control group, † - p < 0,05 in comparison with the control group and intragroup indicators).

A positive correlation was found between the level of anxiety, depression and the severity of clinical manifestations of the disease ($R = 0.353$ and $R = 0.291$ $p < 0.05$). A negative correlation was observed between the severity of dyspepsia and the QOL of patients ($R = -0.264$, $p < 0.05$). The linear correlation was found between the QOL (PCS) and depression ($R = -0.311$, $p = 0.004$). The linear regression equation is: $PCS = -0.6441 * HADS-D + 50.27$.

Conclusion: Mental disorders are associated with changes in visceral sensitivity in FD patients, who perceive pain impulses as aggravated. This includes the interaction and feedback mechanisms between changes in the gastrointestinal tract and psychological factors. The HADS assessment showed that anxiety outweighed depression.

The most significant factors influencing the level of anxiety and depressive disorders in FD group were the patient's gender and the severity of clinical symptoms. Self-reported symptom severity, anxiety and depression were clearly and independently associated with the QOL. This became an important tool for assessing the severity of the disease and the effectiveness of therapy.

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P0043

DEFINING A THRESHOLD OF SEVERE FUNCTIONAL DYSPESIA FOR USE IN A CLINICAL SETTING

M.P. Jones¹, N.J. Talley², Y.A. Saito-Loftus³, F. Carbone⁴, J. Tack⁵
¹Macquarie University, School of Psychological Sciences, North Ryde, Australia, ²University of Newcastle, Faculty Of Health & Medicine, New Lambton Heights, Australia, ³Mayo Clinic, Gastroenterology & Hepatology, Rochester, United States, ⁴University of Leuven, TARGID, Leuven, Belgium, ⁵University of Leuven, University Hospital Gasthuisberg, Gastroenterology, Leuven, Belgium

Contact E-Mail Address: mike.jones@mq.edu.au

Introduction: The Rome IV criteria for functional dyspepsia¹ are the generally accepted diagnostic criteria for this condition and can be used to funnel patients into therapy. However these criteria are based primarily on symptom frequency rather than severity and therefore a diagnosis according to these criteria does not automatically mean that a patient has a symptomatically severe condition. Symptom severity might affect the clinician's decision on whether to initiate treatment and what form of treatment to apply. Other equivalent conditions do have thresholds set for defining mild, moderate and severe symptoms including irritable bowel syndrome².

Aims & Methods: This study aimed to define a threshold for symptoms that define a severe condition.

Study data: Data from two completed clinical trials were employed in this study. The first was the Functional Dyspepsia Treatment Trial (FDTT, $n = 292$)³ which compared two antidepressants and a placebo while the second was a trial comparing the prokinetic Itopride with placebo⁴ ($n = 100$). Since only the baseline (pretreatment) time point was used in each study all patients from all study arms were included.

Symptom thresholds: The symptom severity was first evaluated from the symptom score from the Nepean Dyspepsia Index (NDI)⁵ was considered once including all symptoms (AllSx) and again considering only symptoms relevant to the Rome IV criteria (RomeSx). Generalizability was enhanced by replicating with the Leuven Postprandial Distress Scale (LPDS)⁶.

Analytic approach: The shape of the relationship between symptom severity measures and independent anchors was evaluated in the FDTT and a threshold for severe symptoms was established based on the upper tertile (1/3) of the distribution symptom scores. These results were replicated in the Itopride trial in which additional patient psychosocial anchors were available.

Finally, discrimination of high scores on the overall symptom score (OSS) measure by the defined severity thresholds were evaluated for the NDI symptom score and the LPDS.

Results: In the FDTT RomeSx correlated well with the gastrointestinal symptom rating scale (GSRS, $r = 0.56$), all dimensions of the NDI ($r = -0.43$ to -0.53) physical ($r = -0.46$) but not mental ($r = -0.20$) of the SF-36, nutrient drink test volume ($r = -0.35$) but not scintigraphy measured gastric emptying half-time ($r = -0.01$). Similar correlations were obtained for AllSx. The upper tertile for RomeSx was scores of 78 or greater while for RomeSx it was 29 or greater. Use of this threshold was associated with Cohen d effect sizes of 1.04 (> 0.8 indicates large effect) for the GSRS and between 0.87 and 1.26 for the NDI QoL domains.

In the Itopride trial, the AllSx and RomeSx correlations with the NDI QoL were replicated and additional correlations with the PAGI-Sym⁷ and OSS ($r = 0.44$ and 0.47) were demonstrated. Further, the LPDS correlated with the OSS ($r = 0.55$ for PDS and $r = 0.41$ for EPS). Use of the FDTT-defined thresholds yielded Cohen d values -0.80 for AllSx and -1.11 for RomeSx. The upper tertile of the PDS domain of the LPDS corresponded to values of 2.4 and above while for the EPS domain it was values 0.7 or above. Use of these thresholds yielded Cohen d values -1.27 for PDS and -0.82 for EPS for the OSS and based on the total PAGI-SYM score values of -0.98 for PDS and -1.53 for EPS.

Conclusion: Symptomatically severe functional dyspepsia can be defined by scores on either of two validated measures, the NDI and LPDS. Thresholds defined for both instruments have been demonstrated to correspond to symptomatically severe disease and with impact on other aspects of patient wellbeing.

Disclosure: Nothing to disclose.

P0044

DUAL ASSESSMENT OF GASTRIC FUNCTION WITH SIMULTANEOUS GASTRIC EMPTYING AND BODY-SURFACE GASTRIC MAPPING IN PATIENTS WITH GASTROPARESIS-LIKE SYMPTOM AND FUNCTIONAL DYSPESIA

I.-H. Huang^{1,2}, A.A. Gharibans^{3,4}, G. Schamberg³, S. Calder³, S. Pellens¹, L. Holvoet¹, C. Varghese⁴, K. Verbeke¹, G. O'Grady^{4,3}, J. Tack¹

¹Translational Research Center for Gastrointestinal Disorders, University of Leuven, Leuven, Belgium, ²Tri-Service General Hospital, National Defense Medical Center, Department of Gastroenterology and Hepatology, Taipei, Taiwan, ³Alimetry Ltd, Auckland, New Zealand, ⁴University of Auckland, Auckland, New Zealand

Contact E-Mail Address: albertstgsh@gmail.com

Introduction: The distinction between patients with gastroparesis (GP) from those with functional dyspepsia (FD) is a matter of ongoing debate. The current diagnostic armamentarium is limited to the endoscopy and gastric emptying tests (GET). The recent European consensus defined GP as a condition characterized by delayed gastric emptying in the absence of mechanical obstruction, with a symptom pattern of predominant nausea and/or vomiting and overlapping postprandial distress syndrome (PDS)¹. FD is defined by predominant PDS or epigastric pain syndrome (EPS) symptoms². Body surface gastric mapping (BSGM) has recently emerged as a new non-invasive diagnostic strategy.

Aims & Methods: Aim: To investigate myoelectrical abnormalities in patients with GPLS and FD using BSGM.

Methods: Consecutive patients with chronic gastric symptoms undergoing a GET (breath tests with a C13-octanoic acid labelled 250 kcal solid meal) were invited to participate. Exclusion criteria were organic gastrointestinal diseases and history of abdominal surgery. BSGM was performed simultaneously using a novel medical device (Gastric Alimetry, Alimetry, New Zealand), employing stretchable electronics attached to a wearable Reader over the epigastrium (8x8 electrodes; 225 cm²).

Symptoms of nausea, bloating, upper gut pain, heartburn, stomach burn, and excessive fullness were logged at 15 min intervals in a validated app (30min fasting, 4hr postprandially) and combined to form a "Total Symptom Burden" score. GPLS (nausea and/or vomiting ≥ 1 day/week and simultaneous PDS) and FD (PDS or EPS) were defined based on the Rome IV diagnostic questionnaires.

BSGM data included amplitude, dominant frequency, stability index (percentage of activity concentrated in a narrow frequency band across time), meal response (fed-fasting power ratio) and slow wave direction. Data are presented as median (interquartile range). Mann-Whitney U and Pearson's chi-square tests were performed, with comparisons to a reference range of >100 healthy controls.

Results: At interim analysis, 21 patients with GPLS and 16 with FD (14 PDS, 1 EPS, 1 overlap PDS-EPS) were analyzed. BSGM abnormalities were detected in 20 patients (54.1%). The prevalence of delayed gastric emptying (half gastric emptying time (T1/2) > 109 min) was 21.6% in GPLS and 12.5% in FD (p=0.24). Total Symptom Burden Score was not significantly different between GPLS and FD (14.3 (7.2-38.2) vs 9.8 (2.6-18.1), retrospectively, p=0.11).

There were no significant differences in dominant frequency, meal response and percent of retrograde propagation between the two groups. FD patients demonstrated lower average postprandial amplitudes (32.70 μ V (26.52-36.75) vs 42.04 μ V (33.70-50.74), p=0.04) and less stable myoelectrical activity evidenced by a lower stability index (27.6 (24.7-31.2) vs 33.0 (27.8-37.3), p=0.03).

Characteristics	GPLS (n=21)	FD (n=16)	P value	BSGM variables	GPLS (n=21)	FD (n=16)	P value
Female	17 (81.0%)	13 (81.3%)	1.00	Dominant frequency (CPM)	3.03 (2.95-3.16)	3.05 (2.87-3.26)	0.97
Age (years)	29.0 (26.0-41)	31.0 (22.8-58.5)	0.81	Amplitude (μ V)	42.04 (33.70-50.74)	32.70 (26.52-36.75)	0.04
BMI	22.5 (20.5-25.5)	23.4 (20.7-25.5)	0.74	Stability index	0.33 (0.28-0.37)	0.27 (0.25-0.31)	0.03
T1/2 (min)	87.0 (66.0-111.0)	87.5 (79.5-97.8)	0.77	Meal response	1.17 (1.05-1.80)	1.50 (1.24-1.89)	0.21
Delayed gastric emptying	6 (28.6%)	2 (12.5%)	0.24	Retrograde propagation (%)	0 (0-6.7)	0 (0-2.8)	0.72

Table.

Conclusion: Patients with GPLS and FD demonstrated a high rate of gastric myoelectrical abnormalities on BSGM. Attenuated amplitude and reduced stability index in FD indicates contributing underlying neuromuscular abnormalities. Adding BSGM to a diagnostic pathway is feasible in clinical settings and may increase identification of gastric dysfunction vs GET alone. Ongoing patient recruitment will further define relationships between BSGM and these two groups of patients.

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P0045

CHRONOTYPES CORRELATES WITH PRESENCE AND SEVERITY OF UPPER GASTROINTESTINAL TRACT SYMPTOMS AND AFFECTS PATIENT'S QUALITY OF LIFE

S. Rurgo¹, M. Pesce¹, V. Vaino¹, M. Pagliaro¹, P. Senneca¹, G. Di Giorgio¹, B. Guida¹, G. Sarnelli¹

¹University of Naples "Federico II", Clinical Medicine and Surgery, Naples, Italy

Contact E-Mail Address: sararurgo91@hotmail.it

Introduction: Chronotype is the phenotype of behaviors controlled by the unique circadian rhythm possessed by individuals. Chronotype is under the control of finely regulated neuro-hormonal pathways and affects the sleep-wake cycle of a person. Circadian rhythms regulate multiple aspects of gastrointestinal physiology and recent evidence suggested their implication in symptoms' generation. Symptoms associated with disorder of gut-brain interaction negatively affect patients' quality of life and are associated with sleep disturbances. No structured studies have examined the chronotypes in patients with non-organic symptoms of the upper gastrointestinal tract.

Aims & Methods: To clarify the association between chronotypes, presence and severity of upper gastrointestinal tract diseases and their impact on quality of life. The subjects were 130 consecutive patients referring to the outpatients clinic for upper gastrointestinal symptoms (88 female, age 37 $\pm$ 13 years).

All subjects had a clinical and instrumental diagnosis of GERD or functional dyspepsia (FD). Subjects with underlying organic diseases were excluded. The standardized PAGI questionnaire was administered to all participants in order to assess the type, the severity and the impact on quality of life of specific symptoms.

Participants' chronotype, was assessed by the standardized Morningness-Eveningness Questionnaire (MEQ). The MEQ consists of 19 multiple-choice questions regarding sleep habits and daily performance, such as when feeling most productive in physical or mental activities, when feeling most tired, and when feeling most energetic. Patients were classified into morning, or evening chronotypes and GI symptoms analyzed, respectively.

Results: Thirty-four and 96 were classified as evening or morning chronotypes, respectively. Symptom's severity and relative impact on QoL significantly correlated with chronotype score ($r^2=0.1$ and 0.2 , respectively, all $p<0.05$). Patients with evening chronotype had significantly higher severity score than morning behavior (30 ± 17 vs. 15 ± 9 , $p<0.01$). A further analysis showed that dyspeptic (25 ± 14 vs. 11 ± 9 , $p<0.01$) but not Gerd-related symptoms (5 ± 3 vs. 3.8 ± 1.2 , $p=ns$) were significantly increased in evening chronotypes, with higher severity scores for postprandial fullness and epigastric bloating being observed (3.3 ± 0.8 vs. 1.8 ± 0.5 and 2.6 ± 0.6 vs. 1.3 ± 0.3 , $p<0.05$ and $p<0.01$, respectively). No significant differences were observed for the other symptoms.

Conclusion: We showed that chronotype correlates with upper gastrointestinal symptoms, with patients with an evening chronotype having more severe dyspeptic symptoms. Our findings suggest the involvement of disrupted circadian rhythms in the pathophysiology of dyspepsia and pave the way to alternative and personalized therapeutic approaches.

Disclosure: Nothing to disclose.

P0046

ASSESSING PREVALENCE AND CLINICAL FEATURES OF POSITIVE HYDROGEN BREATH TESTS IN PATIENTS REFERRED TO A TERTIARY UNIT, WITH SPECIAL ATTENTION TO FUNCTIONAL GASTROINTESTINAL CONDITIONS AND HEDS

H. Dervin¹, N. Zarate¹, R. Sweis¹, A. Mensah¹, K.C. Fragkos¹, C. Brugaletta¹, A. Raeburn¹, A. Emmanuel¹

¹University College London Hospitals NHS Foundation Trust, Gastrointestinal Physiology, London, United Kingdom

Contact E-Mail Address: humayra.abdul-razakq@nhs.net

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 (Rezai et al. 2017).

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 type Ehlers Danlos Syndrome (hEDS).

Aims & Methods: We aimed to:

1. Assess the prevalence of positive HBT in patients referred to a tertiary unit with particular interest in the prevalence of patients with functional gut disorders and hEDS,
2. Evaluate the potential predictive value of GI symptoms on different cohorts of patients referred for SIBO test,
3. Evaluate the potential role of other factors such as PPIs on influencing a positive HBT diagnosis.

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. 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 Maldigestion/malabsorption (i.e IBD, pancreatitis), Sensorimotor Disorders (i.e diabetes mellitus, radiation enteritis) and hEDS.

Descriptive statistics and median with interquartile ranges were used to describe the patient groups. A univariate analysis was used to compare the effect of the underlying disease on SIBO outcome using multiple predictors and chi-squared test.

Results: Over the 3-year period, a total of 1,062 HBT were performed. Seventy percent were female, with median age of patients being 47 (35- 60) years. Only, 7.5% (80/1062) patients were diagnosed as having a positive HBT. Prevalence of positive HBT was highest in patients with GI Maldigestion/Malabsorption (17.9%), Sensorimotor (15.9%), followed by functional disorders (1.6%). Interestingly, none of the hEDS patients tested positive for HBT (Table 1).

	N (Valid)	Gender [female (n, %)]	Age (years) [Median (IQR 25- 75 percentiles)]	Negative Test	Positive Test	Positive (%)
Functional	609	430 (70.6%)	43 (34.0-56.0)	599	10	1.6%
GI Maldigestion/ Malabsorption	273	183 (67.0%)	53.0 (37.0-68.5)	224	49	17.9%
Sensorimotor	132	86 (65.2%)	56.0 (43.0- 64.0)	111	21	15.9%
hEDS	48	45 (93.8%)	34.0 (28.0- 46.0)	48	0	0%
Total	1062	744 (70.0%)	47.0 (35.0-60.0)	982	80	7.5%

Table 1. Gender, age, percentage, frequency and total of each of the patient groups.

For the diagnostic accuracy of HBTs for all groups combined, the individual symptoms that had the highest diagnostic yield were diarrhoea, followed by fluctuating bowel habit. The remaining symptoms have no predictive value. A total of 531 patients had PPI usage recorded, with 137 of these patients (25.8%) fulfilling the criteria for long-term PPI use. Patients on PPIs were more likely to have a positive HBT than patients off PPI (16.1%vs6.9%; $p<0.0001$).

Conclusion: We have demonstrated that patients with a medical history of GI maldigestion/malabsorption disorders and sensorimotor disorders have greater prevalence and incidence of positive HBT, compared to patients with functional disorders and hEDS. Patients on PPIs are more likely to have a positive HBT compared to those that are not. Symptoms, along with the patient's medical history, can be a helpful triage tool in making appropriate therapeutic decisions and avoiding unnecessary hydrogen breath testing.

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Disclosure: Nothing to disclose.

P0047

QUANTIFYING THE BURDEN OF FOOD RELATED ALLERGIC REACTIONS IN HYPERMOBILE EHLERS DANLOS SYNDROME

R. Topan¹, S. Pandya¹, S. Williams², J. K Ruffle¹, N. Zarate-Lopez³, Q. Aziz¹, A. Fikree¹

¹Wingate Institute of Neurogastroenterology, Neurogastroenterology, London, United Kingdom, ²Barts Health NHS Trust, Gastroenterology, London, United Kingdom, ³University College London Hospital, Gastrointestinal Physiology Unit, London, United Kingdom

Contact E-Mail Address: r.lalani@qmul.ac.uk

Introduction: Patients with Hypermobile Ehlers Danlos Syndrome (hEDS) – a connective tissue disorder with high prevalence of Gastrointestinal (GI) symptoms – commonly report allergic reactions. Mast Cell Activation Syndrome (MCAS) is often diagnosed, although the evidence for this association is unclear. Food is reported as a typical symptom trigger of these reactions, but there are no large scale studies to quantify this.

Aims & Methods: We aimed to investigate patient-reported reactions which are interpreted as allergic by hEDS patients, to determine the incidence and commonly associated triggers. We conducted a cross-sectional study from August '21 to January '22. hEDS patients from the charity organisation Ehlers-Danlos Support UK and tertiary Neurogastroenterology clinics completed questionnaires to identify reactions interpreted as allergic across four domains: gastrointestinal(GI), skin, cardiovascular and respiratory, and whether specific foods triggered symptoms.

Additional questionnaires assessed for the presence of Mast Cell Activation Syndrome(MCAS), Postural Orthostatic Tachycardia Syndrome(PoTS)), Anxiety and Depression(HADS-A/D),somatic symptoms(PHQ-15), autonomic symptoms(COMPASS 31) and Avoidant Restrictive Food Intake Disorder(ARFID). We used logistic regression with stepwise feature selection to ascertain which of the above factors were predictive of GI reactions interpreted as allergic.

Results: 681 participants responded (median: 39 years(range: 16-76), 95% female). 33.6% reported a diagnosis of MCAS; 49.0% reported a diagnosis of PoTS and 64.6% had an abnormal HADS-A score. Atopy was common – 42.8% asthma, 33.6% eczema and 50.2% hay fever. 64.7% reported allergic reactions, most commonly GI (abdominal pain(58.9%), bloat-

ing(58.4%) and diarrhoea(55.3%)) of which 85.4% were provoked by food. Food also provoked symptoms in skin(50.8%), cardiovascular(40.7%) and respiratory(35.6%) systems. 81% of patients reporting food-related allergies eliminated their food triggers; of these 90.1% reported subsequent symptom improvement. Specific foods associated with GI allergic type reactions included pickles(OR: 1.85, $p=0.03$), highly processed snacks(OR: 1.70, 95%, $p=0.03$) and wheat(OR: 1.70, $p=0.01$).

All other foods, including milk/dairy, nuts, eggs, fish, shellfish and alcohol were not significantly associated. After food, the most commonly reported triggers for GI reactions interpreted as allergic were stress(46.1%), medication(41.9%) and exercise(21.2%). Having a reported diagnosis of MCAS($p=0.04$) and a high HADS-A score ($p=0.04$) predicted having food related GI-symptoms, yet a reported diagnosis of PoTS or high COMPASS-31 score did not. 8.5% ($n=26$) of those reporting food related GI-symptoms were taking the supplement Quercetin of whom 96.2%($n=25/26$) found it helpful.

Although there was more use of antihistamines and mast cell stabilisers in those who reported GI symptoms compared to those who did not, these differences were not statistically significant.

Conclusion: The most frequent reactions interpreted as allergic in hEDS patients are abdominal pain, bloating and diarrhoea. Further work is needed to objectively determine whether these reactions are true allergies/intolerances. Food is the most common trigger whereby fermentable carbohydrates and highly processed foods are frequent culprits which can be considered for elimination. Quercetin is a potentially useful supplement which requires further study. Anxiety plays a role in the association between food and GI reactions interpreted as allergic, therefore addressing stress may be a crucial component of the management plan.

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P0048

NO GENDER DIFFERENCES IN EOE DISEASE PRESENTATION, TREATMENT, AND COMPLICATIONS IN THE DANISH DANEEO COHORT – A POPULATION-BASED STUDY OF 236 PATIENTS

I. Kozon¹, L.T. Frandsen², B. Izgi¹, M.S. Trabjerg¹, L.E.M. Hansen³, D. Melgaard³, A.L. Krarup¹

¹Aalborg University Hospital, Department of Emergency Medicine and Trauma Care, and Department of Gastroenterology and Hepatology, Aalborg, Denmark, ²North Denmark Regional Hospital, Department of Gastroenterology, Hjørring, Denmark, ³North Denmark Regional Hospital, Center for Clinical Research, Hjørring, Denmark

Contact E-Mail Address: line.frandsen@rn.dk

Introduction: It is well known that there is a gender difference in the incidence eosinophilic oesophagitis (EoE) with more men affected. However, there is a lack of knowledge of gender difference in most other aspects of the disease.

Aims & Methods: This is a retrospective, registry-based, DanEoE cohort study of 236 adult EoE patients, (178 adult men and 58 adult women) diagnosed in 2007-2017 in the North Denmark Region. Medical registries were searched for patient files and pathology reports. We aimed to estimate the differences in phenotype, treatment, and complication rate between gender.

Results: There were no statistical or clinical significant differences in the phenotype regarding symptoms reported, macroscopic or histological findings at the diagnose (all $p>0.3$). However, a trend was observed towards 14% more men reporting allergy or asthma compared to women (61% men versus 47% women, $p=0.06$). A comparable number of men and

women were followed up symptomatically and histologically (all $p>0.3$). More men reported “no symptoms” on PPI (men 56% versus 39% women, $p=0.04$) although the histological response was not different between genders ($p=0.4$). The proportion of food bolus obstructions and dilations were comparable (all $p>0.4$).

Conclusion: In this study very few gender differences were found. Results suggests that men and women with EoE can be managed equally clinically. We did not find the expected gender differences as described in other gastrointestinal diseases.

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P0049

POPULATION-BASED INCIDENCE AND PREVALENCE OF EOSINOPHILIC OESOPHAGITIS IN DENMARK: A NATIONWIDE STUDY 2008 – 2018

K.H. Allin¹, G. Poulsen¹, D. Melgaard², L.T. Frandsen³, T. Jess¹, A.L. Krarup⁴

¹Aalborg University, Center for Molecular Prediction of Inflammatory Bowel Disease (PREDICT), Department of Clinical Medicine, Copenhagen, Denmark, ²North Denmark Regional Hospital, Center for Clinical Research, Hjørring, Denmark, ³Aalborg University Hospital, Department of Gastroenterology and Hepatology, Aalborg, Denmark, ⁴Aalborg University Hospital, Department of Emergency Medicine and Trauma Care, and Department of Gastroenterology and Hepatology, Aalborg, Denmark

Contact E-Mail Address: apslk@rn.dk

Introduction: Eosinophilic oesophagitis (EoE) is a chronic, immune-mediated, or antigen-mediated oesophageal disease characterized by symptoms related to oesophageal dysfunction and eosinophil-predominant inflammation.

Aims & Methods: To estimate the incidence and prevalence of EoE in Denmark during the period 2008-2018.

Based on data from nationwide registers we identified cases of EoE using two definitions: a broad definition based solely on oesophageal biopsies registered in the Danish Pathology Register and a narrow definition also including symptoms of oesophageal dysfunction registered in the Danish National Patient Registry.

The annual incidence and prevalence were standardized by sex and age in 5-year intervals to the 2013 study population.

Results: From 2008 to 2011, the standardized incidence of EoE (using the broad definition) was stable, but from 2011 to 2018 it increased from 3.9 (95% CI 3.3-4.4) to 11.7 (95% CI 10.8-12.6) per 100,000 person-years. Similar temporal trends were observed when using the narrow EoE definition.

The increase in incidence was most pronounced in men and in individuals above 40 years of age. In children, the EoE incidence was a fourth of the incidence in adults aged 40-64 years: 4.4 (95% CI 3.2-5.6) vs 17.6 (95% CI 15.7-19.5) per 100,000 person-years.

Overall, the biopsy rate as well as the proportion of oesophageal biopsies with detected eosinophilia increased during the study period.

Conclusion: This study of the entire population of Denmark during the period 2008 to 2018 shows that the incidence and prevalence of EoE is not yet plateauing and that EoE could be severely underdiagnosed in children.

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P0050

THE DESCRIPTION OF THE EOE COPENHAGEN COHORT OF PATIENTS WITH EOSINOPHILIC OESOPHAGITIS [ALK1]REFERRED TO A TERTIARY FACILITY IN DENMARK COMPARED TO THE POPULATION BASED DANEOE COHORT

C.O. Mortensen¹, I.B. Andersen¹, D. Melgaard², L.T. Frandsen³, A.L. Krarup⁴

¹Hvidovre University Hospital, Gastro-Unit, Copenhagen, Denmark,

²North Denmark Regional Hospital, Center for Clinical Research, Hjørring, Denmark, ³Aalborg University Hospital, Department of Gastroenterology and Hepatology, Aalborg, Denmark,

⁴Aalborg University Hospital, Department of Emergency Medicine and Trauma Care, and Department of Gastroenterology and Hepatology, Aalborg, Denmark

Contact E-Mail Address: Christian.Otto.Mortensen@regionh.dk

Introduction: The population-based DanEoE cohort in the North Denmark Region is well described. Little is known of difference in EoE complications in the general population compared to patients at tertiary centres.

Aims & Methods: The aims of the study were to describe the EoE patient phenotypes and complications in a new cohort of adult EoE at an academic Hospital in the capital of Denmark. Secondly, to compare them to the population-based DanEoE cohort.

The EoE Copenhagen cohort included dysphagia patients with eosinophilia starting May 1st, 2013. Exclusion criteria were other causes of eosinophilia in oesophagus than EoE. From May 2013 to 20th of October 2017, strictly clinical data limited to the direct handling were recorded: Allergic disease, histological responses to treatment, pH and manometry results and complications. From 20th of October 2017 to 31st of December 2020 detailed information were entered in the same database as the population-based DanEoE cohort.

Two experienced gastroenterologists and EoE experts (IBA, CM) evaluated and entered all data. The index endoscopy was defined as the first endoscopy with biopsies showing oesophageal eosinophilia. In both cohorts the EoE diagnose followed the AGREE consensus.

Results: The 245 EoE patients in the Copenhagen cohort were 1) less likely to have comorbid GORD, 2) be of male gender, 3) younger both at symptom debut, and at the EoE diagnose (all $p < 0.05$). At the index endoscopy less endoscopists had suspected EoE as a diagnose (EoE Copenhagen: 11 % versus DanEoE: 78 %, $p < 0.001$). The findings at the endoscopy were very similar except for edema being described more often in the EoE Copenhagen cohort ($p = 0.01$).

Dilations were rarely necessary in both cohorts. However, dilations after the diagnose was more frequently done in patients from the Copenhagen cohort (EoE Copenhagen cohort 9.5 % versus DanEoE cohort 7.1 %, $p = 0.5$).

Conclusion: The results indicated that patients referred to the Danish academic centre had earlier symptom debut, were diagnosed earlier, had more fibrotic disease, and less comorbid GORD. This indicate that studies based on patients from Academic centres are not comparable to studies based on the general population.

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Dellon ES, Liacouras CA, Molina-Infante J, et al. Updated International Consensus Diagnostic Criteria for Eosinophilic Esophagitis: Proceedings of the AGREE Conference. *Gastroenterology*. 2018;155(4):1022-1033.e10. doi:10.1053/j.gastro.2018.07.009

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P0051

DELAYED DIAGNOSIS OF EOSINOPHILIC OESOPHAGITIS IN THOSE PRESENTING TO THE EMERGENCY DEPARTMENT WITH FOOD BOLUS IMPACTION

D.A. Gyimah¹, H. Khan¹, B. Abdalla¹, H. Haboubi¹

¹University Hospital Llandough, Cardiff & Vale University Healthboard, Gastroenterology, Cardiff, United Kingdom

Contact E-Mail Address: dagymah1@gmail.com

Introduction: Food bolus impaction can be a manifestation of chronic untreated inflammation in those with underlying eosinophilic oesophagitis (EoE). The eosinophil predominant inflammation of the oesophagus is associated with a higher prevalence of fibrosis when it remains undetected and untreated. Non-malignant food bolus impaction is strongly associated with an underlying diagnosis of EoE, but outside of gastroenterology and other oesophageal interested specialists there remains poor understanding of how to diagnose and manage this condition.

Aims & Methods: We conducted a retrospective study of patients presenting to a tertiary emergency unit with oesophageal food bolus impaction between November 2018 and May 2021. Electronic attendance records and the endoscopy database were examined to determine the associations between demographics, comorbidities, endoscopic findings, biopsy findings and follow up. We also evaluated the effect of the pandemic on food bolus management with statistical analysis undertaken using IBM SPSS software.

Results: Of the 938 patients who presented to the emergency department with food bolus impaction, 83.6% were sent home with no follow up. Only 7.2% went on to have an endoscopy. In those with macroscopic evidence of inflammation, only 35.8% of patients had the correct number of biopsies taken to establish a histological cause for their symptoms. 1.6% of patients demonstrated histological evidence of EoE, of whom 80% were male and 20% female. The COVID-19 lockdown did not negatively impact access to endoscopy with mean wait time improving from 121-days prior to lockdown compared to 69-days during lockdown, $p < 0.01$.

Conclusion: Our findings highlight significant shortcomings in the management of those presenting emergently with food bolus impaction and possible undiagnosed EoE. There remains a need for clear management pathways to aid risk-stratification, discharge planning and endoscopic practices in the diagnosis of EoE. We therefore propose an algorithm for food bolus management to facilitate early endoscopy, effective diagnosis, and appropriate follow-up, ensuring optimal management for patients with non-malignant dysphagia requiring emergency admission for resolution of food impaction.

Disclosure: Nothing to disclose.

P0052

CHROMOENDOSCOPY WITH IODINE-POTASSIUM IODINE SOLUTION IMPROVES THE DETECTION OF EOSINOPHILIC ESOPHAGITIS - A COMPARATIVE STUDY

K.D.-C. Pham¹, S.S. Lauritzen¹, S. Akerkar¹, E. Tjora², O.H. Gilja^{3,1}, J.G. Hatlebakk^{1,3}, R.F. Havre^{1,3}, Bergen Research Group for Advanced Gastrointestinal Endoscopy (BRAGE)

¹Haukeland University Hospital, Medicine, Bergen, Norway,

²Haukeland University Hospital, Pediatrics, Bergen, Norway,

³University of Bergen, Clinical Medicine, Bergen, Norway

Contact E-Mail Address: sigurd.lauritzen@gmail.com

Introduction: Eosinophilic esophagitis (EoE) is a chronic immune-mediated condition characterized by eosinophilic infiltration of the esophageal mucosa. Endoscopic findings in EoE may be non-specific. The diagnosis is confirmed by histology with the finding of ≥ 15 eosinophilic granulocytes per high power field (HPF). The distribution of EoE may be patchy, hence, multiple biopsies from ≥ 2 segments are generally recommended to avoid false-negative diagnosis.

Aims & Methods: This study aims to evaluate whether chromoendoscopy with Iodine-Potassium iodine solution (IPIS) can improve the detection of EoE. Normal mucosa takes up IPIS and is stained dark brown, while mucosa with diminished uptake of IPIS becomes egg-yellow. Patients with dysphagia underwent gastroscopy with IPIS 1 % staining of the esophagus. A minimum of two biopsies were taken in ≥ 2 segments of the esophagus. In patients with heterogeneous staining after IPIS, selective biopsies were taken from areas with and without IPIS uptake, and forwarded separately for histological analysis.

Results: 52 patients were recruited prospectively. 31 (60%) of them had histologically proven EoE, of whom 11 (35 %) had normal endoscopic findings before installation of IPIS. All patients with EoE had diminished uptake of IPIS in whole or parts of the esophagus, giving a sensitivity of 100 % and a specificity of 78 %. The area under the receiver operating characteristic curve was 0.86. We identified three IPIS uptake patterns in EoE; 16 patients (53%) had diminished uptake in the whole esophagus, five (17%) had segmented and nine (30%) had a patchy pattern.

Of the 21 patients without EoE, seven (33 %) had diminished uptake of IPIS, of whom all had other identifiable diseases of the esophageal mucosa, including scleroderma, lymphocytic esophagitis, and squamous cell neoplasia. In patients with EoE and segmental or patchy IPIS patterns, the median number of eosinophils was significantly higher in areas with diminished uptake of IPIS, compared to areas with normal uptake (86 versus 7 eosinophils/HPF, $p=0.01$).

Conclusion: Our study suggests that around 35% of patients with EoE have normal endoscopic findings. Three IPIS uptake patterns can be seen in EoE. Biopsies taken from areas with diminished IPIS uptake show a significantly higher number of eosinophilic granulocytes, suggesting that the IPIS stain reflects the distribution of inflammation in the esophageal mucosa. Chromoendoscopy with IPIS may therefore be an useful in vivo technique for identifying EoE during endoscopy, allowing targeted biopsies, and thus increasing diagnostic sensitivity. IPIS staining is also useful for the identification of other mucosal conditions which cause dysphagia such as scleroderma, lymphocytic esophagitis, and squamous cell neoplasia.

Disclosure: Khanh Do-Cong Pham is a consultant for Boston Scientific and Ambu, and a speaker for Taewoong and Olympus.

Roald Flesland Havre has received lecture fees from Bristol-Myers-Squibb. The other co-authors have nothing to disclose.

P0053

THE PHENOTYPE OF PATIENTS WITH COMPLICATED EOSINOPHILIC OESOPHAGITIS - A POPULATION BASED STUDY OF THE DANEEO COHORT

S.D. Henriksen¹, D. Melgaard², A.L. Krarup^{3,4}

¹Aalborg University Hospital, Surgery, Aalborg, Denmark, ²North Denmark Regional Hospital, Center for Clinical Research, Hjørring, Denmark, ³Aalborg University Hospital, Department of Emergency Medicine and Trauma Care, and Department of Gastroenterology and Hepatology, Aalborg, Denmark, ⁴Aalborg University Hospital, Department of Gastroenterology and Hepatology, Aalborg, Denmark

Contact E-Mail Address: apslk@rn.dk

Introduction: The DanEoE is a previously described population- and register-based cohort of 236 adult patients with eosinophilic oesophagitis (EoE) in a well-defined Danish region with a population of 580.000 and free medical treatment.

Aims & Methods: To compare the phenotype and treatment response between EoE patients with complications to patients without complications at diagnosis.

Results: At the diagnostic endoscopy 61 % had never had a complication, and 39 % had had either FBO (n 77) or been dilated (n 15). The Complicated group had the same mean age at symptom debut (37 (16) versus 37 (17) years, $p = 1.0$), but were diagnosed significantly later (age: 49(15) versus 45(15) years, $p = 0.04$) with a resulting longer diagnostic delay (13(13) versus 7.9(11) years, $p = 0.01$). The complicated group were more often on a proton pump inhibitor at the time of diagnosis, complained more often of dysphagia, had rings or stenosis more frequent, but less often erosive oesophagitis (all $p < 0.05$).

Almost half of all patients were never treated to symptomatic remission (uncomplicated 40 %, complicated 49 %). The histological remission were not secured in the majority (uncomplicated 68 %, complicated 70 %). Despite this, less than 15 % of patients with previous FBO experienced this after the diagnose.

Conclusion: Results indicated that the complicated EoE phenotype at time of diagnosis was a patient with a five year longer diagnostic delay, and rings or stenosis already present. In the current study complication status did not determine treatment responses.

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P0054

TOLERANCE TO STERILIZED COW'S MILK IN PATIENTS WITH EOSINOPHILIC ESOPHAGITIS TRIGGERED BY MILK

A.J. Lucendo¹, M.P. Navarro Sánchez¹, M. Cobo-Palacios²,

R. Juárez-Tosina³, J.M. Olalla³, N. Serrano-Moya¹,

C. Alcolea-Valero¹, T. Angueira¹, J. González-Cervera⁴,

Á. Arias Arias⁵, Eosinophilic Inflammation and Mucosal

Immunology Research Lab (EIMIRLab)

¹Hospital General de Tomelloso, Dept. de Gastroenterology,

Tomelloso, Spain, ²Hospital General de Tomelloso, Nutrition and

Dietetics, Tomelloso, Spain, ³Hospital General La Mancha Centro,

Pathology, Alcázar de San Juan, Spain, ⁴Hospital General de

Tomelloso, Allergy, Tomelloso, Spain, ⁵Hospital La Mancha Centro,

Research Unit, Alcazar de San Juan, Spain

Contact E-Mail Address: mpilar_ns@hotmail.com

Introduction: Cow's milk protein is the main food trigger for eosinophilic esophagitis (EoE) in both children and adults, and should be continuously avoided from diet once identified as such.

Aims & Methods: This study evaluates tolerance of sterilized cow's milk (boiled instead of UHT processing) with regards to EoE remission maintenance, quality of life, nutritional intake and allergic sensitization in patients of all ages with milk-triggered EoE.

Eighteen patients in whom cow's milk was demonstrated to trigger EoE after empiric food elimination diet-based study, were prospectively recruited. They were given 200 mL of sterilized cow's milk twice daily for 8 weeks. Endoscopic assessment, intraepithelial peak eosinophil counts, esophageal-related symptoms, quality of life, blood eosinophils, eosinophil cationic protein, skin prick test and serum total and specific IgE to major milk proteins, were monitored before and after sterilized milk intake.

Results: Eighteen patients (mean±SD age 32±13.4 years, range 13 to 59 years; 13 male) with EoE triggered by milk who were in clinical and histologic remission underwent to a challenge with commercially available sterilized milk. After 8 weeks of daily intake, EoE remained in histological remission (<15 eos/hpf) in 12 out of the 18 EoE patients (66.7%), but EoE recurrence (≥15 eos/hpf) was documented in the remaining 6 patients.

Median±IQR baseline symptoms scored with DSS were 4±6 (range: 0-9) in the whole series, with no significant differences between patients who tolerated and not the sterilized milk. After sterilized milk challenge, tolerant patients maintained symptoms unchanged, but these tended to increase to 9±3.8 among milk-reactive subjects.

The esophagus was described as normal in all patients at baseline (ERFES score being 0), and remain unchanged in patients who maintained histological remission. In contrast, the median±IQR ERFES score increased up to 2.5±2.5 (range: 0-4) in patients who presented EoE recurrence after sterilized milk challenge. This increase was evidenced at the expense of inflammatory findings (edema, furrows and exudates), since no features of fibrosis were observed.

No differences in age, gender, symptoms score, endoscopic appearance, or personal/family allergic background were observed between those patients who tolerated the sterilized milk and those who did not.

Blood eosinophilia were in normal values at baseline, and tended to increase after sterilized milk challenge only in reactive patients who presented EoE recurrence. As for milk sensitization evaluation, total and milk specific IgE serum levels did not changed after sterilized milk consumption, with the exception of cow's milk specific IgE in reactive-EoE patients (median ± IQR increasing from 0.07±0.08 to 0.12±0.11, p=0.041 after sterilized milk challenge). Changes in eosinophilic cationic protein and tryptase were not significant from baseline in either tolerant and reactive patients. SPT to milk resulted negative in all the 18 but one participant at baseline. EoE-QoL-A score did not change significantly from baseline among patients who tolerated sterilized milk.

However, QoL significantly impaired among patient who did not tolerate sterilized milk, both in terms of the global score and the subscores corresponding to the dimensions Diet/eating Impact, Social Impact and Emotional Impact.

Conclusion: Most patients with EoE triggered by milk proteins are able to tolerate sterilized milk, with no signs of disease recurrence. This allows to improve patient's diets while maintaining an adequate disease control.

Disclosure: Nothing to disclose.

P0055

SPORADIC VERSUS FAMILIAL PRESENTATION OF EOSINOPHILIC ESOPHAGITIS: A COMPARATIVE ANALYSIS OF THE EOE CONNECT REGISTRY ON DEMOGRAPHIC, CLINICAL CHARACTERISTICS AND EARLY-LIFE EXPOSURES

M.P. Navarro Sánchez¹, L. Arias-Gonzalez¹, E.J. Laserna-Mendieta^{1,2}, S. Casabona-Francés³, E.V. Savarino⁴, M. Ghisa⁵, I. Pérez-Martínez⁶, D. Guagnozzi⁷, J. Barrio Andrés⁸, M.A. Perello⁹, A. Guardiola Arévalo¹⁰, A. Granja-Navacerrada¹⁰, L. Blas-Jhon¹¹, J. Alcedo¹², F. Racca¹³, A.L. Krarup¹⁴, G. Pellegatta¹⁵, C. Gutiérrez-Junquera¹⁶, S. De la Riva¹⁷, S. Fernandez-Fernandez¹⁸, S. Carrión Bolorino¹⁹, J.E. Naves²⁰, E. Amorena-Muro²¹, M.L. Masiques-Mas²², N. Garcia Morales²³, J. Cobián²⁴, C. Teruel²⁵, R. Dainese Plichon²⁶, S. Oliva²⁷, A. Rodríguez-Sánchez²⁸, J.A. Rodríguez Oballe²⁹, C. Ciriza de Los Ríos³⁰, M.T. Palomeque³¹, M. Votto³², S. Tamarit-Sebastian¹, C. Santander^{3,2,33}, A.J. Lucendo^{2,33,1}

¹Hospital General de Tomelloso, Department of Gastroenterology, Tomelloso, Spain, ²Instituto de Investigacion Sanitaria La Princesa, Madrid, Spain, ³Hospital Universitario de La Princesa, Gastroenterologist, Madrid, Spain, ⁴University of Padua, Division of Gastroenterology, Department of Surgery, Oncology and Gastroenterology, Padua, Italy, ⁵Azienda Ospedaliera di Padova, DISCOG - UOC Gastroenterologia, Padova, Italy, ⁶Hospital Universitario Central de Asturias, Oviedo, Spain, ⁷University Hospital Vall de Hebron, Gastroenterology Department, Barcelona, Spain, ⁸Rio Hortega University Hospital, Valladolid, Spain, ⁹Hospital De Viladecans, Barcelona, Spain, ¹⁰Hospital Universitario de Fuenlabrada, Gastroenterology, Aranjuez (Madrid), Spain, ¹¹Hospital Universitario Fundación Jiménez Díaz, Department of Gastroenterology, Madrid, Spain, ¹²Miguel Servet University Hospital, Digestive Diseases Department, Zaragoza, Spain, ¹³Humanitas Research Hospital, Personalized Medicine Asthma and Allergy Clinic, Rozzano, Italy, ¹⁴Aalborg University Hospital, Aalborg University Hospital, Aalborg, Denmark, ¹⁵Humanitas Research Hospital, Gastroenterology Unit, Rozzano, Italy, ¹⁶Hospital Puerta de Hierro, Pediatric Gastroenterology, Madrid, Spain, ¹⁷Clínica Universitaria de Navarra, Department of Gastroenterology, Pamplona, Spain, ¹⁸Hospital Universitario Severo Ochoa, Pediatric Gastroenterology, Leganes, Spain, ¹⁹Hospital de Mataró, Department of Gastroenterology, Mataró, Spain, ²⁰Parc de Salut Mar, Gastroenterology Department, Barcelona, Spain, ²¹Complejo Universitario de Navarra, Pamplona, Spain, ²²Hospital de Granollers, Pediatric Gastroenterology, Granollers, Spain, ²³University Hospital Álvaro Cunqueiro, Gastroenterology, Vigo, Spain, ²⁴Hospital Universitario de Donostia, San Sebastian, Spain, ²⁵Hospital Universitario Ramón y Cajal, Department of Gastroenterology, Madrid, Spain, ²⁶Centre Hospitalier d'Antibes Juan-les-Pins, France, Antibes, France, ²⁷University Hospital Umberto I - Sapienza University of Rome, Pediatric Gastroenterology and Liver Unit, Roma, Italy, ²⁸Hospital Universitario Santa Lucía, Department of Gastroenterology, Cartagena, Spain, ²⁹Hospital Universitari Arnau de Vilanova, Gastroenterology, Lerida, Spain, ³⁰Hospital Clínico Universitario San Carlos, Department of Gastroenterology, Madrid, Spain, ³¹Complejo Hospitalario Universitario de Albacete, Allergy, Albacete, Spain, ³²University of Pavia, PEDIATRIA, Pavia, Italy, ³³Centro de Investigación Biomédica en Red Enfermedades Hepáticas y Digestivas, Madrid, Spain

Contact E-Mail Address: mpilar_ns@hotmail.com

Introduction: Eosinophilic oesophagitis (EoE) is a chronic inflammatory disease characterised by a dense eosinophilic infiltration of the oesophagus.

gus and symptoms of oesophageal dysfunction. EoE represents a particular form of non-IgE-mediated food allergy that frequently associates to concomitant Th2 atopies. EoE often occur in families with several members affected. In addition, environmental factors and early life exposures have been involved in triggering EoE. However, limited information has been provided on the clinical differences between sporadic and familial EoE, and we do not know whether environmental risk factors to EoE influence differently on patients who have a family history of the EoE and those who do not.

Aims & Methods: To assess differences in demographic, clinical, endoscopic, pathological and environmental characteristics of familial EoE compared to sporadic cases. A cross-sectional analysis of the “European Registry of Clinical, Environmental and Genetic Determinants in Eosinophilic Oesophagitis” (EoE CONNECT) was performed to evaluate demographic, clinico-histological and early life factors in familial and sporadic cases of EoE. Statistical analyses (Mann-Whitney test and Kruskal-Wallis test for continuous variables and Chi-squared test for categorical variables) were performed using SPSS software.

Results: Data from 1,422 patients of EoE were analyzed (1,281 sporadic and 141 EoE patients with other relatives affected). Age at diagnosis was significantly lower in patients with familial EoE compared to sporadic disease (26.7±16.2 vs. 31.6±16.2; p=0.001). Patients with sporadic EoE tended to present greater diagnostic delay than familial cases (4.15±6.32 vs. 3.53±5.61 years; p=0.112), higher EREFS (Edema-Rings-Exudates-Furrows-Stricture) score (2.48±1.97 vs 2.71±1.73, p=0.13), peak eosinophil count (53.4±37.6 vs 50.2±29.8; p=0.79) and stricturing or mixed phenotypes, compared to familial cases.

However, none of this comparison achieved statistical significance. Regarding early-life exposures, antibiotic use during the first year of life, cesarean section delivery, preterm birth, contact with animals, place of residence (rural, urban or mixed), consumption of fast food in childhood and breast, formula-only or mixed (infant formula and breast milk) feeding did not present significant differences (p>0.05) between the group of patients with family history of EoE and those without.

	Overall (n=1422)	Esporadic cases (n=1281)	Familial cases (n=141)	p-value
Gender (n,%)				
Male	1084 (76,2)	981 (76,6)	103 (73)	0,35
Female	338 (23,8)	300 (23,4)	38 (27)	
Birth weight (Kg)	3,30±0,63	3,29 ±0,64	3,31±0,47	0,97
Age at diagnosis (years)	31,11±16,22	31,59 ± 16,16	26,73± 16,23	0,001
Diagnostic delay (years)	4,09±6,25	4,15 ± 6,32	3,53 ± 5,61	0,112
EoE Phenotype (n,%)				
Inflammatory	1035 (72,8)	923 (77,1)	112 (81,8)	0,40
Mixed	149 (10,5)	138 (11,5)	11 (8)	
Stenosing	150 (10,5)	136 (11,4)	14 (10,2)	
EREFS	2,64±1,68	2,73 ±1,69	2,61 ±1,86	0,32
DSS	8,16±3,36	7,79 ±3,58	7,95±3,32	0,73
peak eosinophils (eos/hpf)	53,19±35,61	53,42 ±37,57	50,20 ±29,78	0,79

Mean ± SD, Mann-Whitney test for continuous variables and Chi-squared test for categorical variables

Table 1. Demographic, clinical and histologic characteristics of familial EoE compared to sporadic cases.

Conclusion: This study suggests that patients with familial EoE are diagnosed at an earlier age than those presenting as sporadic cases, but neither the clinico-histological characteristics of the disease nor the early life exposures showed a differential influence over patients with or without familial EoE.

Disclosure: Nothing to disclose.

P0056

BURP-EXCRETED NITRIC OXIDE (BUENO): SETTING THE STANDARDS

F. Racca¹, E. Nappi^{1,2}, G. Paoletti^{1,2}, S. Ferri¹, M.R. Messina¹, F. Puggioni¹, G.W. Canonica^{1,2}, E. Heffler^{1,2}

¹IRCCS Humanitas Research Hospital, Personalized Medicine, Asthma and Allergy Clinic, Rozzano, Italy, ²Humanitas University, Department of Biomedical Sciences, Pieve Emanuele, Italy

Contact E-Mail Address: racca.fr@gmail.com

Introduction: Nitric oxide (NO) measurement is currently used in the setting of asthma patients' management as a marker of type 2 airway inflammation (1). NO is a crucial mediator also in the esophageal mucosa: luminal NO derives from exogenous (dietary) or endogenous sources, deriving from both constitutive and inducible isoforms of NO synthase (NOS): endothelial (eNOS) and neuronal (nNOS) NOS are physiological mediators of NO production at low concentrations, while inducible NO (iNOS) is an inflammation-induced enzyme, which can mediate production of high amounts of NO (2).

The esophageal luminal NO levels at fasting state might approximate iNOS activity and therefore mucosal inflammation. Non-invasively assessing esophageal inflammation might be important in the management of eosinophilic esophagitis (EoE). A non-invasive method for luminal esophageal gas sampling could consist in belch collection. The aim of this study was to assess the feasibility and standardize belch sample collection and NO analysis (Burp-Excreted++ Nitric Oxide – BuENO).

Aims & Methods: We consecutively enrolled 11 healthy subjects (6 females, mean age 41y±16; range 21-74). Belching samples were collected in the morning, after at least 8 hours of fasting to avoid exogenous NO formation. Subjects were instructed to close their nose with a clip and drink up to 500 ml of sparkling water to induce belching. When belching occurred, patients were instructed to keep the air in the closed mouth and expel it in an exhalation bag equipped with a unidirectional valve without blowing. The process had to be repeated until a sample of at least 200 ml was obtained. Samples were subsequently analyzed with a NO analyzer.

Results: Mean NO values were 734±889 ppb (Range 134-2585 ppb). No statistically significant difference was found between males and females. Values did not correlate with age or with the amount of sparkling water used. Two subjects showed values >1000 ppb, both referred typical gastroesophageal reflux symptoms during the night before the sample collection.

Conclusion: We set a protocol for belch collection and NO analysis. A first small sample of subjects showed values <1000 ppb with 2 exceptions, both referring gastroesophageal reflux disease, compatible with a situation of esophageal inflammation leading to activation of iNOS. The next phases of this study will enlarge sample size to obtain a normal range of values and to evaluate repeatability, and then assessing BuENO in patients with EoE. If validated, BuENO could represent a non-invasive method to detect esophago-gastric inflammation.

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P0057

HOW TO PREDICT PROTON PUMP INHIBITORS RESPONSES IN EOSINOPHILIC ESOPHAGITIS PATIENTS. AN IMPOSSIBLE MISSION?

M. Machín Delgado¹, V. Roales Gómez¹, I. Cacho Soblechero¹, C. López Martínez¹, S. Molina Tejedor¹, I. Blanco Nodal¹, E. Velasco Martínez¹, C. Ciriza de los Ríos¹, E. Rey Díaz-Rubio¹
¹Clínico San Carlos Hospital, Madrid, Spain

Contact E-Mail Address: mariamacdel@gmail.com

Introduction: Eosinophilic esophagitis (EoE) is an allergic inflammatory disease triggered by exposure to environmental or food allergens whose prevalence is increasing. It's clinical presentation is caused by altered motility resulting from permanent tissue swelling that causes subepithelial fibrosis.

Severe or long-standing cases develop fibrostenotic esophageal strictures that sometimes require endoscopic dilations, which carries the risk of complications. Therefore, treatment is necessary to achieve a clinical, endoscopic and histological response, either with proton pump inhibitors (PPI), topical corticosteroids or exclusion diets.

As of today, it is unknown whether there are characteristics to predict patients responding to PPI (PPI-REE) or non-PPI-REE, or if there is a correlation between non-PPI-REE and fibrostenotic development.

Aims & Methods: The aim is to determine whether patients with PPI-REE have personal history, environmental factors or clinical phenotype other than non-PPI-REE, to avoid using PPI in patients we know will not respond. A retrospective observational cohort study has been conducted. Patients diagnosed with EoE under the European and American Clinical Guide were included. Patients treated with exclusion diets and those with poor therapeutic adherence were excluded.

According to the clinical, endoscopic (EREFS score) and histologic response, patients were classified as complete, partial (clinical but not histologic) PPI-REE or non-PPI-REE. In addition, according to endoscopic findings, patients were classified as having an inflammatory or fibrostenotic phenotype.

The variables studied (Table 1) were obtained from the review of clinical, endoscopic and pathological reports. Statistical analysis was carried out by χ^2 of Pearson using the SPSS application.

Results: A group of 152 patients were analyzed in which the mean age of diagnosis was 40 years with a mean of 7 years of symptoms.

In 52.7% (80) complete PPI-REE was presented, 20.7% (32) presented partial PPI-REE and 26.6% (40) was non-PPI-REE. In the latter subgroup, 21.3% responded to corticosteroids and 5.3% did not respond to fluticasone/budesonide.

The analysis of variables (Table 1) did not show statistically significant differences between the PPI-REE and non-PPI-REE group, except for caesarian delivery, with a strong trend in favor of the non-PPI-REE group.

According to PPI response, 85.5% (94) of PPI-REE presented an inflammatory phenotype compared with 14.5% (16) of fibrostenotic. In non-PPI-REE patients, 75% (31) showed an inflammatory phenotype and 17.5% (7), a fibrostenotic phenotype. No association was observed between response type and phenotype (p 0.57).

Variables	Asthma	Rhinitis	Atopic dermatitis	Environmental allergy	Food allergy	Tobacco exposure	Pet exposure	Caesarean delivery
PPI-REE	35,5	50	31,8	68,5	31,2	46,4	22,7	10,1
NO PPI-REE	32,5	50	22,5	64,1	46,2	41,0	15,0	25,0
p valor	0,730	1	0,268	0,614	0,093	0,565	0,301	0,020

Table 1. Analysis of variables.

Conclusion: Given the exponential expansion in the incidence of EoE over the last two decades in the West, the possibility of knowing factors of non-PPI-REE patients would be a key tool for a therapeutic step-up strategy, which would reduce costs, endoscopies and active disease time.

This *ad hoc* study has not identified differentiating elements between the two cohorts, except for the caesarian delivery. It is clear that we still do not know about the response and the fibrous evolution of EoE, which prevents us today from predicting the natural history of the disease and the different clinical responses to the treatments available to us. Therefore, although it may be redundant, further research is needed.

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P0058

EOSINOPHILIC ESOPHAGITIS: MOST NON-RESPONDERS TO FIRST COURSE OF PPIS ACHIEVE SUSTAINED HISTOLOGICAL REMISSION FOLLOWING SEQUENTIAL TREATMENT WITH TOPICAL STEROIDS AND SECOND COURSE OF PPIS MONOTHERAPY

P. Visaggi¹, A. Venturini¹, D. Stefani Donati¹, F. Baiano Svizzero¹, L. Mariani¹, M. Ghisa², B. Barberio², M. Bellini¹, E.V. Savarino², N. de Bortoli¹

¹Gastroenterology Unit, University of Pisa, Translational Research and New Technologies in Medicine and Surgery, Pisa, Italy,

²University of Padua, Division of Gastroenterology, Department of Surgery, Oncology and Gastroenterology, Padua, Italy

Contact E-Mail Address: pierfrancesco.visaggi@gmail.com

Introduction: Proton pump inhibitors (PPIs) can be considered as first line treatment for eosinophilic esophagitis (EoE). When PPIs fail to achieve histological remission (i.e., eosinophils/high-power field - eos/HPF < 15), topical steroids (TS) can be used as second line. When patients report steroid-related side effects and decline treatment with elimination diets (ED), management becomes challenging. Little data regarding the efficacy of a second course of PPIs (scPPIs) in primary PPI non-responders is currently available.

Aims & Methods: We aimed at investigating if EoE patients who did not respond to a first course of PPIs and achieved histologic remission with subsequent TS treatment could be maintained in histologic remission with scPPIs monotherapy. We enrolled EoE patients who did not respond histologically (i.e., eos>15/HPF) to a 12-week course of high-dose PPIs who subsequently achieved histological remission following 12 weeks of second line therapy with topical steroids.

Among steroid responders (SR), those who complained of any steroid-related adverse event after a minimum of 12 weeks of treatment were offered a therapeutic switch to either ED or scPPIs. SR who had adverse events and opted for a therapeutic switch to scPPIs were evaluated histologically (minimum 4 esophageal biopsies) after 12 weeks of scPPIs.

Results: Among 68 primary PPIs non-responders who were SR, 18 patients (14M; 35.1±13yrs) reported adverse events after a minimum of 12 weeks of treatment (7 irritability, 6 edema, 4 oral candidiasis, 1 fatigue) and opted for scPPIs. Based on endoscopy with biopsies, 12 patients (10M, 34.3±13.8yrs) were scPPIs responders (scPPIs-R, i.e., eos/HPF<15), and 6 (4M, 36.8±13.4yrs) were scPPIs non-responders (scPPIs-NR, i.e., eos/HPF<15) at week 12. The two groups were comparable in terms of sex distribution, age at enrollment, age at diagnosis, smoking habits and coffee use, clinical presentation (dysphagia, chest pain, heartburn, regurgitation), history of asthma and food allergy. In contrast, scPPIs-NR more frequently drank >2 units of alcohol per day. Significantly more scPPIs-NR patients reported history of bolus impaction (scPPIs-NR=4 vs scPPIs-R=1, p=0.022) and had nasal polyposis (scPPIs-NR=5 vs scPPIs-R=1, p=0.004). Peak eosinophil count (PEC) was higher in scPPIs-NR at each histologic evaluation. scPPIs-R had higher although not significant prevalence of deep remission (i.e., eos<6/HPF) following steroid treatment (41.6% vs 0%, p=0.05). The EREFS score improved in scPPIs-R. Table 1 reports the most relevant clinical, endoscopy, and histology findings

	scPPIs responders (n=12)	scPPIs non-responders (n=6)	p value
EREFS score baseline (mean±sd)	3.5 ± 2.8	3.2 ± 2.6	0.82
EREFS score after first PPI course (mean±sd)	3 ± 1.9	3.2 ± 2.9	0.86
EREFS score after scPPIs (mean±sd)	1.3 ± 0.6	3.1 ± 2.4	0.02
PEC baseline (mean±sd)	31.5 ± 13.8	47.5 ± 16.4	0.04
PEC after first PPI course (mean±sd)	21.3 ± 3.2	32.9 ± 7.6	<0.001
PEC after scPPIs (mean±sd)	10.4 ± 4.1	27.9 ± 9.3	<0.0001
Previous bolus impaction (n/%)	1 (8.3%)	4 (66.7%)	0.02
Nasal polyposis (n/%)	1 (8.3%)	5 (83.3%)	<0.01
Alcohol >2 units/day (n/%)	1 (8.3%)	4 (66.7%)	0.02

Table 1.

Conclusion: scPPIs maintained histological remission for at least 12 weeks in 67% of primary PPI non-responder EoE patients who achieved histological remission with TS. History regarding bolus impaction, nasal polyposis, PEC, and deep remission following steroid treatment may identify patients more likely to achieve histological remission after scPPIs in case of primary PPI failure. Larger multicentric studies are needed to establish if this therapeutic strategy could be effective and widely applicable in the EoE setting.

Disclosure: Nothing to disclose.

P0059

CLINICAL HISTORY REPRESENTS A PERFECT SCREENING STRATEGY FOR EOSINOPHILIC ESOPHAGITIS IN PATIENTS REPORTING DYSPHAGIA: A CROSS-SECTIONAL CASE-CONTROL STUDY

P. Visaggi¹, D. Stefani Donati¹, F. Baiano Svizzero¹, A. Venturini¹, G. Del Corso², M. Ghisa³, B. Barberio³, R. Penagini⁴, M. Bellini¹, E.V. Savarino³, N. de Bortoli¹

¹Gastroenterology Unit, University of Pisa, Translational Research and New Technologies in Medicine and Surgery, Pisa, Italy,

²GSSI, Gran Sasso Science Institute, L'Aquila, Italy, L'Aquila, Italy,

³University of Padua, Division of Gastroenterology, Department Of Surgery, Oncology And Gastroenterology, Padua, Italy, ⁴Università degli Studi di Milano, Department of Pathophysiology and Transplantation, Milan, Italy

Contact E-Mail Address: pierfrancesco.visaggi@gmail.com

Introduction: Eosinophilic esophagitis (EoE) is a chronic disease of the esophagus characterized by symptoms of esophageal dysfunction, including dysphagia and food impaction, which frequently presents in combination with atopy. The diagnosis requires at least 15 eosinophils per high-power field (eos/HPF) on at least one esophageal biopsy collected during an esophagogastroduodenoscopy (EGDS). Screening strategies to reduce the diagnostic delay of EoE are lacking.

Aims & Methods: We investigated if clinical characteristics could be used for the screening of EoE in patients with dysphagia. We included patients referred for dysphagia to the Esophageal Diseases Clinic of Pisa and Padua who had undergone an EGDS to rule out obstructive neoplasia within six months. All patients were screened for EoE with an EGDS (minimum 4 esophageal biopsies). Patients without EoE (eos/HPF<15) underwent esophageal high-resolution manometry (HRM) with reflux monitoring in case of gastroesophageal reflux disease (GERD) symptoms.

Consecutive patients with EoE complaining of dysphagia and controls with non-EoE dysphagia (NED) were enrolled in a 1:1 ratio. A detailed clinical history including age, sex, interval between symptoms onset and conclusive diagnosis (i.e., diagnostic delay), history of food impaction, allergic rhinitis, asthma, atopic dermatitis, and autoimmunity was recorded.

Differences in clinical characteristics between EoE and controls were assessed using the Student's *t*, Mann-Whitney *U*, or Chi-squared test when appropriate. Normality and heterogeneity of variances were investigated. A Monte-Carlo approach was used to find the optimal combination of clinical features providing a diagnosis of EoE. Significance threshold was *p* < 0.05.

Clinical characteristics	EoE patients (n = 20)	NED patients (n = 20)	p-value
Age (mean±sd)	40±14	54±18	0.005
Males/Females	16/4	10/10	0.047
Allergic Rhinitis (n/%)	15 (75%)	1 (5%)	<0.001
History of food impaction (n/%)	13 (65%)	4 (20%)	0.004
Asthma (n/%)	8 (40%)	3 (15%)	0.07
Atopic dermatitis (n/%)	2 (10%)	1 (5%)	0.08
Autoimmunity (n/%)	8 (40%)	3 (15%)	0.07

Table.

Results: Twenty patients with EoE (mean age 47±17 years, 16M) and 20 NED (mean age 54±18 years, 10M) were enrolled. The median diagnostic delay was 6 years (1.5-10.5) for EoE, and 3 years (1.3-6) for NED, *p*=0.4.

Among patients with NED, six had achalasia, five had a normal HRM (two GERD, one either myasthenia gravis, myotonic dystrophy, or no found cause), three had esophagogastric junction outflow obstruction, three hypercontractile esophagus, two absent peristalsis, and one distal esophageal spasm. Patients with EoE were significantly younger ($p < 0.01$), more frequently male ($p = 0.04$), more frequently reported a history of allergic rhinitis ($p < 0.001$) and food bolus impaction ($p = 0.004$) compared to NED. In contrast the two groups did not differ in terms of asthma, atopic dermatitis, and autoimmunity history.

Monte-Carlo analysis of the clinical characteristics that differed significantly between the two groups generated >50 predictive models for the screening of EoE. Among these, the model investigating male sex and/or the presence of allergic rhinitis performed best, with 100% sensitivity and 50% specificity for a diagnosis of EoE.

Conclusion: Performing an EGDS with multiple esophageal biopsies in a patient referred for non-neoplastic dysphagia, who is male or has allergic rhinitis, identifies 100% of EoE cases and avoids unnecessary biopsies in 50% of NED.

Despite this was a small cohort, the homogeneity of the two groups and the significance obtained strongly suggest that age, gender, history of rhinitis and bolus impaction segregate EoE from NED. Studies with larger cohorts of patients are needed to validate a clinical history-based screening for EoE.

Disclosure: Nothing to disclose.

P0060

EOSINOPHILIC ESOPHAGITIS, PREVALENCE, INCIDENCE AND PRESENTING FEATURES IN SOUTHWEST SWEDEN: A 20-YEAR POPULATION-BASED STUDY

J. Plate¹, T. Söderbergh¹, H. Larsson¹

¹NÄL County Hospital, Department of Otorhinolaryngology Head and Neck Surgery, Trollhättan, Sweden

Contact E-Mail Address: john.plate@vgregion.se

Introduction: Eosinophilic Esophagitis (EoE) is a chronic eosinophilic inflammatory condition of the esophagus and was first recognized in the 1990's as an own disease entity (1, 2) Symptoms in adults are mainly esophageal dysphagia but can also present as acute food bolus obstruction of the esophagus. Diagnosis requires symptoms of esophageal dysfunction and esophageal biopsy with ≥ 15 eosinophils/HPF. (3)

EoE seems to be rising in both prevalence and incidence (4).

The reported prevalence in USA and Europe is 45-55/100 000(6), though a Spanish study from 2018 reports a prevalence of 112/100 000.(5;6) Not until 2012 the disease could be registered via an own diagnostic code (K20.9A) in Sweden.

Aims & Methods: The aim of this study was to study prevalence, incidence and presenting symptoms among patients with EoE in the catchment area of NÄL county hospital, Sweden, 290 000 inhabitants. (7)

Patient records marked with the diagnostic code of EoE between 2012.01.01 - 2022.01.01 were studied. Incidence of acute food bolus obstruction and endoscopic findings were noted. Patients who did not meet the diagnostic criteria of EoE were excluded.

A search was made in the local data base for histological samples using the keywords Esophagus and Inflammation with a timeframe of 2000-01-01 - 2022-01-01. The patients with more than 15 eosinophils/HPF had their records studied. The patients who met the diagnostic criteria for EoE were included.

Results: 360 patients met the criteria for EoE diagnosis. 19 patients were diseased, leaving a total of 341 patients alive who had the diagnosis, giving a prevalence of 118/100 000.

Of the 341 patients the mean age at diagnosis was 40 years(1-79 years), 66% are men. 65 patients are under 18 years of age (16 girls and 49 boys) 42% had at least one acute bolus obstruction before diagnosis, 40% had endoscopic findings of fibrosis (trachealisation/stricture).

The mean yearly incidens was 8/100000 (2005-2021) and seems to be rising, mean incidence 5/100000 (2005-2010).

Conclusion: The prevalence of EoE January 2022 in the catchment area of NU-sjukvården is 118/100 000, which is significantly higher than generally reported.

42% had acute food bolus obstruction as presenting symptom possibly an effect of that patients was diagnosed late after symptom onset.

The incidence seems to be increasing, whether this is due to a real increase in diagnosed patients or increased awareness among practicing physicians remains unknown.

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P0061

HISTOPATHOLOGY BUT NOT MENTAL HEALTH ASSESSMENT DISTINGUISHES INDIVIDUALS WITH AND WITHOUT EROSIIVE REFLUX DISEASE AND CONTROLS WITHOUT REFLUX DISEASE – A CROSS-SECTIONAL POPULATION-BASED STUDY

A. Andreasson^{1,2}, M.P. Jones², M.M. Walker³, M. Vieth⁴, B. Wallner⁵, P.M. Hellström⁶, A. Forsberg⁷, L. Agréus⁸, N.J. Talley⁹
¹Stockholm University, Stress Research Institute, Stockholm, Sweden, ²Macquarie University, Psychology, North Ryde, Australia, ³University of Newcastle, Dept. of Anatomical Pathology, Newcastle, Australia, ⁴Klinikum Bayreuth Abt. Pathology, Abt. Pathologie, Bayreuth, Germany, ⁵Umeå University, Surgical and Perioperative Sciences, Surgery, Umeå, Sweden, ⁶Uppsala University, Specialmedicine / Gastroenterology, Uppsala, Sweden, ⁷Karolinska Institutet, Institution of Medicine Solna, Stockholm, Sweden, ⁸Karolinska Institutet, Division of Family Medicine and Primary Care, Huddinge, Sweden, ⁹University of Newcastle, Faculty of Health & Medicine, New Lambton Heights, Australia

Contact E-Mail Address: nicholas.talley@newcastle.edu.au

Introduction: Gastroesophageal reflux disease (GERD) is defined as weekly or more frequent gastroesophageal reflux symptoms (GERS) and/or visible mucosal changes, erosive esophagitis (EE), on an oesophago-gastroduodenoscopy (OEGD) (1). GERD is a chronic disease, but only a minority with GERS have EE (1). The role of histology in diagnosis of GERD is controversial (1, 2). A recent systematic review concluded poor mental health is a risk factor for GERD but community-based studies are very few (3). We investigated differences in histological markers and mental health in EE, non-erosive reflux disease (NERD) and subjects free from GERD from a random population sample who were endoscoped.

Aims & Methods: In a cross-sectional study investigating a random sample of individuals from the general population in a Swedish municipality, 384 subjects completed an upper endoscopy (OEGD). Biopsies were taken at three locations, at the Z-line, just above the Z-line and 2 cm above the Z-line. Participants reported gastrointestinal symptoms, including heartburn and acid regurgitation, on the Abdominal Symptom Questionnaire and mental health on the Hospital Anxiety and Depression Scale. Logistic regression was used to test differences in histological parameters and mental health between individuals with EE with or without GERS, NERD and individuals without any GERD. The models were adjusted for age, sex, body mass index (BMI) and proton pump inhibitor (PPI)/histamine (H₂) blocker treatment.

	Non GERD	NERD	EE without GERS			EE with GERS	
Z-line		RRR	95 % CI	RRR	95 % CI	RRR	95 % CI
Total thickness	Reference	1.002	1.000-1.005	1.004	1.000-1.007*	.999	.995-1.003
Papilla length	Reference	1.003	.999-1.006	1.006	1.001-1.010*	1.003	.999-1.008
Above Z-line							
Total thickness	Reference	1.001	.998-1.004	1.002	.997-1.006	1.008	1.004-1.013***
Basal layer	Reference	1.005	.991-1.020	1.006	.988-1.024	1.019	1.004-1.034*
Papilla length	Reference	1.001	.997-1.005	1.005	.999-1.011	1.011	1.005-1.016***
2 cm above Z-line							
Spongiosis	Reference	5.32	1.500-18.85*	-	-	-	-
*p<0.05; ***p<0.001							

*p<0.05; ***p<0.001

Table 1. Differences in histological parameters and mental health between individuals with and without erosive reflux disease and controls without reflux disease

Results: EE was found in 58 participants (15.1%: LA-A:9.4%, B:4.9%, C:0.8%). Compared to participants without GERD (n=242), participants with EE without GERS (n=33) showed changes at the Z-line: increased total

thickness and papilla length while participants with EE with GERS (n=25) displayed an increase in total thickness, basal layer thickness and papillary length just above the Z-line, see Table 1.

NERD (n=84) was associated with increased spongiosis 2 cm above the Z-line. No differences in anxiety and depression were observed.

Conclusion: Histological changes at the Z-line may provide useful information about GERD. There is no evidence in this study that mental health is linked to GERD in the community.

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P0062

OESOPHAGEAL DYSMOTILITY AND GASTROESOPHAGEAL REFUX IN RESPIRATORY DISEASE: AN ONGOING CONUNDRUM OF WHO SHOULD UNDERGO LUNG TRANSPLANTATION

A. Alghubari¹, R. Cheah¹, S. Shah², K.R. DeVault³, L.A. Houghton^{1,3}

¹University of Leeds, Leeds Institute of Medical Research at St James's, Division of Gastroenterology and Surgical Sciences, Leeds, United Kingdom, ²Mayo Clinic, Department of Transplantation, Jacksonville, United States, ³Mayo Clinic, Division of Gastroenterology and Hepatology, Jacksonville, United States

Contact E-Mail Address: umaifa@leeds.ac.uk

Introduction: Oesophageal dysmotility and gastroesophageal reflux (GER) are common in patients with respiratory disease and following lung transplantation (LTx). However, the effect of LTx and how oesophageal dysfunction prior to LTx influences outcome remains unclear. This leads to patients with abnormal pH-metry or significant dysmotility prior to LTx often been excluded from transplant waiting-lists, out of concern for adverse allograft outcomes.

Aims & Methods: Our aim is to further understand the effect of LTx on oesophageal motility and GER in patients with respiratory disease.

High Resolution Oesophageal Impedance Manometry (HRIM, CCv4.0) along with 24hr-pH/impedance was performed on 38 patients before and after LTx (mean age 60 yrs (range; 37-75 yrs), 25 males) between November 2017 and September 2021.

Results: Of 38 patients identified, 28 had restrictive lung disease, 6 obstructive disease, 3 combined restrictive/obstructive disease, and 1 pulmonary arterial hypertension.

HRIM: Pre-LTx, 17(45%) patients exhibited abnormal motility, of which 10(59%) had ineffective oesophageal motility (IEM), 6(35%) oesophago-gastric junction outflow obstruction (EGJOO) and 1(6%) absent contractility. Post-LTx, distal contractile integral increased from 793(414-1296) (median(IQR)) to 985(478-3136)(p=0.03). However, this was associated with a variety of changes in manometric diagnoses.

Of the 21 with normal motility pre-LTx, 11(52%) remained normal, 5(24%) changed to EGJOO, 2(10%) to IEM, 2(10%) to Jackhammer, and 1(4%) to distal oesophageal spasm post-LTx (Fig. 1). Of the 10 patients with IEM pre-LTx, 5(50%) remained IEM, 3(30%) changed to normal, and 2(20%) to EGJOO; and of the 6 patients with EGJOO pre-LTx, 3(50%) remained EGJOO, 2(33%) changed to normal, and 1(17%) to IEM.

The patient with aperistalsis pre-transplant changed to IEM.

24hr-pH/impedance: Pre-LTx 11(30%) patients had abnormal bolus exposure time (TBET) and 4(11%) abnormal number of reflux events reaching the proximal oesophagus. Post-LTx the number of patients with abnormal number of proximal events had doubled to 8(21%), although this did not reach significance($p=0.20$). The latter had no effect on TBET. Pre-LTx, patients with IEM (1.45(1.0-1.6) median(IQR)) had greater TBET than both patients with normal motility (0.5(0.4-1.1); $p=0.05$) and EGJOO (0.9(0.1-1.1); $p=0.05$).

Similarly, patients with IEM (12.5(5-17)) had more reflux events reaching the proximal oesophagus than those with normal motility (4(3-8); $p=0.07$) and EGJOO (3(0-7); $p=0.04$). Post-LTx these differences were lost (TBET: normal, 1.1(0.3-1.9); IEM, 0.9(0.6-2.1); EGJOO, 0.6(0-1.4); No. prox events: normal, 8.5(2-34); IEM, 7(2-26) and EGJOO, 4.5(1-11)).

Conclusion: Following LTx approximately half of motility diagnoses remained the same as pre-LTx, with the rest showing no consistent change. GER better associated with motility pre- than post-LTx. We conclude that pre-op testing remains valuable to allow optimal management of the patient till LTx, but post-op testing may be more important for the long-term outcome and allograft survival of patients.

Disclosure: None of the authors have anything to declare.

P0063

EFFECT OF HIATUS HERNIA ON REFLUX PATTERNS AND MUCOSAL INTEGRITY IN PATIENTS WITH NON-EROSIVE REFLUX DISEASE

A. Sawada¹, B. Rogers², P. Visaggi³, N. de Bortoli⁴, C.P. Gyawali⁵, D. Sifrim⁶

¹Osaka Metropolitan University Graduate School of Medicine, Department of Gastroenterology, Osaka, Japan, ²Washington University in St. Louis, Gastroenterology, Louisville, United States, ³Gastroenterology Unit, University of Pisa, Translational Research and New Technologies in Medicine and Surgery, Pisa, Italy, ⁴University of Pisa, Department Translational Research and New Technologies in Medicine and Surgery, Division of Gastroenterology, Pisa, Italy, ⁵Washington University School of Medicine, Division Of Gastroenterology, St Louis, United States, ⁶Queen Mary University London, Blizard Institute, Wingate Institute, London, United Kingdom

Contact E-Mail Address: a.sawada@omu.ac.jp

Introduction: Hiatus hernia (HH) facilitates reflux by several pathophysiological mechanisms including abnormal reflux patterns, delayed acid clearance, and proximal displacement of a postprandial acid pocket, which could also contain bile. Esophageal reflux exposure contributes to abnormal esophageal mucosal integrity, which can be measured using mean nocturnal baseline impedance (MNBI) during impedance pH monitoring.

Aims & Methods: The aim of this study was to investigate the influence of HH on reflux patterns using impedance-pH monitoring and bile spectroscopy (Bilitec 2000), and compare distal esophageal mucosal integrity and bile exposure between non-erosive reflux disease (NERD) patients with similar acid burden with and without HH. We retrospectively analyzed data from PPI-refractory NERD patients referred to three tertiary referral centers who had undergone endoscopy, esophageal high-resolution manometry (HRM), and impedance-pH studies off PPI with or without Bilitec monitoring.

Inclusion criteria of the study consisted of patients who had distal acid exposure time (AET) of 6-12%, HH >2 cm (HH group) or no HH (non-HH group) on HRM. Prior to the reflux testing, endoscopy confirmed that none of the patients had reflux esophagitis or Barrett's esophagus. Patients who had obstructive motor disorders, pathological supragastric belching, ru-

mination or prior foregut surgery were excluded. HRM evaluated esophageal motility and the esophagogastric junction morphology. Impedance-pH monitoring measured AET, the number of reflux episodes, acid and bolus clearance, MNBI, (normal>1350 ohms) and post reflux swallow induced peristaltic wave index (PSPWI) whereas Bilitec 2000 measured esophageal bile reflux exposure time (normal $\leq 1.8\%$ bilirubin absorbance time).

These parameters were compared between the patients with and without HH. Univariate logistic regression, multivariable regression and correlational analyses were performed to identify factors influencing the distal esophageal MNBI.

Results: We identified 42 patients in the HH group and 40 patients in the non-HH group. Age, gender, BMI, esophageal motility, AET and esophageal clearance were similar between the two groups. The HH group had higher numbers of total reflux episodes ($p=0.015$) with similar proportion of acid/non-acid reflux compared to the non-HH group. Mean nocturnal baseline impedance (MNBI) in the distal esophagus was significantly lower in the HH group than the non-HH group at both 5cm ($p=0.002$) and 3cm ($p=0.015$) above the lower esophageal sphincter.

Multivariable regression analysis showed that HH, low number of non-acid reflux and PSPWI were independently associated with MNBI. Among 31 patients tested with bile spectrophotometry, the HH group had significantly longer bile exposure time than the non-HH group ($p=0.011$), and bile reflux inversely and significantly correlated with MNBI ($\rho=-0.75$, $p<0.001$).

Conclusion: In NERD patients with similar acid burden, the presence of HH, fewer non-acid reflux episodes and lower PSPWI were independently associated with impaired mucosal integrity. Correlational analysis suggested that HH damages mucosal integrity potentially through excessive bile reflux.

Disclosure: Nothing to disclose.

P0064

STRAIGHT LEG RAISE TEST: A NOVEL PROVOCATIVE TEST TO ASSESS ESOPHAGEAL CONTRACTION RESERVE

P. Visaggi¹, A. Venturini¹, F. Baiano Svizzero¹, D. Stefani Donati¹, L. Mariani¹, S. Siboni², L. Bonavina², M. Bellini¹, R. Penagini³, E.V. Savarino⁴, N. de Bortoli¹

¹Gastroenterology Unit, University of Pisa, Translational Research and New Technologies in Medicine and Surgery, Pisa, Italy,

²Department of Surgery, IRCCS Policlinico San Donato, San Donato Milanese, Italy, ³Università degli Studi di Milano, Department of Pathophysiology and Transplantation, Milan, Italy, ⁴University of Padua, Division of Gastroenterology, Department Of Surgery, Oncology And Gastroenterology, Padua, Italy

Contact E-Mail Address: pierfrancesco.visaggi@gmail.com

Introduction: Provocative manoeuvres are increasingly being performed during esophageal high-resolution manometry (HRM) in an attempt to increase the yield of the test. Recently, straight leg raise manoeuvre (SLR) (i.e., wet swallow with raised straight legs in supine position) has been proposed as novel provocative test to evaluate esophageal reflux barrier and contraction reserve (CR) (i.e., augmentation of the esophageal contractile vigor following multiple rapid swallow, MRS). The rationale is that SLR augments intra-abdominal pressure, which has been shown to augment the contractile vigor of the esophagus.

Aims & Methods: The aim of this study was to investigate the relationship between the CR after MRS and contractile vigor following SLR (i.e., obstructive stress reserve, OSR). Between Nov 2021-Jan 2022, consecutive patients reporting GERD symptoms who underwent high-resolution manometry (HRM) were enrolled. GERD symptoms, height and weight were

recorded for all patients. Distal contractile integral (DCI) was analyzed during single water swallows (SS) (10 × 5 mL), MRS (3 × 10 mL), and during SLR (2x5 mL). Preserved esophageal CR was defined as MRS/SS ratio was >1. Preserved OSR was defined as SLR/SS ratio >1. Data comparisons were performed using independent sample t test or the chi-square test, as appropriate. The Pearson's correlation coefficient was used to investigate the correlation between the DCI following MRS and DCI during SLR.

Results: 32 patients (17 female, mean age: 49.8±13.3 years) were enrolled. All patients reported heartburn as main symptom. Mean BMI was 23.8±2.2. Esophageal HRM was normal in 25/32 (78.1%) and ineffective esophageal motility (IEM) was detected in 7/32 (21.9%). Esophageal CR was observed during MRS in 21/32 (65.6%) and OSR was seen in 26/32 (81.3%) following SLR. The DCI response following MRS correlated with the DCI response following SLR (Table 1).

		Number of patients with MRS/SS ratio>1, n (%)		p value
		YES	NO	
Number of patients with SLR/SS ratio>1, n (%)	YES	21 (65.6%)	6 (18.8%)	<0.001
	NO	1 (3.1%)	4 (12.5%)	

Table 1.

The Pearson's correlation coefficient was 0.74 ($p < 0.001$). Mean±sd DCI was 1508.7±1074.9 mmHg-s-cm; mean DCI during MRS was 1672.1±1079.1 mmHg-s-cm and mean DCI during SLR was 2094.3±1521.8 mmHg-s-cm ($p=NS$).

Conclusion: Swallowing against the resistance of increased intra-abdominal pressure from SLR improves esophageal body peristaltic performance and correlates with esophageal body CR.

Disclosure: Nothing to disclose.

P0065

POST-REFLUX SWALLOW-INDUCED PERISTALTIC WAVE INDEX CORRELATES WITH BODY MASS INDEX AND IMPROVES WITH BARIATRIC SURGERY-INDUCED WEIGHT LOSS, REGARDLESS OF ESOPHAGEAL ACID EXPOSURE

M. Pesce¹, M. Pagliaro¹, P. Senneca¹, V. Vaino¹, G. Di Giorgio¹, M. Andreozzi¹, S. Rugo¹, E. Efficie¹, G. Sarnelli¹

¹University of Naples 'Federico II', Clinical Medicine and Surgery, Naples, Italy

Contact E-Mail Address: mapesc@hotmail.com

Introduction: The Post-reflux swallow-induced peristaltic wave (PSPW) is an esophago-salivary reflex that allows the chemical clearance of the refluxate. As a result, when impaired, it progressively increases the risk of gastro-esophageal reflux disease (GERD) and its complications. Obesity is one of the major risk factors for GERD and progression to erosive esophagitis, Barrett esophagus and esophageal adenocarcinoma. Weight loss in severely obese subjects improves GERD by decreasing esophageal acid exposure time (AET) and reflux symptoms; but its impact on PSPW index (PSPWi), a novel pH-impedance (MII-pH) parameter, has never been systematically explored. However, achieving weight loss by means of bariatric surgical procedures has a still controversial effect on both esophageal motility and AET, which in turn could affect PSPWi.

Aims & Methods: Our aim was to verify how bariatric surgery, namely Mini-Gastric bypass (MGB) and Laparoscopic Sleeve Gastrectomy (LSG) affects MII-pH parameters and if weight loss is correlated to PSPWi. 57 morbidly obese subjects (37F, BMI 47.2±6.1) were enrolled in this prospective randomized, open-label, controlled trial to evaluate MII-pH parameters in the preoperative phase (T0) and at 6 (T1) and 12 months (T2) after MGB and

LSG, respectively. All subjects performed a preoperative upper gastrointestinal endoscopy, ruling out the presence of esophagitis or Hiatus Hernia, a high-resolution manometry (HRM) and an off-PPI 24h MII-pH. A standardized questionnaire assessing upper gastrointestinal symptoms severity (PAGI SYM) was administered at all time points. Data are expressed as mean±SD.

Results: 25 subjects underwent MGB (14F, BMI 47±7.3) while 32 patients were treated with LSG (23F, BMI 46±5.1). At baseline, no differences were found between the two groups in terms of BMI, PAGI-SYM scores and HRM or MII-pH data. At both time points, a significant weight loss from baseline (expressed as ΔBMI) was found in both groups with no differences between the two procedures (T0vsT1: -11 vs -11.2 kg/m² and T0vsT2: -14.5 vs -16.2 kg/m² in MGB and LSG group respectively, $p=ns$). At T2, AET was significantly increased in the LSG as compared to the MGB group (9.2±7.7 vs 1.4±2.4, $p < 0.01$), while the total number of reflux episodes did not differ between the two groups (61.5±36.9 vs 53.6±19.5, $p=ns$). At baseline, PSPWi values were equally reduced in both groups (42±11.2 and 42.6±15.2 in MGB and LSG, respectively).

Following bariatric surgery, a progressive increase in PSPWi was observed at both time points in MGB (T1 63.5±11.6; T2 72.4±8.8) and LSG groups (T1 62.9±16.1; T2 67.2±13.5; all $p < 0.001$). PSPWi improvement directly correlated with the reduction of BMI ($r^2=0.28$; $p < 0.0001$). When all variables were computed in a multivariate analysis, PSPWi was the only significant factor associated with BMI decrease ($r^2=0.058$; $p < 0.05$).

Conclusion: Severely obese subjects show a reduced PSPWi that improves in parallel with weight loss, independently from the bariatric surgical procedure. There was a strong inverse association between BMI decrease and PSPWi improvement, regardless of the acid exposure time. Our results suggest that a low PSPWi might be a marker of impaired visceral esophageal sensitivity influenced by obesity, which could contribute to the risk of GERD and its complications.

Disclosure: Nothing to disclose.

P0066

CENSORING REFLUX EPISODES BY THE WINGATE CONSENSUS REDUCES SUPPORTIVE EVIDENCE FOR GERD PROVIDED BY PH/IMPEDANCE MONITORING

S. Kindt¹, M. Surmont¹

¹UZ Brussels, Gastroenterology and Hepatology, Brussel, Belgium

Contact E-Mail Address: sebastien.kindt@telenet.be

Introduction: The Lyon consensus classifies the evidence of gastro-oesophageal reflux (GERD) based on endoscopic features and results of pH/impedance monitoring (pH-MII). Where only an acid exposure time > 6% represents conclusive evidence for GERD, presence of more than 80 impedance episodes, low post-reflux swallow-induced peristaltic wave (PSPW) index and low mean nocturnal baseline impedance (MNBI) on pH-MII provide adjunctive evidence. The Wingate consensus established criteria to reduce inter-reviewer variability when assessing reflux episodes and PSPW by impedance.

Aims & Methods: This study aims to assess the influence of the Wingate criteria on the different pH-MII parameters obtained by automated analysis. Forty consecutive pH-MII were reviewed manually according to Wingate criteria. Number of impedance episodes censored from automatic analysis were recorded. Reflux categorisation according to Lyon consensus between censored and uncensored data was compared by Chi square. Pearson correlations between impedance parameters and censored episodes were calculated.

Results: On average 27.6 (range 3-94) impedance episodes were censored. Reasons for censoring were: 1/ antrograde episode: 13 (range 1-70), 2/ impedance drop < 50%: 4,1 (0-60), 3/ duration < 4s: 1,5 (0 - 10), 4/ <2 distal

channels: 3.9 (0-20) and 5/ artefacts: 5.1 (0 – 19). Applying the Wingate criteria altered the categorisation of impedance episodes (<40 episodes, 7 vs 17 for resp. uncensored vs censored tracings, 40-80 episodes: 19 vs 19, and > 80 episodes: 14 vs 4, $p=.008$). MNBI and PSPW index were significantly correlated ($r=.47$, $p=.002$). The percentage of censored episodes was inversely correlated with the number of acidic impedance episodes ($r=-0.61$, $p=0.000$) and positively correlated with PSPW index ($r=.64$, $p=.000$).

Conclusion: Manual interpretation of impedance tracings based on the Wingate consensus reduces supportive evidence for GERD. The observed correlations indicate that acidic reflux episodes and reflux episodes followed by a PSPW are less likely to be censored, harbouring a potential at improving automatic pH-MII analysis.

Disclosure: Nothing to disclose.

P0067

VALIDATION OF THE LYON CONSENSUS CRITERIA FOR GERD DIAGNOSIS IN A GREEK POPULATION: A RETROSPECTIVE STUDY

T. Voulgaris¹, V. Lekakis¹, A. Orfanidou¹, J. Vlachogiannakos¹, D. Kamberoglou¹, G. Papatheodoridis¹, G. Karamanolis¹
¹National and Kapodistrian University, Laiko General Hospital, Department of Gastroenterology, Athens, Greece

Contact E-Mail Address: georgekaramanolis@yahoo.co.uk

Introduction: Gastroesophageal Reflux Disease (GERD) affects globally 8%–33% of worlds population, it is observed among all ages and does not differ among sex. The gold standard examination in diagnosing GERD is 24hrs pHmetry ± impedance. Recently new diagnostic criteria were introduced by the Lyon consensus for GERD diagnosis.

Aims & Methods: Our aim was to investigate the diagnostic yield of pHmetry ± impedance using the Lyon consensus criteria and to evaluate possible changes in the rate of GERD diagnosis with the adaptation of those new diagnostic criteria. Our study included 249 consecutive patients (M/F: 120/129, mean age 50±15 years (min 18 – max 86) who underwent 24-hour pH± impedance monitoring in the laboratory for esophageal disorders of our department during a five year period (6/2016-6/2021).

Acid exposure time (AET) was calculated as the percentage of time during which the pH was below 4 at the esophageal pH sensor, and AETs of 4.2% or 6% and greater were designated as abnormal thresholds. Number of reflux episodes (NRE), reflux-symptom association (symptom index-SI and symptom association probability –SAP) as well as mean nocturnal baseline impedance (MNBI) was also calculated. Epidemiological, endoscopic, clinical and 24-hour pH± impedance data were retrospectively collected.

Results: Typical GERD symptoms were reported by 140/249 (56.2%) patients, whereas 99/249 (39.6%) patients reported various extra-esophageal symptoms. The majority (137/249, 55%) of patients reported no amelioration of their symptoms when previously treated with Proton Pump inhibitors (PPis).

Endoscopic findings supportive of GERD by Lyon consensus (Esophagitis according to LA classification of grade A/B and/or hiatal hernia) were present in 42/185 (22.7%). An AET>6% was observed in 60/249 (24.1%), 22/249 between 4 and 6% and 147/249 <4%. The mean number of reflux episodes was 32±27 (min 0-max 198), 12/249 (4.8%) had over >80 reflux episodes and 62/249 (24.9%) >40, while 74 (29.7%) patients had a De Meester score over 14.7. Symptomatic Index was positive in 16/172 while Symptoms Associated Probability in 30/172.

Abnormal Mean Nocturnal Basal Impedance (MNBI) was observed in 38/249 patients. Hypersensitive esophagus was diagnosed in 26/249 patients (10.4%). GERD diagnosis according to the Lyon Consensus criteria was set in 63/249 (25.3%) patients; a rate significantly lower compared to

the rate observed by implementing the older criteria (32.1%), $p<0.001$. In the multivariate analysis the existence of endoscopic findings supportive to GERD diagnosis as defined by the Lyon consensus ($p=0.036$), a De Meester score over 14.7 and the presence of typical GERD symptoms were correlated to GERD diagnosis ($p<0.001$, respectively) by the criteria defined for pH- impedance monitoring. In the univariate analysis, response to PPis was closely correlated to GERD diagnosis by the Lyon consensus criteria (43/112, 38.4% among responders to PPis compared to 26/137, 19.0%, of non-responders, $p<0.001$), as also the existence of abnormal MNBI (16/63, 25.4% vs. 22/186, 11.8%, $p=0.027$), findings not observed in the multivariate analysis.

Conclusion: Changes in 24-hrs pH-impedance monitoring diagnostic criteria of GERD by the Lyon consensus led to a conclusive GERD diagnosis in approximately 25% of patients. This rate of GERD diagnosis is reduced in comparison to the one confirmed with the use of previous established criteria. Moreover, presence of typical symptoms, as well as existence of endoscopic supportive evidence of GERD was independently correlated with GERD diagnosis by pH-impedance-monitoring.

Disclosure: Nothing to disclose.

P0068

LCI IMPROVES THE VISIBILITY OF MINIMAL CHANGE ESOPHAGITIS - A LAB COLOR VALUE BASED QUANTITATIVE ANALYSIS

L. Wang¹, X. Lin¹, L. Zhang¹, X. Li¹, Y. Wang¹, PKUIH Upper-GI Disorder Study Group
¹Peking University International Hospital, Gastroenterology Department, Beijing, China

Contact E-Mail Address: wangli5@pkuih.edu.cn

Introduction: GERD (Gastroesophageal reflux disease) can be divided into NERD (non-erosive reflux disease) and RE (Reflux esophagitis. RE) according to endoscopic manifestation[1-3]. MCE (minimal change esophagitis) refers to the changes of mucosa above the dentate line including redness, edema and whitening but without mucosal damage[4-5].

Previous literatures found that traditional white light endoscopy had some difficulty in the diagnose of RE Grade-A and MCE, and the consistency with the golden standard 24-hour pH monitoring was also limited[6]. LCI (Linked color imaging) is a novel image enhanced technique. It can increase the contrast of mucosal color and highlight the red lesions. Therefore, we speculated that LCI has an advantage over white light in detecting the red lesions of GERD, especially MCE and Grade-A esophagitis as well.

Aims & Methods: We use quantitative analysis to explore whether LCI technology is helpful for the diagnosis of MCE and Grade-A esophagitis. The outpatients aged 18-75, regardless of gender, with typical acid reflux and heartburn in the past week, and had positive results of GERD-Q questionnaire (8 points or above) were selected for this research. Patients that had a history of gastrectomy or were highly suspicious of upper gastrointestinal tumors or achalasia were excluded. The termination criteria were esophagitis grade B or above, malignancies, Barrett esophagus, or whose cardia area could not be exposed sufficiently under endoscopy. We completed the gastroscopy in routine steps with Blue Laser Imaging Endoscope system and observed the area 5cm above the dentate line.

Then the pictures under both WLI (white light) and LCI were obtained respectively. These images were analyzed and scored by Adobe Photoshop software based on Lab color value in the CIELAB color space system[7]. L, a, and b color values were transformed into L* a* b* color values in CIELAB as follows[8]: $L^* = L/256 \times 100$, $a^* = a - 128$, $b^* = b - 128$. The color differences were calculated as follows: $\Delta L^* = L^*(red\ area) - L^*(normal\ mucosa)$, so as Δa^* and Δb^* . $\Delta E^* = [(\Delta L^*)^2 + (\Delta a^*)^2 + (\Delta b^*)^2]^{1/2}$. SPSS 24.0 software was used for data analysis.

Results: A total of 56 patients were obtained including 26 males and 30 females, aged 26 to 70. 112 qualified WLI and LCI images were selected. The L*, a*, b* values between red area and normal mucosa under both LCI and white light mode were compared respectively. The results showed that there were significant differences in L*, a*, b* between the red area and the normal mucosa in both mode (P<0.05). The scatter plot of a* and b* color values in CIELAB revealed that the spots separation of LCI mode is higher, suggesting that the color difference between red and normal mucosa in LCI mode is greater than that in white light mode. The color difference of ΔL^* , Δa^* , Δb^* and ΔE^* were calculated and compared between LCI and WLI mode, the results revealed that Δa^* , Δb^* and ΔE^* of LCI mode were all significantly higher than WLI (P<0.001), see Table-1.

L*, a* b* values	WLI	LCI	P
Δa^*	6.917±5.683	21.048±8.131	0.000
Δb^*	8.685±6.764	127.703±6.497	0.000
ΔE^*	13.589±6.969	130.011±6.514	0.000

Table-1. Color differences of Δa^* , Δb^* and ΔE^* between WLI and LCI.

Conclusion: LCI improved the color difference between the red area and surrounding mucosa in MCE and RE Grade-A and might therefore be helpful for the diagnosis.

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Disclosure: Nothing to disclose.

P0069 LOW ESOPHAGEAL BASELINE IMPEDANCE AND NUMBER OF CHANNELS INVOLVED ARE ASSOCIATED WITH BARRETT'S ESOPHAGUS SEGMENT LENGTH

N. Bar¹, K. Staller², C. Velez², B. Kuo²
¹Tel Aviv Medical Center, Department of Gastroenterology and Hepatology, Tel Aviv, Israel, ²Massachusetts General Hospital, Center for Neurointestinal Health, Boston, United States

Contact E-Mail Address: nirb@tlvmc.gov.il
Introduction: Gastroesophageal reflux disease increases mucosal permeability, reducing the mucosal baseline impedance (BI) measured in multichannel intraluminal impedance pH studies (MII-pH). Low BI is reported in patients with increased acid exposure time (AET), erosive oesophagitis, and Barrett's oesophagus (BO).

Aims & Methods: As data about BI in BO are few, we aimed to examine the predictive capabilities of BI in BO.

We included all patients over a 10-year period undergoing 24h MII-pH and upper endoscopy with clinical suspicion for BO, knowing some patients will not have BO, and could serve as controls. The Medtronic software measures BI in the distal (Z6) channel only. To validate proximal channel BI measurements, MII-pHs were reanalyzed with blinded BI measurement at Z6: mean nocturnal BI (MNBI) in three 10-minute periods an hour apart during sleep (standard method) and point BI (PBI) measured BI during a stable (no swallow/reflux for ~20 minutes) supine period in all 6 channels. We tested the correlation between MNBI and PBI and compared the PBI in all patients with BO and without to validate the measurement methods. BO was diagnosed as >1 cm salmon-colored mucosa in tubular oesophagus with intestinal metaplasia; long segment was ≥3 cm. Abnormal MII-pH was defined as either distal acid exposure time (AET) >6% or >80 total reflux episodes. Those not meeting criteria were used as controls. P values were adjusted by Bonferroni correction as needed.

Results: The cohort included 110 patients. Patients with long BO had significantly lower distal channel MNBI, see table 1. To examine overall ability to diagnose BO, we excluded patients with increased acid exposure. The area under the ROC curve for MNBI detecting BO was excellent 0.91, (0.83-1.0). A cut-off of 0.6 kOhm had 100% sensitivity and 75% specificity. In multivariate logistic regression adjusting for age, sex, and race showed: MNBI was associated with BO or abnormal MII-pH with OR=0.52 (0.4-0.7, p<0.001) for every 1 kOhm, and having MNBI< 0.6 kOhm had an OR= 12.9 (1.6-102.3, p=0.016).

Studies with a normal MII-pH and a MNBI under 0.6, 1, 1.6 kOhm: the prevalence of BO was 2/3 (67%), 7/10 (70%), and 14/19 (74%), respectively. To validate the use of PBI in assessing BO extent, we found excellent correlation between PBI and MNBI in the distal channel MNBI (spearman's rho): 0.958 p<0.001. Patients with long BO had significantly more channels with low PBI compared to short BO and normal, see table 1.

	Total cohort (n=110)	Barrett's oesophagus (n=45)	Control (n=41)
Age [years, median (IQR)]	59 (25 - 85)	59.4 (53.3-70)	57.3 (48.8-65.2)
Female n (%)	63 (57)	21 (47)	26 (63)
Race - White n (%)	91 (83)	39 (87)	30 (73)
On PPI MII-pH n (%)	95 (86)	43 (96)	33 (81) *
	Long BO (n=13)	Short BO (n=32)	Abnormal MII-pH (n=24) Control (n=41)
Mean baseline impedance (kOhm) n=13	0.6 (0.5-0.97)	1.9 (0.8-3.2)*	1.3 (0.6-2.8) 3.6 (2.1-4.7)***
Patients with multiple low baseline impedance channels n (%)	11 (85)	8 (25)***	8 (33)** 1 (2)***

PPI- proton pump inhibitor; MII-pH – multichannel intraluminal impedance – pH study; BO- Barrett's oesophagus. *. p<0.05, **. p<0.01, *** - p<0.001. All p-values are Bonferroni corrected for multiple comparisons and compared to the long BO group as reference

Table 1.

Conclusion: We showed the extent of BO is associated with the extent of oesophageal mucosa with low BI and confirmed the association between BO and lower BI values. This supports the utility of BI in detecting reflux complications. Clinicians reading MII-pH studies should consider BO in the differential when encountering a MII-pH with low supine BI, especially when this spans across impedance channels.

Disclosure: Nothing to disclose.

P0070

BARIUM OESOPHAGRAM DOES NOT RELIABLY DETECT CLINICALLY RELEVANT REFLUX DEFINED BY 24-HOUR MULTICHANNEL INTRALUMINAL IMPEDANCE PH

N. Bar¹, K. Staller², C. Velez², B. Kuo²

¹Tel Aviv Medical Center, Department of gastroenterology and hepatology, Tel Aviv, United States, ²Massachusetts General Hospital, Center for Neurointestinal Health, Boston, United States

Contact E-Mail Address: nirb@tlvmc.gov.il

Introduction: Barium oesophagram is an important tool in the assessment of oesophageal disease, and its utility for identifying structural abnormalities or as a functional test of oesophageal emptying is well known. Spontaneous gastrooesophageal reflux (GOR) or GOR induced by different maneuvers are routinely reported, but scarce data exist about the relevance of these findings.

Aims & Methods: We aimed to examine the performance characteristics of oesophagram as a test for GOR disease (GORD)

Consecutive patients with both a multichannel intraluminal impedance-pH study (MII-pH), and a oesophagram reporting GOR degree were included. Patients were excluded if they had achalasia or reflux surgery between oesophagram and MII-pH. For oesophagram: We recorded presence and degree of oesophagram diagnosed reflux (oesophagram-R) and other parameters. For the MII-pH we recorded total oesophageal acid exposure time (AET), total reflux episodes, and whether the test was done on/off proton pump inhibitors (PPI). We also collected manometry parameters and diagnosis.

We calculated the Kappa coefficient for inter-test agreement, sensitivity (Se), specificity (Sp), and positive and negative predictive values (PPV, NPV) using MII-pH as the gold standard. We used different cut offs for off (1,2) and on (3) PPI studies to define abnormal GORD. As sensitivity analysis, we analyzed the utility of oesophagrams to detect GORD defined by reflux number only. All MII-pHs were analyzed on Reflux reader 6.1.1.11 (Medtronic Inc, Minneapolis, Minn)

Results: There were 113 patients included between Jul-Oct/2021. Median (IQR) age was 58.2 (47.8-65), with 70 (62%) females. Median (IQR) time between oesophagram and MII-pH studies was 2.6 (0.7-6.6) months. PPs were used in 64% of MII-pH studies. oesophagram-R was noted in 53% of oesophagrams, and 40% reported hiatal hernias (HH).

Sixty (53%) patients had some degree of oesophagram-R and were more likely to be female (69% vs. 51%), have a hiatal hernia (52% vs 29%), and had higher median (IQR) number of reflux episodes [81 (45-129) vs 50 (27-76)], $p < 0.05$ for all. Oesophagram-R was also associated with ineffective oesophageal motility (Chicago classification V4.0, 26% vs 9%, $p < 0.05$).

The AET, and the proportion of studies performed on PPIs were similar between groups.

To diagnose clinically significant GORD we used different cut offs (1-3) to define pathologic GOR, including specific cut offs for MII-pH done on PPI. We found fair agreement at best between the gold standard MII-pH and oesophagram by Kappa coefficients ($\kappa = 0.18-0.31$) and unsatisfactory test characteristics (universally poor Se/Sp/PPV/NPV) (Table 1). Performing the same analyses with only moderate or severe grade oesophagram-R showed similar results.

Reference -	Lyon (1)	Reflux only	Reflux only	Lyon (1) + Gyawali 2021 (3)	Zerbib 2013 (2)
Pathologic GORD definition	pH<6% or more than 80 refluxes	Total reflux (>80)	Total reflux (>40)	Off PPI see Lyon; On PPI AET>0.5% or >40 refluxes	Off: AET>5.8% reflux>53. ON: AET>0.4%, refluxes>57
Kappa	0.31	0.28	0.31	0.30	0.18
Se	55%	50%	85%	75%	71%
Sp	77%	79%	45%	54%	46%
PPV	74%	74%	65%	66%	62%
NPV	59%	58%	73%	65%	56%
†LR+	2.42	2.41	1.56	1.63	1.31
†LR-	0.58	0.63	0.32	0.46	0.63

Clinically relevant pathologic GORD was diagnosed by MII-pH. The different cut-offs in the top row were used. PPI- proton pump inhibitor; AET- Acid exposure time; Se – sensitivity; Sp – specificity; PPV – positive predictive value; NPV negative predictive value. LR – likelihood ratio. † LR+ is considered robust when > 10 , and LR- when < 0.1 .

Table 2. Barium oesophagram's test performance parameters.

Conclusion: While oesophagram has proven value in some aspects of the assessment of oesophageal structure and function, its ability to identify clinically-significant reflux is limited compared to a MII-pH gold standard. GORD diagnosis based on oesophagram may lead to unwarranted and uncomfortable work up.

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Disclosure: Nothing to disclose.

P0071

HEALING WATER LEADS TO REDUCTION OF HEARTBURN: RANDOMISED, PLACEBO-CONTROLLED PHASE-III TRIAL (STOMACH STILL)

J. Labenz¹, M. Anschütz², J. Walstab³, F. Donath³, R.-S. Wedemeyer², H. Wolters⁴, B. Schug²

¹Diakonie Klinikum Jung-Stilling Hospital, Medizinische Klinik I, Siegen, Germany, ²Socra Tec R&D GmbH, Oberursel, Germany, ³Socra Tec R&D GmbH, Erfurt, Germany, ⁴Fachingen Heil- und Mineralbrunnen GmbH, Birlenbach, Germany

Contact E-Mail Address: j.labenz@t-online.de

Introduction: The healing water Staatl. Fachingen STILL has been used for decades for symptomatic treatment of gastrointestinal (GI) disturbances including heartburn. Its beneficial effect has not been systematically investigated in a placebo-controlled trial so far.

Aims & Methods: The primary objective of the multicentre, double-blind, randomised, placebo-controlled trial STOMACH STILL was to demonstrate superiority of the healing water (verum) over conventional mineral water (placebo) with respect to alleviation of heartburn. Efficacy in GI symptom reduction ("heartburn", "dyspepsia", "regurgitation") was assessed using the validated *Reflux Disease Questionnaire* (RDQ). Primary endpoint was the percentage of patients with a reduction of ≥ 5 points in the RDQ score for the dimension "heartburn" (responder rate). Secondary objectives included health-related quality of life (HRQOL) using the questionnaire *Quality of Life in Reflux and Dyspepsia* (QOLRAD), intake of rescue medication and safety/tolerability (adverse events, AEs). The trial population comprised adult patients with frequent heartburn episodes since ≥ 6 months (RDQ ≥ 8 within 7 days prior to screening, absence of reflux oesophagitis >Los Angeles Grade A) who drank 1.5L/day verum or placebo over the course of the day for 6 weeks.

Results: Overall, 148 patients with symptomatic heartburn were randomised (verum: n=73, placebo: n=75); 143 patients completed the trial. The responder rate was 84.72% in the verum group compared to 63.51% in the placebo group (p=0.0035, number needed to treat <5). Symptom improvement under verum compared to placebo was statistically significant for the dimension “heartburn” (p=0.0003) and the RDQ total score (p=0.0050) [exploratory analysis]: from baseline to treatment end, the RDQ score for “heartburn” decreased by (mean±standard deviation) 9.17±4.82 points in the verum group and by 6.33±5.07 points in the placebo group, and the RDQ overall score decreased by 20.65±14.04 and 14.31±12.83 points under verum and placebo, respectively. The RDQ dimension scores for “dyspepsia” and “regurgitation” numerically improved during treatment with verum compared to placebo. The absolute reductions of all three RDQ dimension scores in the verum group exceeded the previously determined minimal important changes for a beneficial treatment effect [1].

The reduction in symptom complaints was paralleled by an improved HRQOL: from baseline to treatment end, statistically significant improvements under verum compared to placebo were reported for QOLRAD domains “emotional distress” (p=0.0147), “food/drink problems” (p=0.0125) and “vitality” (p=0.0393) [exploratory analysis].

Consistent with the superior efficacy of verum over placebo, mean intake of rescue medication decreased from 0.73 tablets/day at baseline to 0.47 tablets/day in week 6 and thereafter in the verum group, whereas in the placebo group the intake of rescue medication remained constant during the course of the trial (baseline: 0.56 tablets/day, week 6 and thereafter: 0.60 tablets/day). Treatment-related AEs were only reported in 1 patient of the verum group and in 2 patients of the placebo group.

Conclusion: For the first time, superiority of the healing water Staatl. Fachingen STILL over placebo in the reduction of heartburn, accompanied by an improved quality of life, was demonstrated in a controlled clinical trial. Thus, STOMACH STILL provides the clinical evidence for a recommendation of Staatl. Fachingen STILL in the symptomatic treatment of GI disturbances including heartburn.

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Disclosure: Joachim Labenz served as Medical Advisor to Socra Tec R&D GmbH and Staatl. Fachingen GmbH.

P0072
VONOPRAZAN OR MORE THAN DOUBLE-DOSE PROTON PUMP INHIBITOR MAINTENANCE THERAPY SHOULD BE PERFORMED IN PATIENTS WITH SYSTEMIC SCLEROSIS WITH ABSENT CONTRACTILITY

S. Kuribayashi¹, F. Nakamura², S.-i. Moteji³, K. Hara⁴, H. Hosaka¹, M. Ishikawa³, Y. Endo³, M. Obokata⁵, T. Harada⁵, M. Uchida⁶, T. Uraoka¹, Gunma Systemic Sclerosis Study Group
¹Gunma University Graduate School of Medicine, Department of Gastroenterology and Hepatology, Maebashi, Gunma, Japan, ²Kohseichuo General Hospital, Digestive Disease Center, Bunkyo-ku, Japan, ³Gunma University Graduate School of Medicine, Department of Dermatology, Maebashi, Gunma, Japan, ⁴Gunma University Hospital, Allergy and Respiratory Medicine, Integrative Center of Internal Medicine, Maebashi, Gunma, Japan, ⁵Gunma University Graduate School of Medicine, Department of Cardiovascular Medicine, Maebashi, Gunma, Japan, ⁶Gunma University Graduate School of Medicine, Department of Public Health, Maebashi, Gunma, Japan

Contact E-Mail Address: shikokuri@yahoo.co.jp
Introduction: Proton pump inhibitor (PPI) refractory reflux esophagitis (RE) is often seen in patients with systemic sclerosis (SSc). We reported earlier that standard-dose PPI therapy could not control reflux esophagitis (RE) enough in SSc patients with absent contractility and weak esophago-gastric junction (EGJ) barrier function, and that vonoprazan (VPZ) maintenance therapy may be more effective than standard-dose PPI therapy in patients with SSc. The aims of this retrospective observational study were to clarify prevalence and risk factors for PPI or VPZ refractory RE in patients with SSc in a clinical setting.

Aims & Methods: A total of 188 consecutive patients with SSc who underwent both high-resolution esophageal manometry (HRM) and esophago-gastroduodenoscopy (EGD) between May 2009 and February 2021 at Gunma University Hospital were reviewed. Patients who underwent gastro-intestinal surgery were excluded. Esophageal motility was assessed retrospectively according to the Chicago classification v3.0. The second and subsequent EGDs were performed when patients had reflux symptoms. The presence of RE and grades of the gastroesophageal flap valve (GEFV) were assessed. Administration of acid secretion inhibitors and doses were decided based on patients’ reflux symptoms. The presence of RE or changes of medications were investigated. When RE was seen on any dose of PPI or VPZ, it was defined as medication-refractory RE. Observation periods were from the day of HRM to the final visit (median observation period: 4.36 years).

Variables	Number of patients	Univariate analysis		Multivariate analysis	
		Odds ratio (95%CI)	p value	Odds ratio (95%CI)	p value
≥ 65 years	73	0.625 (0.283-1.425)	0.271		
Male	36	1.451 (0.593-3.553)	0.415		
dcSSc	63	2.518 (1.172-5.409)	0.018	1.710 (0.729-4.012)	0.217
Observation periods ≥ 5 years	78	1.637 (0.770-3.483)	0.201	1.939 (0.823-4.564)	0.130
Gastric atrophy	77	0.480 (0.209-1.099)	0.083	0.517 (0.211-1.265)	0.148
GEFV Grade III or IV	47	2.724 (1.236-6.004)	0.013	1.908 (0.766-4.753)	0.165
Absent contractility	50	5.429 (2.452-12.017)	< 0.001	3.642 (1.519-8.734)	0.004

Table.

Backward stepwise regression analysis was used to select potential variables, and odds ratios and 95% confidence intervals were calculated for each potential variable using multiple logistic regression analyses.

Results: Ineffective esophageal motility (IEM) or absent contractility were seen in approximately 25% of SSc patients. Most of the patients (82%) received acid secretion inhibitor maintenance therapy to control their reflux symptoms. Medication-refractory RE was seen in 17.6% of patients. Most cases of the medication-refractory RE were seen on the standard-dose of PPI (11%), but was rarely seen on more than double-dose PPI (3%) or half-dose and standard-dose of VPZ (4% and 2%). GEV, absent contractility, and diffuse cutaneous SSc were significant factors in medication-refractory RE in a univariate analysis; however, only absent contractility was a significant factor in a multivariate analysis (Table).

Conclusion: Maintenance therapy of inhibition of acid secretion is required to control reflux symptoms in most patients with SSc. Medication-refractory RE is seen in a certain proportion of patients. Patients with absent contractility should receive more than double-dose PPI or VPZ maintenance therapy.

Disclosure: Authors did not have any Conflict of Interest regarding the abstract.

P0073

EFFICACY AND SAFETY OF HIP1601 (DUAL DELAYED-RELEASE ESOMEPRAZOLE) 40MG IN EROSIIVE ESOPHAGITIS COMPARED TO HGP1705 (DELAYED-RELEASE ESOMEPRAZOLE) 40MG: A MULTICENTER, RANDOMIZED, DOUBLE-BLIND, NON-INFERIORITY STUDY

H. Lim¹, H.-Y. Jung²

¹University of Hallym College of Medicine, Hallym University Sacred Heart Hospital, Internal Medicine, Anyang, Korea (Republic of), ²University of Ulsan College of Medicine, Asan Medical Center, Gastroenterology, Seoul, Korea (Republic of)

Contact E-Mail Address: lh10004ok@hanmail.net

Introduction: Proton pump inhibitors (PPIs) are the most effective drugs for treating acid-related disorders. However, once-daily oral dosing with conventional PPIs does not completely control acid secretion over 24 hours. HIP1601, the newly developed esomeprazole formulation with dual delayed-release emission, has an extended duration of therapeutic plasma drug concentrations and is expected to improve the nocturnal symptoms of gastroesophageal reflux disease (GERD) by inhibiting nocturnal acid breakthrough.

This study aims to compare the clinical efficacy and safety of HIP1601 (dual delayed-release esomeprazole) 40mg and HGP1705 (delayed-release esomeprazole) 40mg in patients with erosive esophagitis (EE).

Aims & Methods: This study was designed as a multicenter, double-blind, randomized-controlled, non-inferiority trial of patients with EE. The patients with EE were randomized to receive either HIP1601 40mg (n = 107) or HGP1705 40mg (n = 106) for 4 or 8 weeks.

The primary endpoint was the complete healing rate of EE confirmed by endoscopy by week 8 in the per protocol set (PPS) population, including patients with healed EE at week 4. The secondary endpoints were:

1. The complete healing rate of EE confirmed by endoscopy at week 4,
2. The complete resolution rate of symptoms at week 4 or 8,
3. The proportion of symptoms-free days and nights after 1, 2, 4, 8 weeks of treatment,
4. The time to sustained resolution of symptoms, and 5) the number of rescue medication administered.

Results: Based on PPS analysis by week 8, estimated healing rates of EE were 97.8% in HIP1601 group and 96.8% in HGP1705 group with -4.7 to 7.2 of 95% confidence interval on the difference. This result was greater than the -10%, acceptable range for non-inferiority.

After 4 or 8 weeks of treatment, the healing rate of EE at week 4, the complete resolution rate of symptoms, the time to sustained resolution of symptoms, and the number of rescue medication use were similar in both

groups. The proportion of heartburn- and acid regurgitation-free nights by week 4 were higher in HIP1601 group compared to HGP1705 group, but the difference did not reach a clinical significance (87.7% vs 85.8%, $P = 0.514$, 87.5% vs 85.8%, $P = 0.774$). Adverse events were not significantly different between the two groups.

Conclusion: This study demonstrated that HIP1601 40mg is a highly effective and well-tolerated drug in healing EE and resolving GERD symptoms. And, the efficacy and safety of HIP1601 40mg is not inferior to HGP1705 40mg after both 4 and 8 weeks of treatment.

Disclosure: This study was funded by Hanmi Pharmaceuticals Co, Ltd, Seoul, Korea.

P0074

EFFECTS OF TRANSCUTANEOUS ELECTRICAL STIMULATION SYSTEM ON HEARTBURN, REGURGITATION AND ESOPHAGEAL ACID EXPOSURE IN GERD PATIENTS

R. Brun¹, M. Siterman², S. Levy³, Y. Ron⁴, T. Rainis⁵, T. Naftali⁶, M. Hazani-Pauker², G. Saidov², V. Shay², D. Boltin², R. Fass⁷, R. Gingold-Belfer², R. Dickman²

¹Rambam Health Care Campus, Gastroenterology, Haifa, Israel, ²Rabin Medical Center, Gastroenterology, Petach Tikva, Israel, ³The Academic College of Tel Aviv-Yafo, Statistics Education Unit, Tel Aviv-Yafo, Israel, ⁴The Tel-Aviv Medical Center, Gastroenterology & Hepatology, Tel-Aviv, Israel, ⁵Bnai-Zion Medical center, Faculty of Medicine, Technion Institute, Gastroenterology and Hepatology, Haifa, Israel, ⁶Meir Hospital, Gastroenterology, 69400 Tel Aviv, Israel, ⁷Case Western Reserve University, Digestive Health Center, Cleveland, OH, United States

Contact E-Mail Address: dickmanr1@gmail.com

Introduction: Chronic PPI treatment in GERD is associated with high failure rate and concerns regarding PPI's side effects. In a previously published proof of concept study, a non-pharmacological, non-invasive transcutaneous, electrical stimulation system, reduced esophageal acid exposure in GERD patients unresponsive to standard dose PPI. However, in that study, a symptomatic response to electrical stimulation was not assessed.

Aims & Methods: To determine the effect of a transcutaneous electrical stimulation system (TESS) on symptoms (heartburn and regurgitation) and the percentage of esophageal acid exposure time in GERD patients. Patients suffering from heartburn and regurgitation were recruited into this multicenter study.

The first phase of this study was a one week, run-in period, off-PPI's, during which patients completed symptoms diaries and demographic questionnaires.

Thereafter, all patients underwent upper endoscopy with subsequently wireless esophageal pH capsule placement (off PPI). Based on pH analysis in the first 24-hours, (day 0) only those with increased acid exposure time (percent total time pH <4 above 6%) continued to the next phase. During phase two of the study, patients were treated for two weeks with TESS and documented their symptoms.

Primary end points included the reduction of baseline (pretreatment) number of heartburn and regurgitation episodes as well as 24-hour percent total time pH <4 and/or DeMeester score by at least 50%.

Results: 26 GERD patients (16 male, aged 47±15 years, mean BMI 25±3 kg/m²) completed the study. At baseline, mean number of daily heartburn and regurgitation events was 2.41±0.36 and 1.38±0.35, respectively. Following TESS, mean number of daily heartburn and regurgitation events dropped to 0.69±0.16 and 0.31±0.19, respectively ($p=0.01$). At baseline, mean percent total time pH <4 was 11.8±0.9. Following TESS, mean percent total time pH <4 dropped to 7.3±0.8, 7.8±1.0, 6.7±1.1 and 5.0±0.7

for day 1, 2, 3 and 4, respectively ($p=0.01$). At baseline, mean DeMeester score was 31.4 ± 2.1 . Following TESS, mean DeMeester score dropped to 20.1 ± 2.0 , 20.4 ± 2.5 , 17.3 ± 2.6 and 14.3 ± 2.0 for day 1, 2, 3 and 4, respectively ($p=0.01$).

Conclusion: TESS is effective in reducing both symptoms (heartburn and regurgitation) and esophageal acid exposure time in GERD patients.

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Disclosure: Nothing to disclose.

P0075

MANAGEMENT OF RECURRENT GASTROESOPHAGEAL REFLUX DISEASE AFTER NISSEN OR TRANSORAL INCISIONLESS FUNDOPLICATION UTILIZING EITHER ANTIREFLUX MUCOSECTOMY OR RESECTION AND PLICATION: AN UPDATED MULTICENTER STUDY

N. Randhawa¹, A. Khalyfa², K. Ayub³

¹Pacific Northwest University of Health Sciences, Yakima, United States, ²Franciscan Health Olympia Fields, Olympia Fields, United States, ³Silvercross Hospital, New Lenox, United States

Contact E-Mail Address: randhnhk@gmail.com

Introduction: Gastroesophageal Reflux Disease is a common condition seen in approximately one out of every five Americans. This condition results from acid rising up to the esophagus, resulting in symptoms and further complications. PPIs are an effective first-line treatment for gastroesophageal Reflux Disease, however, the disease is not eradicated through this therapy. Some patients require continuous maintenance therapy for recurrent symptoms. Long-term PPI use can lead to adverse effects including, but not limited to osteoporosis, pneumonia, and hypomagnesemia; thus exploring anatomical treatments is imperative.

Aims & Methods:

Aims: To evaluate the safety and efficacy of Antireflux Mucosectomy or Resection and Plication in symptomatic patients with prior fundoplication.

Methods: This multicenter study was carried out at four hospitals on symptomatic patients with gastroesophageal Reflux Disease who had prior Nissen Fundoplication or TIF. Informed consent was obtained from all of the patients prior to the procedure. A standardized procedure for mucosectomy was performed and an approximately 210-degree area was resected.

Approximately, 1 cm of the distal esophagus and 2 cm of the cardia were resected along the lesser curve. Endoscopic submucosal dissection (ESD) was performed in 6 patients while Endoscopic mucosal resection (EMR) was performed in 12 patients. Suturing was used in 5 patients with Hill Grade 3 valve.

Results: Eighteen patients were enrolled in the study. Ten had prior TIF and 8 had prior Nissen Fundoplication. All patients underwent the ARMS or RAP procedure. Of these patients, 9 patients had a Hill Grade 3 Valve and 9 patients had a Hill Grade 2 valve. Follow-up endoscopy was performed at 4-12 weeks. At follow-up, 11 patients had a Hill Grade 1 valve and 7 patients had a Hill Grade 2 valve.

All patients had improvement in symptoms. Four patients developed dysphagia, 7 patients developed post-procedural pain, 1 patient had bleeding requiring 1 unit of transfusion, and 1 patient required dilation. In the remaining patients, dysphagia and pain resolved spontaneously.

The follow-up was 24 weeks to 32 months. A paired T-Test comparing each patient's pre-Hill compared to post-Hill revealed the procedure produced statistically significant data (difference in means = 1.111, $T=14.5774$, $p<0.001$)

Conclusion: This multicenter, pilot study revealed Antireflux Mucosectomy or Resection and Plication to be safe and effective treatments in symptomatic patients with prior fundoplication procedures.

Disclosure: Nothing to disclose.

P0076

MOSAPRIDE CITRATE COMBINED WITH ESOMEPRAZOLE IS EFFECTIVE IN GASTROESOPHAGEAL REFLUX DISEASE BY IMPROVING DELAYED GASTRIC EMPTYING. – PRELIMINARY RESULTS –

B.J. Kim¹, J.G. Kim², J.Y. Park¹

¹Chung-Ang University College of Medicine, Internal Medicine (Gastroenterology), Seoul, Korea (Republic of), ²Chung-Ang University College of Medicine, Internal Medicine, Seoul, Korea (Republic of)

Contact E-Mail Address: kimbj@cau.ac.kr

Introduction: Previous studies have shown that patients with gastroesophageal reflux disease (GERD) have slower rates of gastric emptying than control subjects. However, the involvement of delayed gastric emptying (DGE) in the pathophysiology of gastro-esophageal reflux disease (GERD) remains debated.

Aims & Methods: The aim of this study was to investigate whether treatment with prokinetics in addition to PPI therapy would improve clinical symptoms in dyspeptic GERD patients with or without delayed gastric emptying.

Thirty consecutive patients refractory to PPI over six month period were included in the study.

DGE by Gastric Emptying Scintigraphy was defined when gastric emptying time ($T_{1/2}$) >70 min.

Patients were divided according to presence of dyspepsia into dyspeptic group ($n = 12$) and non-dyspeptic group ($n = 18$). Mosapride citrate in addition to esomeprazole 40 mg was administered for 4 weeks. Symptoms were evaluated using a standardized questionnaire before and after treatment.

Results: There was no statistical difference in age and gender between dyspeptic group and non-dyspeptic group ($P=0.92$ and $P=0.23$, respectively). Prevalence of esophagitis was similar between dyspeptic group and non-dyspeptic group (58% vs 39%, $P=0.31$). DEG was detected 75% in dyspeptic group and 28% in non-dyspeptic group ($P=0.01$). Symptom improvement was greater in dyspeptic group than non-dyspeptic group (75% vs 33%, $P=0.02$).

Conclusion: Gastric emptying in dyspeptic patients with GERD is significantly slower than in non-dyspeptic patients regardless of esophagitis. Combination therapy with prokinetics in addition to PPI improves typical GERD symptoms in dyspeptic patients with GERD.

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Disclosure: There is no conflict of interest.

P0077

THE EFFECTS OF TEGOPRAZAN VERSUS ESOMEPRAZOLE FOR RELIEF OF NIGHTTIME HEARTBURN AND SLEEP QUALITY IN GERD: A MULTICENTER DOUBLE-BLIND RANDOMIZED CONTROLLED TRIAL

J.S. Kim¹, S.I. Seo², S.H. Kang³, S.K. Lee⁴

¹Incheon St. Mary's Hospital, The Catholic University Of Korea, Seoul, Korea (Republic of), ²Kangdong Sacred Heart Hospital, Hallym University College of Medicine, Seoul, Korea (Republic of), ³Chungnam National University School of Medicine, Internal Medicine, Daejeon, Korea (Republic of), ⁴Yonsei University College of Medicine, Internal Medicine, Seoul, Korea (Republic of)

Contact E-Mail Address: qndrj@naver.com

Introduction: Patients with gastroesophageal reflux disease (GERD) frequently experience nighttime heartburn and sleep disturbance. Tegoprazan is a new potassium-competitive acid blocker which can rapidly block acid secretion.

Aims & Methods: Patients with erosive esophagitis and sleep disturbances were randomized 1: 1 in a double-blind fashion to receive tegoprazan 50 mg or esomeprazole 40 for two weeks.

The primary end point was time to first nighttime heartburn free interval. Percentage of nighttime heartburn-free days were also compared between the two groups.

Results: A total of 46 patients were enrolled in the study. Time to first nighttime heartburn-free interval was shorter for tegoprazan compared to esomeprazole but without statistical significance (1.5 d vs. 3 d). Percentage of nighttime heartburn-free days were higher for the tegoprazan group but without significance (57.8% vs. 43.1%). Adverse events occurred in two patients and were mild in severity.

Conclusion: Tegoprazan may induce faster symptom relief of nighttime heartburn symptoms and improve sleep disorders associated with nighttime heartburn. Further large-scale studies are required to validate our findings. (Clinical Trials NCT04309916).

Disclosure: This study was supported by HK inno.N Corporation.

P0078

EFFECT OF A COMBINATION ORAL FORMULATION OF HYALURONIC ACID WITH CHONDROITIN SULPHATE AND WITH MAGNESIUM TRISILICATE IN GASTRO-ESOPHAGEAL REFLUX DISEASE

A. Geeraerts¹, H. Geysen¹, J. Toth¹, L. Timmermans², H. Van Gucht², K. Geboers², A. Pauwels¹, T. Vanuytsel^{1,2}, J. Tack^{1,2}
¹KU Leuven, TARGID, Leuven, Belgium, ²Neurogastroenterology and Motility, University Hospitals, Department of Gastroenterology, Leuven, Belgium

Contact E-Mail Address: Annelies.Geeraerts@kuleuven.be

Introduction: Gastric acid is the main pathological factor in gastro-esophageal reflux disease (GERD) and the development of proton pump inhibitors (PPIs) was a major break-through in GERD treatment. However, PPIs are most suitable for continued intake and less for intermittent use in patients with intermittent or occasional reflux symptoms. GERDOFF® Plus is a novel chewable nonprescriptive 'medical device', for the relief of GERD symptoms, based on a bioadhesive mixture of hyaluronic acid, chondroitin sulfate and magnesium trisilicate (HA/CS/MT) which has the capability of attaching to the esophageal mucosa, promoting mucosal recovery and neutralizing acidity.

Aims & Methods: To investigate the efficacy and safety of oral HA/CS/MT for improving mucosal integrity and symptom severity in GERD patients with occasional symptoms, not treated with a PPI.

We performed a single-center, randomized, double-blind, placebo-controlled, cross-over pilot study in patients with typical GERD symptoms (heartburn and/or regurgitation), not treated with a PPI in the last 2 months. Patients received either HA/CS/MT (1100 mg) or placebo q.i.d. for 3 weeks followed by a wash-out period of 3 weeks after which patients crossed over to the other treatment arm for another 3 weeks.

At baseline and after each treatment period patients underwent a 24h pH-impedance measurement to assess mean baseline impedance values (primary endpoint) at 3cm, 5cm and 15cm above the esophago-gastric junction (EGJ) (1).

Symptom severity was assessed using the total ReQuest® questionnaire score at screening and before and after each treatment period. Safety was assessed through analysis of laboratory parameters, vital signs and physical examination.

Results: Twenty patients (10 females, mean age 39±15years) completed the study. No significant differences were observed for baseline impedance values at 3cm, 5cm and 15cm above the EGJ between HA/CS/MT and placebo ($p=0.3580$, $p=0.7674$ and $p=0.5987$, respectively).

However, a numerical increase in impedance values was observed at 3cm and 5cm post-treatment (+276.3Ω and +255.2Ω, respectively) with HA/CS/MT, and not in the placebo group (-5.7Ω and -13.3Ω, respectively). The median total ReQuest® questionnaire scores between the two groups were not significantly different both at baseline and post-treatment.

Post-hoc analysis revealed a significant difference in the percentage of patients with nocturnal heartburn after three weeks treatment between HA/CS/MT and placebo (45% vs. 0% and 42.1% vs. 26.3% respectively; p -value=0.014).

Furthermore, the mean changes between baseline and post-treatment were significantly more pronounced after HA/CS/MT treatment compared to placebo for upper abdominal complaints (-2.9±14.1 vs 3.3±8.4 respectively; $p=0.0470$). All the adverse events were classified as unrelated to the investigational product. Laboratory parameters, vital signs and physical examination did not show any safety issues.

Conclusion: HA/CS/MT had no significant effect on baseline impedance, the primary endpoint of this pilot study. However, we observed a numerical trend towards improved impedance values only after HA/CS/MT treatment and not after placebo.

The median total ReQuest® questionnaire scores were not significantly different, although a post-hoc between-group analysis suggests a statistically significant improvement of nocturnal heartburn and an improvement from baseline for upper abdominal symptoms post-treatment with HA/CS/MT.

Finally, the investigational product was safe and well tolerated.

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P0079

COMPARISON OF MEDICAL THERAPIES FOR NON-EROSIVE REFLUX DISEASE: SYSTEMATIC REVIEW AND NETWORK META-ANALYSIS

B. Barberio¹, P. Visaggi², E.V. Savarino¹, N. de Bortoli², C.J. Black³, A.C. Ford⁴

¹University of Padua, Division of Gastroenterology, Department Of Surgery, Oncology And Gastroenterology, Padua, Italy,

²Gastroenterology Unit, University of Pisa, Translational Research and New Technologies in Medicine and Surgery, Pisa, Italy, ³St James's University Hospital, Department of Gastroenterology, Leeds, United Kingdom, ⁴Leeds Institute of Medical Research at St. James's, University of Leeds, Dept. of Gastroenterology, Leeds, United Kingdom

Contact E-Mail Address: pierfrancesco.visaggi@gmail.com

Introduction: Gastro-oesophageal reflux disease (GORD) affects up to 50% of adults worldwide, with the most prevalent subtype being non-erosive reflux disease (NERD). However, the comparative efficacy and safety of medical therapies for gastro-oesophageal reflux symptoms in NERD is unclear.

Aims & Methods: We conducted a network meta-analysis to evaluate efficacy and safety of proton pump inhibitors (PPIs), histamine-2-receptor antagonists, potassium-competitive acid blockers (PCABs), and alginates compared with each other or with placebo in patients with NERD. We searched MEDLINE, EMBASE, EMBASE Classic, and the Cochrane central register of controlled trials from inception to 1st February 2022.

We included randomised controlled trials (RCTs) comparing the efficacy of all drugs versus each other, or versus a placebo, in adult patients with NERD. Results were reported as pooled relative risks (RRs) with 95% confidence intervals (CIs) to summarise effect of each comparison tested, with treatments ranked according to P-score.

Results: We identified 23 RCTs containing 10,735 subjects with NERD. In the short-term (≥ 2 to < 4 weeks), omeprazole 20mg o.d. (RR = 0.43; 95% CI 0.33-0.56, P-score 0.94) was ranked first in terms of failure to achieve complete relief of symptoms, with esomeprazole 20mg o.d. or 40mg o.d. second and third. Rabeprazole 10mg o.d. (RR = 0.73; 95% CI 0.60-0.90, P-score 0.95) ranked first for failure to achieve adequate relief.

In the longer term (≥ 4 weeks), dextansoprazole 30mg o.d. (RR = 0.48; 95% CI 0.35-0.65, P-score 0.95) ranked first for failure to achieve complete relief, with 30ml alginate q.i.d. combined with omeprazole 20mg o.d., and 30ml alginate t.i.d. second and third, although the latter two based on data from one relatively small RCT. Dextansoprazole 60mg o.d. was the most efficacious in terms of failure to achieve adequate relief (RR = 0.45; 95% CI 0.29-0.70, P-score 0.90) with dextansoprazole 30 mg o.d. and rabeprazole 20mg o.d. second and third. All drugs were safe and well-tolerated.

Conclusion: Our results confirm the superiority of PPIs, as a class, compared with other drugs in treating NERD. Future RCTs should aim to better classify patients with NERD, and to establish the role of alginates and PCABs in achieving adequate and complete symptom relief in NERD in both the short and long-term.

Disclosure: Nothing to disclose.

P0080

HIATUS HERNIA: PREVALENCE, PRESENTATION AND EVALUATION OF ESOPHAGEAL SEQUELA

F. Abu Baker¹, A. Mari², A. Beshara¹, B. Ovadia¹, M. Suki¹, S. Perry¹, M. Levin¹, O. Gal¹, Y. Kopelman¹

¹Hillel Yaffe Medical Center, Gastroenterology and Hepatology, Hadera, Israel, ²EMMS Hospital, Gastroenterology, Nazareth, Israel

Contact E-Mail Address: amir.mari@hotmail.com

Introduction: Hiatus hernia (HH) is an everyday encounter in the daily endoscopic practice, but a comprehensive evaluation of its esophageal sequela is lacking.

Aims & Methods: We aimed to investigate HHs' prevalence and clinical presentation and provide a comprehensive evaluation of the esophageal sequela associated with HH. We conducted a retrospective, large cohort study by reviewing the electronic files of almost 75000 consecutive patients who underwent gastroscopy over a 12-year period (2008-2020). All patients with a documented endoscopic diagnosis of HH were included in the study group, while those without any endoscopic evidence of HH served as controls.

We derived comprehensive data concerned with the clinical presentation and a comprehensive assessment of benign and malignant esophageal pathologies, including esophageal diverticulum, Shatzki ring, Mallory Weiss, infectious and other non-reflux related esophagitis, benign esophageal strictures, food impaction, suspected motility disorders, and esophageal polyps' size, type and location. The clinical, procedural, endoscopic, and outcome measures were compared between the HH and control groups and further analyzed based on HH size and subtype. Multivariate analysis was performed to identify reflux esophagitis, Barret's esophagus, and esophageal cancer predictors.

Results: The overall diagnosis rate of HH in the entire cohort was (16.8%). The vast majority of HH patients (89.5%) had small HH, 8.7 % had large HH, while only 2% were considered to have para-esophageal or mixed HH. Female predominance was documented in HH patients (57.1% vs. 54%; $P < 0.001$), and they were significantly older compared to controls (61.1 ± 16.5 vs. 52.7 ± 20.0 ; $P < 0.001$). Indeed, the HH diagnosis rate was significantly higher in those 50 years or older when compared to younger adults below 50 years (21% vs. 10.46%; $P < 0.001$). Clinical indications associated with higher rate of HH detection compared to controls included reflux-related symptoms (20% vs. 7%; $P < 0.001$), nausea and vomiting (4% vs. 2.9%; $P < 0.01$), and dysphagia (5% vs. 3.4%; $P < 0.001$). A prominent and significant association was noted between anemia (18% and 17.4% vs. 8.7%; $P < 0.001$) as well as GI bleeding (15.7% and 17.4% vs. 6%; $P < 0.001$), and large and para-esophageal HHs, respectively. The outcome analysis of esophageal pathology revealed an independent and significant association between HH and erosive reflux esophagitis (25.7% vs. 6.2%; $OR = 3.8$ $P < 0.001$), severe distal esophagitis (4.4% vs. 0.7%; $OR = 4.4$, $P < 0.001$), and Barret's esophagus (3.8% vs. 0.7%; $OR = 4.7$, $P < 0.001$). These associations were more prominent for patients with large HH.

Moreover, Higher rates of benign esophageal strictures (3.8% vs. 0.5%; $P < 0.001$), Cameron's ulcers (5.6% vs. 0.6%; $P = 0.01$) Mallory Weiss tears (4.7 vs. 2.3%; $P = 0.01$), food impactions (0.7% vs. 0.2%; $P = 0.01$), and esophageal polyps (0.8% vs. 0.4%; $P < 0.001$) were documented in patients with large, but not small HH patients. Other esophageal pathology rates, including infectious and unspecified esophagitis, esophageal diverticulum, and suspected motility disorders, didn't differ significantly from controls.

Conclusion: HHs were associated with reflux esophagitis and Barret's esophagus. This association was more prominent for large HHs, which were also linked with higher rates of Cameron ulcers, benign esophageal strictures, food impactions, and esophageal polyps.

Disclosure: Nothing to disclose.

P0081

CONTRIBUTION OF ENZYMATIC ACTIVITY OF HEME OXYGENASE (HMOX) AND ITS BYPRODUCT, CARBON MONOXIDE (CO) IN BARRETT'S METAPLASIA DEVELOPMENT

K. Krukowska¹, E. Korbut¹, D. Wójcik-Grzybek¹, D. Bakalarz^{1,2}, K. Magierowska¹, M. Wierdak¹, U. Głowacka¹, A. Danielak¹, T. Brzozowski¹, G. Buszewicz³, **M. Magierowski¹**

¹Jagiellonian University Medical College, Department of Physiology, Cracow, Poland, ²Institute of Forensic Research, Department of Forensic Toxicology, Cracow, Poland, ³Medical University of Lublin, Department of Forensic Medicine, Lublin, Poland

Contact E-Mail Address: m.magierowski@uj.edu.pl

Introduction: Heme oxygenase (HMOX) is an enzyme involved in heme metabolism leading to the production of ferrous ion, biliverdin, and bioactive gaseous mediator, carbon monoxide (CO). Expressed under pathological conditions in gastrointestinal (GI) tract, inflammation-sensitive and inducible HMOX-1 isoform and CO released from pharmacological tools were shown in our previous studies to contribute in gastric ulcer healing and in esophagoprotection against acute esophagitis. Nevertheless, the role of HMOX-1 and CO in the prevention of Barrett's esophagus (BE) development and progression (BE) has not been elucidated so far.

Aims & Methods: Thus, we aimed to evaluate if the chronic treatment with pharmacological HMOX-1 inducer, hemin or its inhibitor, tin protoporphyrin IX (SnPP) as well as CO-releasing compound, tricarbonyldichlororuthenium(II) dimer(CORM-2) affects BE progression based on experimental in vitro and in vivo models. GEO2R tool and GSE34619, GSE1420, GSE13083 databases were used to assess the alterations in HMOX-1 mRNA expression in clinical BE samples. Human-derived esophageal keratinocytes (EPC2) were treated with bile mixture (BM, 100 µM) for 6 days to reflect clinical BE-specific molecular alterations.

Wistar rats with esophagogastrroduodenal anastomosis (EGDA) implemented to mimic clinical reflux disease (GERD) were treated i.g. for 8 weeks with vehicle or with hemin (0.2-5 mg/kg), SnPP (0.2- 5 mg/kg) or CORM-2 (0.2-5 mg/kg). Macroscopic esophageal lesions index (ELI) was assessed macroscopically and microscopically using standardized scale. Esophageal blood flow (EBF) was measured by laser flowmetry. Esophageal mRNA levels for HMOX-1, BE-specific KRT₇, interleukin 1 agonist (IL-1RA) and suppressor of cytokine signaling 3 (SOCS3) were determined by real-time PCR. COHb content in whole blood samples was evaluated by gas chromatography.

Results: HMOX-1 expression was decreased in BE clinical biopsies vs. normal squamous epithelium. In EPC2 cells treated chronically with BM mRNA expression of HMOX-1 was downregulated. In animal model, CORM-2 but not SnPP and hemin dose-dependently decreased ELI score and reversed BE-like molecular alterations as compared with vehicle by modulation of selected esophageal KRTs mRNA expression.

Enhanced esophageal expression for anti-inflammatory SOCS3 and IL-1RA in EGDA-rats administered with CORM-2 or hemin was observed. Our preliminary data showed that COHb concentration in blood samples was decreased in EGDA-rats.

Conclusion: We conclude based on clinical datasets, in vitro and in vivo animal models analysis that decreased expression of HMOX-1 and possible subsequent fall in CO bioavailability in esophageal mucosa and in systemic circulation contributes in the development of Barrett's metaplasia and its further progression.

Increased CO content due to selected pharmacological donor application may compensate the effect of this alteration leading to prevention of esophageal mucosa against GERD-related chronic and pre-cancerous

pathologies development. This beneficial effect of CO is accompanied by the upregulation of anti-inflammatory response pathways in esophageal mucosa. These observations could serve as a background for the further research targeting the implementation of novel and safe CO-prodrugs in GI pharmacology. [Funding source: National Science Centre, Poland (UMO-2019/33/B/NZ4/00616)]

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Disclosure: Nothing to disclose.

P0082

INSULIN-LIKE GROWTH FACTOR-1 (IGF-1) IS ELEVATED IN SERUM OF PATIENTS WITH BARRETT'S ESOPHAGUS: LONGITUDINAL STUDY

H. Uchima¹, A. Da Fieno¹, M. Cuatrecasas², A. Bonilla¹, J. de Melo Silva¹, H.N. Cordova Guevara¹, A. Gines¹, J.I. Elizalde¹, N. Rakislova², J. Llach-Roca¹, B. González-Suárez², L. Moreira¹, J. Llach¹, F. Balaguer¹, M.G. Fernández-Esparrach¹

¹Endoscopy Unit, Gastroenterology Department, Hospital Clínic, IDIBAPS, CIBEREHD, University of Barcelona, Barcelona, Spain,

²Pathology Department, Hospital Clínic, IDIBAPS, CIBEREHD, University of Barcelona, Barcelona, Spain

Contact E-Mail Address: hugoikuo@hotmail.com

Introduction: Barrett's esophagus (BE) is an entity with a well known histological progression to malignancy. Malignant transformation in patients with BE may arise from alterations of apoptotic regulatory proteins and the insulin-like growth factor (IGF) system is involved in the regulation of cell proliferation, differentiation and apoptosis. Dys-regulation of IGF-1 increases the risk of a number of malignancies and IGF binding protein-3 (IGFBP-3) is over-expressed in BE, dysplastic and tumour tissue of patients with adenocarcinoma.

The possibility of having a plasmatic biomarker of BE diagnosis or progression is very appealing. However, the role of IGF system in BE is not clear with controversial results regarding circulating levels of these proteins.

Aims & Methods: The objective of this study is to evaluate circulating levels of IGF-1 and IGFBP-3 in patients with BE at different histological stages and study its potential relationship with progression to neoplasm.

We performed a prospective study and determined baseline concentrations of IGF-1 and IGFBP-3 in all patients with BE who underwent an upper endoscopy from May 2012 to May 2015.

Endoscopy was performed under conscious sedation and biopsies were obtained following the Seattle protocol. Ten mL of blood were taken and determination of IGF-1 and IGFBP-3 was performed using the ELISA tech-

nique. The IGF-1/IGFBP-3 molar ratio was calculated. Patients without BE were included as a control group. The protocol was approved by the Ethics Committee and patients gave informed consent.

Results: A total of 116 patients with endoscopy and blood samples were included: 36 control and 80 with BE (46 with IM, 19 with LGD and 20 with ADK/HGD).

Mean levels of IGF-1 were higher in BE than in control group (138.43 ± 69.49 and 108.19 ± 46.69 ng/ml, respectively, $p=0.007$), but there not differences between IM, LGD and ADK/HGD groups. The IGF-1/IGFBP-3 molar ratio was also higher in BE than in control group (0.24 ± 0.98 and 0.19 ± 0.06 , $p=0.001$). 54 out of 65 patients with IM or LGD were followed for a median of 58.50 months (12-113) and 11 of them had progression to LGD ($n=8$) or ADK/HGD ($n=3$) with a median time of 30 months (12-112). Levels of IGF-1 and IGF-1/IGFBP-3 molar ratio were not different between the patients who progressed and not. Age, IMC, glucose and length of BE were similar in both groups.

Conclusion: In this small series of patients with BE with a considerable follow-up, circulating levels of IGF-1 and IGF-1/IGFBP-3 ratio were higher than in controls but were not associated with more advanced histology nor with progression, bringing into question its potential role as a biomarker of neoplastic progression in BE.

Disclosure: Nothing to disclose.

P0083

THE NATURAL COURSE OF UNTREATED NEOPLASIA IN BARRETT'S ESOPHAGUS - A CASE-SERIES

E. Verheij¹, S. van Munster^{1,2}, C. Cotton³, B.L.A.M. Weusten^{2,4}, L. Alvarez Herrero³, A. Alkhalaf⁵, B.E. Schenk⁵, E.J. Schoon⁶, W.L. Curvers⁶, A.D. Koch⁷, P.J. de Jonge⁷, T.J. Tang⁸, W.B. Nagengast⁹, J. Westerhof⁹, M. Houben¹⁰, N. Shaheen³, J.J. Bergman^{1,11}, R.E. Pouw^{1,11}, Dutch Barrett Expert Centers
¹Amsterdam UMC location University of Amsterdam, Gastroenterology and Hepatology, Amsterdam, Netherlands, ²St Antonius Hospital, Gastroenterology and Hepatology, Nieuwegein, Netherlands, ³University of North Carolina School of Medicine, Gastroenterology and Hepatology, Chapel Hill, United States, ⁴UMC Utrecht, Gastroenterology and Hepatology, Utrecht, Netherlands, ⁵Isala Hospital, Gastroenterology, Zwolle, Netherlands, ⁶Catharina Hospital, Gastroenterology, Eindhoven, Netherlands, ⁷Erasmus MC - University Medical Center, Gastroenterology and Hepatology, Rotterdam, Netherlands, ⁸IJsselland Hospital, Gastroenterology, Capelle aan den IJssel, Netherlands, ⁹UMC Groningen, Gastroenterology and Hepatology, Groningen, Netherlands, ¹⁰Haga Teaching Hospital, Gastroenterology, Den Haag, Netherlands, ¹¹Amsterdam UMC location Vrije Universiteit Amsterdam, Gastroenterology and Hepatology, Amsterdam, Netherlands

Contact E-Mail Address: e.p.d.verheij@amsterdamumc.nl

Introduction: Endoscopic eradication therapy (EET) is the preferred treatment for Barrett's Esophagus (BE) with high-grade dysplasia (HGD) to prevent progression to advanced esophageal adenocarcinoma (EAC). EET for early neoplasia is a minimally invasive organ-preserving therapy, in contrast, advanced EAC requires major surgery and is associated with a high mortality rate. The annual neoplastic progression risk is $\pm 7\%$ for HGD.

However, these studies originate from the early 2000's, when lower quality equipment may have missed prevalent cancer. Furthermore, these studies report combined rates of progression to early and advanced EAC. For rational use of EET in clinical practice, accurate risk estimates for progres-

sion to symptomatic EAC are also crucial. Therefore, we aimed to evaluate the time between diagnosis of HGD in BE and development of clinically evident EAC.

Aims & Methods: In the Netherlands, care for patients with BE is centralized in expert centers with a joint registry. We identified cases with HGD left untreated due to competing comorbidities or age and a FU period of at least 12 months. We retrospectively collected data from the electronic patient files and by consultation with the general practitioner to determine vital FU. Endoscopic FU was defined as the time between detection of HGD (i.e. baseline) and the last endoscopy. Vital FU was defined as the time between baseline and symptomatic EAC, death, or last data collection in those still alive. Primary outcome was time of progression to clinically evident EAC, defined as symptomatic EAC (i.e. symptoms of dysphagia) or EAC-related death.

Results: From our database, 11 cases were identified and met the inclusion criteria ($n=2091$, 0.5% of the entire database). The mean age was 78 years old, 64% was male and the median Charlson Comorbidity Index was 4 ($p25$ - $p75$ 4-5). At baseline, HGD was found in a visible lesion in 9 of the 11 cases (82%) and in random biopsies from flat BE in the remaining 2 patients (18%). Median endoscopic FU was 21 months ($p25$ - $p75$ 2-32) with median 2 ($p25$ - $p75$ 0-7) endoscopies per patient. Endoscopic FU had been stopped in 10/11 patients at moment of data collection. Median vital FU was 27 months ($p25$ - $p75$ 21-45). Overall, 4/11 patients (36%) progressed to clinically evident EAC. Three had clinical suspicion of cancer at baseline and 1 had flat HGD. All 4 patients presented as symptomatic EAC and died from EAC. Progression occurred median 52 months (range 17-78) after baseline. In all 4 patients, endoscopic FU was terminated median 30 months ($p25$ - $p75$ 16-44) prior to detection of the clinically evident EAC. Among the other patients (7/11), 3 had endoscopic suspicion of progression and underwent curative endoscopic resection for HGD ($n=1$) or T1-EAC ($n=2$) 19-21-26 months after baseline. The remaining 4 patients had median vital FU of 26 months ($p25$ - $p75$ 16-41) without progression and had unrelated death ($n=3$) or were alive without symptoms ($n=1$).

Conclusion: Even though HGD and early EAC are logical targets for minimal invasive EET, the actual progression to symptomatic disease had a significant duration in our case-series. This lag time in progression to symptomatic EAC may be relevant to consider in patients with a limited life expectancy with early neoplasia or during FU after successful EET.

Disclosure: Nothing to disclose.

P0084

CAN ENDOSCOPIC EVIDENCE OF BILE REFLUX PREDICT THE DEVELOPMENT OF BARRETT'S ESOPHAGUS?

Y. Iwaya¹, S. Kako², T. Miyazawa², D. Hara², K. Hashigami², A. Hirayama², T. Okamura², T. Nagaya³, T. Umemura²
¹Shinshu University, School of Medicine, Advanced Therapeutic Endoscopy, Matsumoto, Japan, ²Shinshu University, School of Medicine, Gastroenterology, Matsumoto, Japan, ³Shinshu University Hospital, Endoscopic Examination Center, Matsumoto, Japan

Contact E-Mail Address: yiwaya@shinshu-u.ac.jp

Introduction: Numerous basic researches have shown that bile reflux plays an important role in the development of Barrett's esophagus (BE). However, the relationship between the endoscopic findings of bile reflux and BE remains unknown. We aimed to investigate whether endoscopic evidence of bile reflux is associated with the presence of BE.

Aims & Methods: We conducted a retrospective analysis of a prospectively maintained database comprised of consecutive Japanese patients who underwent screening gastroscopy. Endoscopic findings of BE, reflux esopha-

gitis, atrophic gastritis and sliding hernia were recorded. Evaluation of a BE was based on the Prague criteria. Endoscopic evidence of bile reflux was defined as the presence of bile-stained fluid in the gastric fundus. We performed univariate and multivariate analyses to determine factors that differed significantly between patients with and without BE.

Results: A total of 3,183 patients were enrolled; 715 (23%) had BE and 767 (24%) had endoscopic evidence of bile reflux. On multivariate analysis, endoscopic evidence of bile reflux was the strongest independent factor associated with the presence of BE (odds ratio (OR) 7.78, 95% confidence interval (CI) 6.33-9.56) compared with the presence of sliding hiatus hernia (OR 3.53, 95%CI 2.79-4.48) or male sex (OR 1.73, 95%CI 1.35-2.21).

Conclusion: Our study showed that endoscopic evidence of bile reflux was a strong independent factor associated with the presence of BE, suggesting that bile reflux may therefore predict which patients with gastroesophageal reflux disease are at risk of developing BE and which patients would benefit from gastroscopy surveillance.

Disclosure: Nothing to disclose.

P0085

CIRCUMFERENTIAL ENDOSCOPIC SUBMUCOSAL DISSECTION OF NEOPLASTIC BARRETT'S ESOPHAGUS

M. Omae¹, N. Wang², F. Baldaque-Silva¹

¹Karolinska University Hospital, Stockholm, Sweden, ²Karolinska University Hospital, Pathology, Stockholm, Sweden

Contact E-Mail Address: machami242000@gmail.com

Introduction: Endoscopic submucosal dissection (ESD) is a treatment option in neoplastic Barrett's esophagus (NBE) in cases with severe fibrosis and in which cancer cannot be resected *en bloc* by conventional mucosal resection. In cases of big or multifocal lesions, large ESD resections are performed. Large esophageal ESDs might be associated with high rate of adverse events, namely stricture. The advent of stricture prophylactic strategies, has reduced dramatically that risk. With this study we aimed to evaluate the safety and efficacy of large BE ESDs engaging all luminal circumference.

Aims & Methods: This study was approved by the Stockholm Regional Ethical Committee. All patients with NBE BE and macroscopic lesions were invited for ESD after discussion in a multidisciplinary conference. Procedures were performed under deep anesthesia. Stricture prophylaxis with steroids was performed in all patients. A stricture was defined as esophageal narrowing making it impossible for a 9.9 mm endoscope to pass through the esophagus regardless of dysphagia. Follow-up endoscopies were performed at 2 weeks and 2 months and then yearly, or when patients symptomatic.

The primary outcomes were the rates of adverse events such as bleeding, perforation and stricture. Secondary outcomes were the rates of *en bloc*, R0, curative resection, positive lateral and vertical margins.

Results: From of cohort of total 160 BE ESD, between 2011 to 2022, 6 corresponded to circumferential ESD in 5 patients. The mean age was 72.0 years, mean length of Barrett's mucosa C13 (0-24), 14 (0-25). Mean resection time was 345 minutes and the mean specimen size was 110 (85-170) mm.

Considering primary outcomes, there were strictures in 3/6 of cases, all treated successfully with balloon dilatation (1/3) or balloon dilation plus temporary metallic stent (2/3). No perforation and postoperative bleeding occurred.

Considering secondary outcomes, *en bloc* resection was present in 6/6, R0 resection in 4/6, and curative resection in 4/6 cases. The resected specimens corresponded to high-grade dysplasia in 2/6, intramucosal adenocarcinoma to submucosal adenocarcinoma (SM1) in 4/6 cases. Positive

lateral margins and positive vertical margins rates were 0/6 and 2/6 cases, respectively. The 30 days mortality was 0 and mean hospital stay was 3 days.

Two out of 3 non-curative cases were operated. Resected specimens corresponded to T1b and T2 cancers, both with no lymph node metastasis. One curative ESD in a patient with ultralong Barrett esophagus (ULSBE, C24M25) had recurrence lesion after 2 circumferential ESDs. In this patient, esophagectomy was performed due to esophageal recurrence. Esophagectomy specimen shown pT1b (SM3) cancer with no lymph node metastasis. Twenty months later, patient had a thoracic wall metastasis and received palliative treatment.

Conclusion: Circumferential ESD with steroid therapy shows a high safety profile in patients with HGD or mucosal cancer.

This is the first study evaluating the role of all circumferential ESD for NBE. This cohort shows that this strategy is associated with high rates of *en bloc* resection and of free lateral margins. The most common complication was stricture, however all those cases were managed endoscopically. R1 rate was 33% mainly due positive vertical margins.

Patients with NBE should be strictly selected for ESD and primary esophagectomy should be considered in patients with ultra long BE and suspected SM cancer. Circumferential ESD with steroid therapy shows a high safety profile in patients with HGD or mucosal cancer. Further comparative and larger studies are warranted.

Disclosure: None.

P0086

BARRETT'S ESOPHAGUS SURVEILLANCE – CAN WE DO BETTER?

M. Soliman¹, K. Kapur²

¹Medway Maritime Hospital, Medicine, Gillingham, United Kingdom, ²Barnsley Hospital NHSFT, Gastroenterology, Barnsley, United Kingdom

Contact E-Mail Address: Mina.soliman@nhs.net

Introduction: Barrett's esophagus (BO) has a pre-malignant potential. Several guidelines^{1,2,3} to optimise surveillance and early detection of dysplasia were produced.

A previous audit in our hospital revealed significant departure from the guidelines. Dedicated lists⁴ and educational intervention⁵, were suggested to improve the quality of surveillance.

Aims & Methods: We aim to evaluate the compliance of BO surveillance with the published guidelines in our centre between February 1st 2021 and March 31st 2022 after the introduction of dedicated lists with longer time slots of 30 minutes.

A retrospective database search was performed for the word "Barrett" using the built-in audit tool of Infoflex v.5 reporting system and cross referenced with the histopathology data base. Surveillance details were added to an excel spreadsheet against criteria extracted from both the British Society of Gastroenterology and the European Society guidelines. Results were compared to the previous audit.

Results: 204 BO reports were found during the study period. 112/204 (55%) patients were undergoing surveillance and 92/204 (45%) were newly diagnosed.

In the surveillance group; 80 were males (71%) and 32 females (29%). Age range was between 41-83 years, with a mean age of 62. Barrett's segment was described according to Prague criteria in 111 out of 112 (99 % compared to 89% in the previous audit). 31 were short segment (i.e. less than 3cm) and 81 were long segment (3cm or above).

Seattle protocol of biopsies was followed in 104/112 (93% compared to 70% previously) and Chromoendoscopy (Narrow Band Imaging and 2% acetic acid spray) was performed in 66/112 (59% compared to 33% in

previous audit). Inspection time was recorded in 7 out of 112 (6% vs 2.5% in previous audit). Correct surveillance interval from last examination occurred in 103 (92% as opposed to 88% in previous audit). Intestinal metaplasia (IM) was not confirmed in 6 patients. All were discharged from surveillance as this was second endoscopy with negative IM in compliance with the guidelines. Dysplasia was detected in 10 cases (9 low grade and one high grade). Seven LGD and one HGD were appropriately followed up and managed. A lesion within the Barrett's was seen in 2 cases, both had distance from incisors recorded and targeted biopsies taken but no Paris classification or position described according to the clock face. There was also a discrepancy in the length of the measured Barrett between the initial and follow up endoscopies in 40/112 cases (35%) but a significant difference that affects the surveillance interval was observed in 7 cases only (6%).

Conclusion: Despite significant improvements from previous audit, namely the use of Seattle protocol and chromoendoscopy, dedicated lists have not achieved >90% in all parameters that we intended. There is still more that needs to be done to optimise surveillance in relation to recording the BO inspection time, the accurate measurement of the BO length as well as lesion description. We introduced mandatory fields in the endoscopy reporting that would be triggered once BO surveillance has been chosen, to improve the above with further re-audit.

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P0087

OPTICAL FLOW AS A METHOD FOR QUALITY ASSURANCE IN AI-AIDED EXAMINATION OF BARRETT'S ESOPHAGUS AND BARRETT'S ESOPHAGUS RELATED NEOPLASIA

M. Meinikheim¹, R. Mendel², A. Probst¹, M.W. Scheppach¹, H. Messmann¹, C. Palm², A. Ebigbo¹

¹University Hospital of Augsburg, Department of Gastroenterology, Augsburg, Germany, ²Ostbayerische Technische Hochschule Regensburg, Regensburg Medical Image Computing, Regensburg, Germany

Contact E-Mail Address: michael.meinikheim@uk-augsburg.de

Introduction: In order to offer the best possible performance, Artificial Intelligence (AI) based clinical decision support systems (CDSS) are dependent on high-quality input for real-time evaluation. Even though evaluation of lesions is perceived as real-time, modern AI systems still have to analyze the provided information frame by frame and sometimes pixel by pixel. The movement created by rapid alteration of the scope's position or flushing procedures can confound the AI algorithm and reduce its performance. Optical flow is a method of locating and quantifying motion between consecutive frames.

Aims & Methods: We aim to improve the human-computer interaction (HCI) by establishing a real-time feedback mechanism of the provided data quality for endoscopists using our AI algorithm "Barrett-Ampel" for the evaluation of Barrett's esophagus (BE) and Barrett's esophagus related neoplasia (BERN).

Therefore, unaltered videos in White Light (WL), Narrow Band Imaging (NBI) and Texture and Color Enhancement Imaging (TXI) of eight endoscopic examinations of histologically confirmed BE and BERN were analyzed by our AI algorithm. The motion between consecutive input frames was calculated using Farneback's dense optical flow algorithm and split into per-pixel magnitudes and angles.

The features used to rate the image quality were the mean magnitude and the entropy of the histogram of angles. Frames were automatically extracted, if predefined threshold values of 3.0 for mean magnitude and 9.0 for the entropy of the histogram of angles were surpassed. Experts first reviewed unaltered videos without AI support and evaluated them regarding the imaging quality, subjective perception of distractions like movement or water flushing, and, if applicable, whether they felt those factors would influence their diagnostic accuracy. Secondly, they reviewed the extracted frames.

Results: During steady movement in one direction, like during pushing and pulling of the endoscope, entropy was low, while there was still significant magnitude. Chaotic visual movement observable for example during flushing led to a high entropy as the water spreads in many directions. Increased optical flow appeared when examination videos were not steady, when abundant fluids disturbed the scope's vision or due to esophageal motility, and correlated with the experts' opinion on the quality of the videos.

Directly proportional to the mean optical flow, experts agreed that the imaging quality and distracting motion influenced their performance. When the optical flow's threshold values of 3.0 for magnitude and 9.0 for entropy of the histogram of angles were surpassed, the associated image quality was insufficient for interpretation in 94% of the cases, even for expert endoscopists.

Conclusion: Optical flow as a quality indicator offered real-time feedback on the quality of the provided input data. Optical flow has the potential to improve human-computer interaction and ultimately help to not only unveil the full potential of AI algorithms but also help endoscopists interpret the provided information.

Disclosure: Nothing to disclose.

P0088

DOES BARRETT'S ESOPHAGUS START TOO EARLY IN LIFE? ANALYSIS OF ENDOSCOPIC FINDINGS IN A PEDIATRIC COHORT

P.R. Tripathi¹

¹Ankura Hospital for Women and Children, Pediatric Gastroenterology, Hyderabad, India

Contact E-Mail Address: parijattripathi1986@gmail.com

Introduction: Barrett's esophagus (BE) is a premalignant condition found usually in adults. Long term acid exposure of esophageal mucosa is an important predisposing factor of BE. When do endoscopic changes start appearing and do the children with dyspeptic symptoms develop BE in adulthood, is not clear. We aimed to analyze endoscopic changes in esophagus in children presenting with clinic features of chronic acid reflux and dyspepsia.

Aims & Methods: We have retrospectively analyzed endoscopic findings of the esophagus in children presenting with symptoms suggestive of chronic gastroesophageal reflux disease (GERD) and dyspepsia over two years duration (March 2020 to February 2022). Children who had recurrence or

persistence of symptoms after ≥ 4 weeks of proton pump inhibitor therapy were included in the study. Children with associated neurological diseases were excluded.

Results: 119 (52% male) children with ages ranging from 3-204 months were included. The duration of symptoms ranged from 2 to 60 months (Table 1). One-third of all the patients had endoscopic changes in the lower esophagus (LE). 85% of them had an extension of gastric mucosa in the lower esophagus up to variable length. 4 patients had isolated islands of gastric mucosa in LE, maximum up to 3 cm above GE junction. Majority of patients (71%, $n=25$) had extension <1 cm above GE junction while in 5.7% ($n=2$) it was more than 2 cm. Biopsy in these two patients suggested gastric columnar epithelium without any dysplasia. Repeat endoscopy was performed after one year in both the patients which did not show any changes in endoscopic findings.

Total number of patients, n	119
Age, months $\pm$ SD	74.4 $\pm$ 45.4
Sex, male(%)	62 (52)
Indications	
Predominant pain abdomen, n (%)	43 (36.1)
Predominant vomiting, n (%)	59 (49.6)
Other dyspepsia related complaints, n (%)	17 (14.3)
Duration of symptoms, months $\pm$ SD	13.4 $\pm$ 12.8
Endoscopic findings of acid reflux in the lower esophagus, n (%)	41 (34.5)
Extension of gastric mucosa, n (%)	35 (85.4)
Islands of gastric mucosa, n (%)	10 (24.4)
Nodules in the lower esophagus, n (%)	3 (7.3)
Erosions in the lower esophagus, n (%)	4 (9.8)
Length of gastric mucosa in the esophagus, n	35
<0.5 cm, n (%)	14 (40)
0.5 cm- ≤ 1 cm, n (%)	11 (31.4)
1 - ≤ 2 cm, n (%)	8 (22.9)
≥ 2 cm, n (%)	2 (5.7)
Histopathology of the lower esophagus biopsy	10
Gastric metaplasia	6
Intestinal metaplasia	0
Dysplasia	0
Leiomyoma	1

Table 1: Endoscopic and histological changes in children with chronic gastroesophageal reflux disease and dyspepsia

Conclusion: Endoscopic changes in mucosa develop early in children with chronic dyspepsia and GERD although intestinal metaplasia and dysplasia are rare. Children with endoscopic changes in LE mucosa should be closely monitored for long-term outcomes.

Disclosure: Nothing to disclose.

P0089

EARLY DETECTION OF BARRETT'S ESOPHAGUS AND ESOPHAGEAL CANCER IN PRIMARY CARE USING TRANSNASAL ENDOSCOPY: A PROSPECTIVE COHORT STUDY

L. Huibertse¹, Y. Peters¹, P.D. Siersema¹

¹Radboud University Medical Center, Gastroenterology & Hepatology, Nijmegen, Netherlands

Contact E-Mail Address: y.peters@radboudumc.nl

Introduction: The ongoing increasing incidence of esophageal adenocarcinoma (EAC) during the last few decades and its dismal prognosis have stimulated interest in screening for EAC and its precursor Barrett's esophagus (BE). Screening programs to detect BE followed by endoscopic surveillance and treatment of dysplasia or early neoplasia seem able to reduce EAC incidence and improve survival. Although unsedated transnasal endoscopy (uTNE) is an accurate endoscopic procedure for the detection

of esophageal columnar epithelium only the American College of Gastroenterology considers uTNE to be an alternative to conventional esophago-gastroduodenoscopy (cEGD) for BE screening.

Aims & Methods: The primary aim of this prospective screening study was to assess the feasibility, diagnostic yield, and acceptability of BE/EAC screening using uTNE.

Patients aged 50-75 years who were diagnosed with reflux symptoms in primary care were eligible for participation. Patients underwent uTNE by an experienced endoscopist. BE was diagnosed by the presence of columnar epithelium of any length above the gastroesophageal junction during uTNE. All patients in whom BE was suspected during uTNE underwent cEGD to confirm the diagnosis and obtain biopsies according to the Seattle protocol (standard care). Confirmed BE was defined as the endoscopic presence of >1 cm of columnar epithelium combined with the presence of intestinal metaplasia in biopsies. Before and after uTNE, patients filled out questionnaires for tolerability.

Results: Between April 2021 and April 2022, 370 patients were invited to undergo screening using uTNE, of whom 166 patients were included in four different general practices (participation rate 44.9%; 95% CI 39.9-50.0). During uTNE, fourteen cases of BE were detected (8.4%) of which eleven were confirmed during cEGD. Two were not confirmed during cEGD because no intestinal metaplasia was detected in the obtained biopsies and one patient is scheduled for cEGD. Of the BE cases detected during uTNE, 85.7% were male (12/14), aged 53-74 years, and BE-length ranged from C0M1-C5M6. Other relevant endoscopic findings were reflux esophagitis grade A ($N = 18$, 10.8%), reflux esophagitis grade B ($N = 17$, 10.2%), reflux esophagitis grade C ($N = 3$, 1.8%), and hiatal hernia ($N = 37$, 22.4%). No dysplasia was detected in any of the biopsies. In 77 participants (46.4%), no abnormalities were found. No (severe) adverse events were seen. Mean patient tolerability measured using a validated 10-point visual analogue scale (VAS-scale) was 6.3 (0 being worst and 10 being best experience).

Conclusion: The diagnostic yield of detecting BE using uTNE followed by cEGD was 6.6% (95% CI 3.7-11.5) in patients with reflux symptoms in primary care. uTNE is a safe and well-tolerated alternative to cEGD as a screening tool for BE and EAC that can potentially be used in an office-based setting. As further evidence is needed on the yield of uTNE-guided biopsies to detect neoplasia, uTNE should only be used as a triage test, after which confirmatory cEGD is indicated when BE is suspected.

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P0090

MICROBIAL BIOMARKERS OF ESOPHAGEAL SQUAMOUS CELL CARCINOMA AND PRECANCEROUS LESIONS BY METAGENOMICS

M. Li¹

¹National Cancer Center/National Clinical Research Center for Cancer/Cancer Hospital, Chinese Academy of Medical Sciences and Peking Union Medical College, National Central Cancer Registry, Beijing, China

Contact E-Mail Address: liminjuan9@163.com

Introduction: Esophageal cancer is a kind of gastrointestinal cancer with heavy disease burden worldwide, in which esophageal squamous cell carcinoma (ESCC) is a main subtype. Early detection and early diagnosis are effective methods to decrease the mortality and morbidity of ESCC, and microbiota is associated with the progression of ESCC and precancerous lesions.

With the development of high-throughput sequencing, there is a high possibility and feasibility to early detect and early diagnose the high-risk population of ESCC and precancerous lesions from the view of microbial biomarkers.

Aims & Methods: Based on the national screening project of ESCC in China, we enrolled forty-five participants and collected esophageal swabs and epidemiological information from each participant. Specifically, there were nine in normal, nine in esophagitis, nine in low-grade intraepithelial neoplasia (LGIN), nine in high-grade intraepithelial neoplasia (HGIN), nine in ESCC. Metagenomic sequencing was performed on the Illumina Nova-Seq platform. The microbial diversity and microbial composition at species were analyzed based reads.

Results: There was no statistical difference of alpha diversity among normal, esophagitis, LGIN, HGIN, and ESCC. However, the beta diversity was significant, especially ESCC. Combined the results of LefSe, pairwise comparison in STAMP, and random forest, *Fusobacterium nucleatum* [3183], *Dialister pneumostintes* [2391], *Peptostreptococcus stomatis* [8192], *Streptococcus australis* [6321], *Porphyromonas gingivalis* [3008], and unknown *Neisseria* [3964] were associated with the progression of ESCC. Then, combine normal and esophagitis into one group, LGIN, HGIN, and ESCC into one group.

The decision tree showed only *Porphyromonas gingivalis* [3008], *Fusobacterium nucleatum* [3183], and *Streptococcus australis* [6321] were actually included, of which the accuracy was 82.22%.

Conclusion: Microbial biomarkers can be used for the early detection and early diagnosis of ESCC and its precancerous lesion, which can help concentrate the high-risk population of ESCC then save the resources of endoscopy screening.

Disclosure: Nothing to disclose.

P0091

CLINICAL OUTCOMES OF ENDOSCOPIC RESECTION FOR THE TREATMENT OF ESOPHAGEAL GASTROINTESTINAL STROMAL TUMORS: A TEN-YEAR EXPERIENCE FROM A LARGE TERTIARY CENTER IN CHINA

J.-X. Xu¹, T.-Y. Chen¹, Y.-B. Liu¹, Y.-Q. Zhang¹, P.-H. Zhou¹

¹Endoscopy Centre and Endoscopy Research Institute, Zhongshan Hospital, Fudan University, Shanghai, China

Contact E-Mail Address: xu.jiaxin1@zs-hospital.sh.cn

Introduction: Esophageal gastrointestinal stromal tumors (E-GISTs) are extremely rare and surgical resection is the recommended approach. However, surgical resection has large trauma that may cause significant postoperative morbidity. Endoscopic resection (ER) has developed rapidly recent years, and been widely used in gastrointestinal lesions. However, the feasibility and efficacy of ER in management of E-GISTs are unknown.

Aims & Methods: A total of 28 patients with E-GIST treated by ER were retrospectively collected from January 2011 to December 2020 in a large tertiary center of China.

Results: Of the 28 patients, there were 21 males and 7 females, with a median age of 55 years (40-70 years). The median tumor size was 15 mm (5-80mm). Complete resection rate was 100% (28/28), while en bloc resection rate was 96.4% (27/28). The median operation time was 35 minutes (10-410 minutes). Sixteen (57.2%) tumors were very low risk, six (21.4%) were low risk, six (21.4%) were high risk. The median hospital stay was 2 days (1-8 days). One patient suffered from hydrothorax and required drainage, leading to a major adverse event rate of 3.6% (1/28). There was no conversion to surgery, and no death during 30 days after the procedure. Imatinib was given to two patients after ER under the multidisciplinary team surveillance. During the median follow-up time of 54 months (9-122 months), no recurrences and metastasis were observed.

Conclusion: ER is safe and effective for E-GISTs, and become a promising choice in the future. Multicenter, prospective, large sample with long-term follow-up studies are still needed.

Disclosure: Nothing to disclose.

P0092

COMPREHENSIVE GENETIC ANALYSES IN CHRONIC ESOPHAGITIS AND ESOPHAGEAL SQUAMOUS CELL CARCINOMA CLASSIFIED BY THE SEVERITY OF LUGOL-VOIDING LESIONS

N. Akizue¹, K. Okimoto¹, T. Matsumura¹, T. Kaneko¹, Y. Ohta¹, T. Taida¹, K. Saito¹, J. Kato¹, N. Kato¹

¹Chiba University Hospital, Department of Gastroenterology, Chiba, Japan

Contact E-Mail Address: n.akizue@gmail.com

Introduction: It has been reported that the risk of carcinogenesis of chronic esophagitis varies according to the grade classification by Lugol-voiding lesions (LVLs). However, according to this classification, the differences in genetic characteristics in chronic esophagitis and esophageal squamous cell carcinoma (SCC) are still not apparent. The present study elucidated the details of genetic mutations in chronic esophagitis and esophageal SCC classified by grade of LVLs.

Aims & Methods: We extracted DNA from the background mucosa (Lugol's stained area) and SCC of 23 esophageal SCC cases, respectively. Next-generation sequencing analysis was performed using a system that targets all exon regions of 69 esophageal cancer-related genes to identify somatic mutations with leukocytes as controls. We also checked whether each mutation was oncogenic or not concerning OncoKB. All cases were classified according to the number of LVLs in one field of view (Grade A: 0, Grade B: 1-9, Grade C: 10-).

Results: Of the 23 cases, 5/11/7 were Grade A/B/C.

Patient age was 72(31-72)/73(54-77)/72(49-77) (p=0.272), and the proportion of women was 40%/10%/14% (p=0.308). The proportion of no smoking was 60%/18%/0% (p=0.042) and no drinking was 60%/0%/14% (p=0.013).

In the background mucosa (Grade A/B/C), 3.6/5.9/6 somatic mutations per case (p=0.117) were found. Oncogenic mutations per case (0.2/0.5/1.3) (p=0.038) were significantly more common in the grade C than in the grade A (p=0.013). (p=0.047, after Bonferroni correction).

Only one case in grade A had no mutation at all in the background mucosa. The other cases had at least one somatic mutation.

In SCC, 5.4/6.5/3.4 somatic mutations per case (p=0.450), and 1.0/1.5/0.8 oncogenic mutations per case (p=0.252) were detected.

Conclusion: Patients in grade A were significantly more likely to be non-drinkers and nonsmokers.

The background mucosa of SCC patients contained many genetic mutations, regardless of the grade of LVLs. However, chronic esophagitis caused by exposure to stronger carcinogens, such as drinking and smoking, may have more LVLs and obtain oncogenic mutations.

The results suggest that the risk of carcinogenesis may differ genetically depending on the grade classification of chronic esophagitis.

Disclosure: Nothing to disclose.

P0093

LONG-TERM OUTCOMES AND PROGNOSTIC FACTORS OF SUPERFICIAL ESOPHAGEAL CANCER IN PATIENTS AGED ≥ 65 YEARS

D.H. Jung¹, C.W. Huh²

¹Severance Hospital, Yonsei University College of Medicine, Internal Medicine, Seoul, Korea (Republic of), ²Yongin Severance Hospital, Yonsei University College of Medicine, Internal Medicine, Yongin, Korea (Republic of)

Contact E-Mail Address: leah10042@gmail.com

Introduction: The number of elderly patients with superficial esophageal cancer (SEC) is increasing.

Aims & Methods: We aimed to evaluate the clinical outcomes and prognostic factors of overall survival (OS) in elderly patients undergoing endoscopic submucosal dissection (ESD) or surgical resection for SEC. Between January 2001 and May 2020, 290 patients aged ≥ 65 years who underwent ESD or surgical resection for SEC were evaluated. Their clinical outcomes and prognosis were assessed, and independent risk factors for OS were identified.

Results: The mean patient age (269 men and 21 women) was 70.9 years (range 65-90 years). En bloc, R0, and curative resections were achieved in 94.5%, 90.0%, and 73.4% of the patients, respectively. During the follow-up (mean: 54.6 months [range: 1-210 months]), 79 patients died. The 3-, 5-, and 10-year OS rates were 82.5%, 73.1%, and 59.7%, respectively.

In multivariate analysis, cancer history of the other organs, American Society of Anesthesiologists performance status, and presence of lympho-vascular involvement (hazard ratio=1.852, 1.656, and 1.943, respectively; all $P < 0.05$) were independent risk factors for poor OS. The high-risk group (≥ 2 risk factors) showed a significantly lower OS than the low-risk group (≤ 1 risk factor) ($P < 0.001$).

Conclusion: The three risk factors could be useful in predicting the long-term prognosis of elderly patients with SEC.

Disclosure: Nothing to disclose.

P0094

SCREENING FOR METACHRONOUS ESOPHAGEAL SECOND PRIMARY TUMORS IN PATIENTS WITH HEAD AND NECK CANCER

L. van Tilburg¹, S.E.M. van de Ven¹, P.J. de Jonge¹, W. de Graaf¹, M.C.W. Spaander¹, S. Nikkessen¹, J.A. Hardillo², A. Sewnaik², D.A. Monserez², H. Mast³, S. Keereweer², M.J. Bruno¹, R.J. Baatenburg de Jong², A.D. Koch¹

¹Erasmus Medical Center, Gastroenterology and Hepatology, Rotterdam, Netherlands, ²Erasmus Medical Center, Otorhinolaryngology and Head and Neck Surgery, Rotterdam, Netherlands, ³Erasmus Medical Center, Oral and Maxillofacial surgery, Rotterdam, Netherlands

Contact E-Mail Address: l.vantilburg@erasmusmc.nl

Introduction: Patients with head and neck squamous cell carcinoma (HNSCC) frequently develop second primary tumors (SPTs) in the esophagus or stomach. Metachronous screening could lead to timely detection of SPTs in early stages and therefore improves the survival in these patients.

Aims & Methods: We conducted a metachronous screening study in patients with HNSCC in a Western country. Patients with HNSCC in the oropharynx, hypopharynx or other sub-locations with alcohol abuses diagnosed between January 2017 and August 2020 were included. Included patients received curative treatment and routine follow-up for HNSCC. A metachronous screening esophagogastrroduodenoscopy (EGD) was performed more than 6 months after HNSCC diagnosis.

Primary outcome was the incidence of SPTs, defined as presence of high grade dysplasia (HGD), esophageal squamous cell carcinoma (ESCC) or any other cancer in the upper gastrointestinal tract.

Results: 120 patients (78% male, median age 65 years) were included. HNSCC was located in the oropharynx (32%), larynx (27%), hypopharynx (24%), or oral cavity (17%).

In total, 9 SPTs were detected in 7 patients (6%). 53 (44%) of the included patients had undergone previous synchronous screening, leading to the detection of 3 early-stage SPTs (2 HGD, 1 ESCC). Metachronous screening was performed within 2 years (54%), 2-3 years (15%), or 3-5 years (31%) after HNSCC diagnosis.

SPTs were detected in 6 (5%) patients (2 HGD, 3 ESCC, 1 esophageal adenocarcinoma). Most SPTs (5/6) were detected in early stages and could be curatively treated with endoscopic resection. No SPTs were detected with routine follow-up imaging for HNSCC prior to metachronous screening.

Conclusion: Metachronous SPTs in the esophagus or stomach were detected in 5% of patients with HNSCC. Metachronous screening for SPTs should be considered in a selection of HNSCC patients.

Disclosure: Nothing to disclose.

P0095

ESOPHAGEAL STENTING FOR ESOPHAGOGASTRIC CANCER PALLIATION: HOW TO PROSPECTIVELY EVALUATE QUALITY OF LIFE?

C. Pinto¹, R. Ortigão², I. Pita¹, C. Costa¹, P. Pedrosa¹, C. Taveira¹, P. Medeiros³, P. Redondo³, R.P. Bastos¹, P. Pimentel-Nunes¹, R. Silva¹, M. Dinis-Ribeiro¹

¹Portuguese Oncology Institute of Porto, Gastroenterology, Porto, Portugal, ²Portuguese Oncology Institute of Porto, Gastroenterology, Porto, Portugal, ³Portuguese Oncology Institute of Porto, Pathology, Porto, Portugal

Contact E-Mail Address: claudia.marquespinto@gmail.com

Introduction: Esophageal stents have a well-established role in the palliation of esophageal and esophagogastric cancers. However, there is little prospective data on the impact of esophageal stenting in patients' quality of life (QoL).

Aims & Methods: Our aim was to evaluate the feasibility of a web-based app to assess the impact of esophageal stenting in the QoL of patients with esophageal malignancy.

Prospective study from August 2017 to October 2019. Three validated questionnaires (EORTC-QLQ-C30, QLQ-OES18 and QLQ-OG25) were incorporated in a smartphone app.

Questionnaires were applied to esophagogastric cancer patients before stent placement (baseline) and at three moments after stenting (30, 90 and 180 days), directly through a smartphone app or during a nursing phone consultation. Answers were wirelessly transmitted to the statistics department for analysis.

Results: Eighty esophageal or esophagogastric stents were placed in 72 patients, with an immediate success rate of 100% and no immediate complications.

Ten patients died at 30 days. Sixty-eight patients (94%) answered the baseline QoL questionnaire, 23 at 30 days, 12 at 90 days and 4 at 180 days. We included 23 patients for QoL analysis at 30 days post-stenting: 23 for global health status (QLQ-30) and 15 for esophageal symptoms (QLQ-OES18).

There was a significant improvement in swallowing saliva (mean score 44vs73, $p=0.017$) and constipation (mean score 55vs86, $p=0.015$) and a tendency for dysphagia improvement (37vs61, $p=0.05$) There was a mean score improvement ≥ 10 points in global health status, although not statistically significant.

Conclusion: QoL assessment is paramount to evaluate the effectiveness of endoscopic palliative techniques. In this study, prospective QoL evaluation of stent palliation for esophageal malignancy was feasible and consistent with an improvement in QoL. The main constraint was to abstain from involving health professionals during the follow-up.

Disclosure: Nothing to disclose.

P1027

BLUE LIGHT IMAGING AND LINKED COLOR IMAGING AS A SCREENING MODE FOR ESOPHAGEAL SQUAMOUS CELL CARCINOMA IN HIGH-RISK PATIENTS: A MULTICENTRE RANDOMIZED CONTROLLED TRIAL

Y. Ogata¹, W. Hatta¹, T. Koike¹, S. Takahashi², T. Matsushashi², T. Oikawa³, W. Iwai³, S. Asonuma⁴, H. Okata⁴, M. Ohyauchi⁵, H. Ito⁵, Y. Abe⁶, Y. Sasaki⁶, M. Kawamura⁷, M. Saito¹, K. Uno¹, K. Iijima², A. Masamune¹

¹Tohoku University Graduate School of Medicine, Division of Gastroenterology, Sendai, Japan, ²Akita University Graduate School of Medicine, Department of Gastroenterology, Akita, Japan, ³Miyagi Cancer Centre, Department of Gastroenterology, Natori, Japan, ⁴South Miyagi Medical Centre, Department of Gastroenterology, Shibata-gun, Japan, ⁵Osaki Citizen Hospital, Department of Gastroenterology, Osaki, Japan, ⁶Yamagata University, Faculty of Medicine, Department of Gastroenterology, Yamagata, Japan, ⁷Sendai City Hospital, Department of Gastroenterology, Sendai, Japan

Contact E-Mail Address: gmaps177@gmail.com

Introduction: For curative treatment of esophageal squamous cell carcinoma (ESCC), detection of ESCC at early stage is mandatory. The effectiveness of image-enhanced endoscopy (IEE) for early detection of gastrointestinal neoplasms has been reported. A randomized trial demonstrated that narrow band imaging (NBI), which enables narrow light observation similar to blue light imaging (BLI), had higher detection of ESCC than white light imaging (WLI) had. In another randomized trial, linked color imaging (LCI), which is one of the IEE to emphasize color contrast, was more effective than WLI for detecting neoplastic lesions in the pharynx, esophagus, and stomach. However, it remains to be elucidated which of BLI/NBI or LCI is optimal as a screening mode for ESCC.

Aims & Methods: The aim of this study was to compare the diagnostic performance of BLI with that of LCI in ESCC screening. This is a prospective, multicenter randomized controlled trial (the trial number: JRCT1022190018). Patients with high-risk for ESCC (defined as follows: previous ESCCs or HNSCCs treated with endoscopic resection or radiation therapy, and present HNSCCs) were enrolled and randomly assigned to either primary BLI group (BLI during insertion, followed by LCI during withdrawal) or primary LCI group (LCI during insertion, followed by BLI during withdrawal). Pathological diagnosis of ESCC in biopsy following Lugol chromoendoscopy was regarded as gold standard. The primary endpoint was the detection rate of ESCC in the primary mode. The secondary endpoints included (1) the miss rate of ESCC in the primary mode and (2) the diagnostic parameters, including sensitivity, in the primary mode.

Results: Between January 2020 and April 2021, 351 patients were assigned to the BLI group and 348 to the LCI group. The detection rate of ESCC in the primary mode was 4.0% (14/351) in the BLI group and 4.9% (17/348) in the LCI group, with no significant difference (risk ratio, 0.82; $p = 0.587$) (Table). However, the number of patients with ESCC in the BLI group (19 patients with 20 lesions) tended to be lower than that in the LCI group (30 patients with 42 lesions) ($p = 0.097$). The miss rate of ESCC in the BLI group was significantly lower than that in the LCI group (26.3% [5/19] vs. 63.3% [19/30]; risk ratio, 0.42; $p = 0.012$); in particular, no cases (0/5)

with ESCCs missed by BLI was detected by LCI. In per-lesion analysis, the sensitivity of BLI was significantly higher than that of LCI (75.0% vs 47.6%; $p = 0.042$). On the other hand, the positive predictive value of BLI tended to be lower than that of LCI (28.8% vs 46.5%; $p = 0.076$).

	BLI group	LCI group	RR (95% CI)	pvalue
Patients with ESCC, n/N (%)	19/351 (5.4)	30/348 (8.6)		0.097
Detected by primary mode	14/351 (4.0)	17/348 (4.9) [†]	0.82 (0.41–1.63)	0.565
Missed by primary mode	5/19 (26.3)	19/30 (63.3) [†]	0.42 (0.19–0.92)	0.012
Detected by secondary mode	0/19 (0.0)	15/30 (50.0)		
Detected by Lugol chromoendoscopy	5/19 (26.3)	4/30 (13.3)		

[†] Six patients in the LCI group had both lesions detected and missed by primary mode.

Table. Detection and miss rates of ESCC in each group.

Conclusion: BLI had better diagnostic performance for ESCC than LCI except the detection which would have been affected by the imbalanced prevalence of ESCCs. BLI has the potential to be the standard screening mode for ESCC in high-risk patients.

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P0096

CAN CONCOMITANT USE OF H2RA PLAY AN IMPORTANT ROLE IN PREVENTING THE GASTRIC MUCOSAL INJURIES LIKE P-CAB OR PPI IN PATIENTS TAKING ASPIRIN?

Y. Shimada¹, R. Om¹, Y. Aonuma¹, S. Arii¹, Y. Kita², Y. Ikeda¹, K. Nomura¹, S. Sato¹, A. Murata¹, S. Sato¹, A. Nagahara², T. Genda¹

¹Juntendo University Shizuoka Hospital, Gastroenterology and Hepatology, Izunokuni-city, Japan, ²Juntendo University School of Medicine, Gastroenterology and Hepatology, Tokyo, Japan

Contact E-Mail Address: yshimada@juntendo.ac.jp

Introduction: The mechanism of aspirin-induced gastric mucosal injury is thought to be mediated by multiple processes involving either topical or systemic effects. Recently, it has been found that topical effects play a pivotal role in causing gastric mucosal injury ⁽¹⁾.

In addition, it is revealed that almost all aspirin-induced gastric mucosal injuries were observed in low intragastric pH condition (pH<4) ⁽²⁾.

Therefore, concomitant use of antacids is the standard strategy in preventing aspirin-induced gastric mucosal injury. However, it is not well known how differences in antacids affect the severity of gastric mucosal injuries in patients taking aspirin.

Aims & Methods: The aim of this study is to reveal the differences in preventing ability from aspirin-induced mucosal injuries between histamine-2 receptor antagonist (H2RA) users and proton pump inhibitor (PPI) or potassium competitive acid blocker (P-CAB) users.

This is a case-controlled study conducted at our department. Data were extracted from the records of subjects who underwent upper gastrointestinal endoscopy at our department between April 2015 and March 2020. We focused on the subjects taking only aspirin as an anti-thrombotic agent. We divided into three groups; concomitant use of P-CAB or PPI group (P group), concomitant use of H2RA group (H group) and NO concomitant use of antacids group (N group). In each group, we compared the severity of

gastric mucosal injury, individually. Severity of gastric mucosal injury was evaluated endoscopically according to the modified LANZA score (MLS)^(3,4). Statistical analyses were performed by using Fisher's exact test.

Results: 310 subjects out of 6,031 were taking aspirin. In P group (134 men, 54 women; mean age 72.8 years), average MLS was 0.54±1.32. In H group (11 men, 4 women; mean age 70.1 years), average MLS was 0.67±1.50. In N group (61 men, 46 women; mean age 74.4 years), average MLS was 0.93±1.60. Average MLS in P group was statistically significantly lower than that in N group (p=0.024), but average MLS in H group was not lower than that in N group (p=0.542).

Conclusion: It is suggested that the concomitant use of H2RA is not sufficient in preventing aspirin-induced gastric mucosal injuries. We strongly recommend P-CAB or PPI as antacids for patients taking aspirin to prevent gastric mucosal injuries.

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Disclosure: Nothing to disclose.

P0097

RANDOMIZED CLINICAL TRIAL: EFFICACY AND SAFETY OF FEXUPRAZAN IN PATIENTS WITH ACUTE OR CHRONIC GASTRITIS

G.H. Kim¹, M.-G. Choi², J.I. Kim³, S.T. Lee⁴, H.J. Chun⁵, K.L. Lee⁶, S.C. Choi⁷, J.-Y. Jang⁸, Y.C. Lee⁹, J.G. Kim¹⁰, K.B. Kim¹¹, K.-N. Shim¹², C.I. Sohn¹³, S.K. Kim¹⁴, S.G. Kim¹⁵, J.S. Jang¹⁶, N. Kim¹⁷, H.-Y. Jung¹⁸, H. Park¹⁹, K.C. Huh²⁰, K.J. Lee²¹, S.J. Hong²², S. Baek²³, J.J. Han²³, O.Y. Lee²⁴

¹Department of Internal Medicine, Pusan National University College of Medicine, and Biomedical Research Institute, Pusan National University Hospital, Busan, Korea (Republic of),

²Department of Internal Medicine, Seoul St. Mary's Hospital, College of Medicine, The Catholic University of Korea, Seoul, Korea (Republic of), ³Department of Internal Medicine, Yeouido St. Mary's Hospital, College of Medicine, The Catholic University of Korea, Seoul, Korea (Republic of),

⁴Department of Internal Medicine, Chonbuk National University Hospital, Jeonju, Korea (Republic of), ⁵Department of Internal Medicine, Korea University Anam Hospital, Seoul, Korea (Republic of),

⁶Department of Internal Medicine, SMG-SNU Boramae Medical Center, Seoul National University of College of Medicine, Seoul, Korea (Republic of), ⁷Department of Internal Medicine, Wonkwang University College of Medicine and Hospital, Iksan, Korea (Republic of),

⁸Department of Gastroenterology and Hepatology, College of Medicine, Kyung Hee University, Seoul, Korea (Republic of), ⁹Department of Internal Medicine, Yonsei University College of Medicine, Seoul, Korea (Republic of),

¹⁰Department of Internal Medicine, Chung-Ang University College of Medicine, Seoul, Korea (Republic of), ¹¹Department of Internal Medicine, Chungbuk National University Hospital, Chungbuk National University College of Medicine, Cheongju, Korea (Republic of),

¹²Department of Internal Medicine, Ewha Womans University College of Medicine, Seoul, Korea (Republic of), ¹³Department of Internal Medicine, Kangbuk Samsung Hospital, Sungkyunkwan University School of Medicine, Seoul, Korea (Republic of),

¹⁴Department of Internal Medicine, School of Medicine, Kyungpook National University, Daegu, Korea (Republic of), ¹⁵Department of Internal Medicine, Seoul National University College of Medicine, Seoul, Korea (Republic of),

¹⁶Department of Internal Medicine, Dong-A University College of Medicine, Busan, Korea (Republic of), ¹⁷Department of Internal Medicine, Seoul National University Bundang Hospital, Seoul National University College of Medicine, Seoul, Korea (Republic of),

¹⁸Department of Gastroenterology, Asan Medical Center, University of Ulsan College of Medicine, Seoul, Korea (Republic of), ¹⁹Department of Internal Medicine, Gangnam Severance Hospital, Yonsei University College of Medicine, Seoul, Korea (Republic of),

²⁰Division of Gastroenterology, Department of Internal Medicine, Konyang University College of Medicine, Daejeon, Korea (Republic of), ²¹Department of Gastroenterology, Ajou University School of Medicine, Suwon, Korea (Republic of),

²²Department of Internal Medicine, Soonchunhyang University College of Medicine, Bucheon, Korea (Republic of), ²³Daewoong Pharmaceutical Co., Ltd., Seoul, Korea (Republic of),

²⁴Department of Internal Medicine, Hanyang University College of Medicine, Seoul, Korea (Republic of)

Contact E-Mail Address: doc0224@pusan.ac.kr

Introduction: Fexuprazan is a novel potassium-competitive acid blocker that could benefit patients with gastric mucosal injury.

Aims & Methods: We aimed to assess the efficacy and safety of fexuprazan for 2 weeks in patients with acute or chronic gastritis. In this study, 327 patients with acute or chronic gastritis who had one or more gastric

erosions on endoscopy and subjective symptoms were randomised into three groups receiving fexuprazan 20 mg q.d., fexuprazan 10 mg b.i.d., or a placebo for 2 weeks. The post-treatment assessments were the primary endpoint (erosion improvement rate), secondary endpoints (cure rates of erosion and oedema and improvement rates of redness, haemorrhage, and subjective symptoms) and drug-related adverse events.

Results: Among the patients, 57.8% (59/102), 65.7% (67/102), and 40.6% (39/96) showed erosion improvement 2 weeks after receiving fexuprazan 20 mg q.d., fexuprazan 10 mg b.i.d., and the placebo, respectively. Both fexuprazan 20 mg q.d. and 10 mg b.i.d. showed an efficacy superior to that of the placebo. Likewise, both fexuprazan 20 mg q.d. and 10 mg b.i.d. also showed erosion healing rates higher than that of the placebo.

No difference was noted in the oedema healing rate and the improvement rates of redness, haemorrhage, and subjective symptoms between the fexuprazan and placebo groups. No significant difference was noted in the incidence of adverse drug reactions.

Full analysis set	Fexuprazan 20 mg q. d.	Fexuprazan 10 mg b.i.d.	Placebo
No. of patients	102	102	96
Erosion improvement rate (%)	59 (57.8)	67 (65.7)	39 (40.6)
Common risk difference (95% CI)	17.0 (3.3–30.6)	25.1 (11.7–38.6)	
P-value (compared with the placebo group)	0.0167	0.0004	

Table

Conclusion: Using fexuprazan 20 mg q.d. and 10 mg b.i.d. for 2 weeks showed therapeutic efficacy superior to that of the placebo and a favourable safety profile in patients with acute or chronic gastritis.

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Disclosure: The corresponding author, Lee OY, had been a member of outside directors at the Daewoong Pharmaceutical Co., Ltd, from the period March 24 2018 to Nov 2 2021. All other authors declare no conflict of interest regarding this study.

P0098

THE EFFICACY AND SAFETY OF KEVERPRAZAN (H008) IN THE TREATMENT OF DUODENAL ULCER: A MULTICENTERED, RANDOMIZED, DOUBLE-BLIND, ACTIVE-CONTROL TRIAL IN CHINA

N. Tan¹, X. Miao², A. Liao³, C. Liu⁴, H. Wu⁵, H. Chen⁶, F. Li⁷, Q. Guo⁸, S. Li⁹, Y. Tang¹⁰, M. Xia¹¹, Y. Liu¹², X. Li¹³, H. Chen¹⁴, X. Liu¹⁵, Y. Zhang¹⁶, Z. Zhang¹⁷, M. Su¹⁸, M. Chen¹, Y. Xiao¹

¹The First Affiliated Hospital, Sun Yat-Sen University, Department of Gastroenterology, Guangzhou, China, ²Hainan Central Hospital, Department of Gastroenterology, Haikou, China, ³The First Hospital, University of South China, Department of Gastroenterology, Hengyang, China, ⁴Binzhou Medical University Hospital, Department of Gastroenterology, Binzhou, China, ⁵The Second Affiliated Hospital and Yuying Children's hospital of WMM, Department of Gastroenterology, Wenzhou, China, ⁶The Second Hospital, University of South China, Department of Gastroenterology, Hengyang, China, ⁷Chenzhou First People's Hospital, Department of Gastroenterology, Chenzhou, China, ⁸The First Hospital of Lanzhou University, Department of Gastroenterology, Lanzhou, China, ⁹Taihe Hospital, Department of Gastroenterology, Shiyan, China, ¹⁰Tianjin Hospital of ITCWM Nankai Hospital, Department of Gastroenterology, Tianjin, China, ¹¹Wuxi People's Hospital, Department of Gastroenterology, Wuxi, China, ¹²The People's Hospital of Xuancheng City, Department of Gastroenterology, Xuancheng, China, ¹³JiangXi PingXiang People's Hospital, Department of Gastroenterology, Pingxiang, China, ¹⁴Huizhou Municipal Central Hospital, Department of Gastroenterology, Huizhou, China, ¹⁵Xiangya Hospital Central South University, Department of Gastroenterology, Changsha, China, ¹⁶Zigong Fourth People's Hospital, Department of Gastroenterology, Zigong, China, ¹⁷Nanjing First Hospital, Department of Gastroenterology, Nanjing, China, ¹⁸Jiangsu Carephar Pharmaceutical Co., Ltd, Pharmaceutical Research Institute, Nanjing, China

Contact E-Mail Address: tannd3@mail.sysu.edu.cn

Introduction: Keverprazan is a novel potassium-competitive acid blocker for the treatment of acid-related disorders.

Aims & Methods: This study aimed to establish the non-inferiority of keverprazan to lansoprazole in patients with duodenal ulcer (DU).

In this phase III, double-blind, multicentered study, 360 Chinese patients with endoscopically confirmed active DU were randomized 1:1 to either keverprazan (20 mg) or lansoprazole (30 mg) treatment groups for up to 6 weeks.

The primary endpoint was DU healing rate at 6 weeks. The secondary endpoints were DU healing rate at 4 weeks and symptom improvement. Safety was also assessed.

Results: Full analysis set showed the cumulative healing rates at week 6 were 94.44% (170/180) and 93.26% (166/178) for keverprazan and lansoprazole, respectively (difference: 1.19%; 95% CI: -4.03% to 6.54%). At week 4, the respective healing rates were 83.89% (151/180) and 80.34% (143/178).

Per-protocol set showed the 6-week healing rates with keverprazan and LPZ were 98.19% (163/166) and 97.60% (163/167), respectively (difference: 0.59%; 95% CI: -3.08% to 4.42%); the 4-week healing rates were respectively 86.75% (144/166) and 85.63% (143/167).

Keverprazan was non-inferior to lansoprazole in DU healing at 4 and 6 weeks. The incidence of treatment-emergent adverse events was comparable among groups.

	Keverprazan (n=180)	Lansoprazole (n=178)	Pvalue
TEAEs, patients (%)	104 (57.78)	105 (58.99)	0.8309
Mild	92(51.11)	101(56.74)	
Moderate	11(6.11)	4(2.25)	
Severe	1(0.56)	0(0.00)	1.0000
Study drug related	46 (25.56)	58 (32.58)	0.1627
Leading to study drug discontinuation	3 (1.67)	2 (1.12)	1.0000
Leading to study drug discontinuation (study drug-related)	1 (0.56)	1 (0.56)	1.0000
Serious adverse events	3 (1.67)	1 (0.56)	0.6229
Serious adverse events (study drug-related)	1 (0.56)	0	1.0000
TEAEs, treatment-emergent adverse events.			

Table 1. Treatment-emergent adverse events and serious adverse events (safety analysis set).

Conclusion: Keverprazan 20 mg was not inferior to lansoprazole 30 mg once daily for healing of DU with a good safety profile.

Disclosure: Nothing to disclose.

P0099

DEVELOPMENT AND VALIDATION OF A NOMOGRAM PREDICTING THE OVERALL SURVIVAL FOR PATIENTS WITH PRIMARY GASTRIC MUCOSA-ASSOCIATED LYMPHOID TISSUE LYMPHOMA: A SEER-BASED STUDY

D. Wang¹, X. Shi², W. Xu³, R. Shi³

¹Clinical Medical School of Southeast University, Zhongda Hospital, Affiliated Hospital of Southeast University, Gastroenterology, Nanjing, China, ²Affiliated Hospital of Yangzhou University, Respiratory and Critical Care Medicine, Yangzhou, China, ³Zhongda Hospital, Affiliated Hospital of Southeast University, Gastroenterology, Nanjing, China

Contact E-Mail Address: wd920625@sina.com

Introduction: Increasingly extranodal marginal B-cell lymphoma of mucosa-associated lymphoid tissue, known as MALT lymphoma, is a type of non-Hodgkin's lymphoma. Approximately one-third of cases of MALT lymphoma and 85% of gastrointestinal MALT lymphomas present in the stomach as the affected site¹. Primary MALT lymphoma (GML) has a rare incidence and only accounts for approximately 5% of all primary gastric neoplasms².

This disease demands high attention. Researchers have observed that GML patients had significant risk of atrophic gastritis, intestinal metaplasia and secondary tumors³. Compared to the healthy population, the incidence of gastric adenocarcinoma in GML patients was 6 times higher in the GML population⁴.

The prognosis of primary GML patients can be affected by many factors. Clinical risk factors, including age, type of therapy, sex, stage and family hematologic malignancy history, also have significant effects on the development of the disease⁵. Meanwhile, previous studies demonstrated a good prognosis of the disease, with 5-year survival rates of up to 99%. However, more than 95% of studies were only based on stage I/II patients with a small sample size, and few of them even used different staging standards^{6,7}.

Matysiak-Budnik, T *et al.*⁸ conducted a multicenter study in France, and 416 GML patients were retrospectively enrolled. They surprisingly found that 25% of subjects diagnosed at stage III/IV and 11% of patients obtained missed or false diagnoses, which was similar to other studies.

Furthermore, the available data are mainly focused on epidemiology; in contrast, few studies have investigated the prognostic variables for overall survival (OS) in patients with primary GML. Based on the realities above, we searched a large amount of data on patients diagnosed with primary GML in the SEER database. The aim was to develop and verify a survival nomogram model that can predict the OS prognosis of primary GML by combining prognostic and determinant variables.

Aims & Methods: Aim: To create an effective survival nomogram for patients with primary gastric mucosa-associated lymphoid tissue (MALT) lymphoma (GML).

Methods: All data of patients with primary GML from 2004 to 2015 were collected from the Surveillance, Epidemiology, and End Results (SEER) database. The primary endpoint was overall survival (OS). Based on the LASSO and COX regression, we created and further verified the accuracy and effectiveness of the survival nomogram model by the concordance index (C-index), and time-dependent receiver operating characteristic (td-ROC) curves.

Results: A total of 2604 patients diagnosed with primary GML were selected for this study. A total of 1823 and 781 people were randomly distributed into the training and testing sets at a ratio of 7:3. The median follow-up of all patients was 71 months, and the 3- and 5-year OS rates were 87.2% and 79.8%, respectively. Age, sex, race, Ann Arbor stage and radiation were independent risk factors for OS of primary GML (all $p < 0.05$). The C-index values of the nomogram were 0.751 (95% CI: 0.729-0.773) and 0.718 (95% CI: 0.680-0.757) in the training and testing cohorts, respectively, showing the good discrimination ability of the nomogram model. Td-ROC curves and calibration plots also indicated satisfactory predictive power and good agreement of the model. Overall, the nomogram shows favorable performance in discriminating and predicting the OS of patients with primary GML.

Conclusion: Nomograms are a low-cost and convenient clinical tool in assessing individualized prognosis and treatment for patients with primary GML.

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P0100

LOCAL RECURRENCE AFTER ENDOSCOPIC SUBMUCOSAL DISSECTION OF EARLY GASTRIC CANCER

C.W. Choi¹, D.G. Ryu¹, D.-H. Kang², H.W. Kim³, S.B. Park³, S.-J. Kim¹, H.S. Nam¹

¹Pusan National University Yangsan Hospital, Yangsan, Korea (Republic of), ²Pusan National University Hospital, Gastroenterology, Pusan, Korea (Republic of), ³Pusan National University Yangsan Hospital, Internal Medicine, Yangsan, Korea (Republic of)

Contact E-Mail Address: luckyace@hanmail.net

Introduction: Endoscopic submucosal dissection (ESD) is considered the treatment of choice for early gastric cancer (EGC) with a negligible risk of lymph node metastasis. However, locally recurrent lesions on artificial ulcer scars are difficult to manage.

Therefore, predicting the risk of local recurrence after ESD is important to manage and prevent the event. This study aimed to elucidate risk factors associated with local recurrence after ESD of EGC.

Aims & Methods: Between November 2008 and February 2016, consecutive patients (n=641; mean age, 69.3±9.5 years; men, 77.2%) with EGC who underwent ESD at a single tertiary referral hospital were retrospectively analyzed to evaluate the incidence and factors associated with local recurrence. Local recurrence was defined as the development of neoplastic lesions at or adjacent to the site of the post-ESD scar.

Results: En bloc and complete resection rates were 97.8% and 93.6%, respectively. The local recurrence rate after ESD was 3.1%. The mean follow-up period after ESD was 50.7±32.5 months. One case of gastric cancer-related death (0.15%) was noted, wherein the patient had refused additive surgical resection after ESD for EGC with lymphatic and deep submucosal invasion. Lesion size ≥15 mm, incomplete histologic resection, undifferentiated adenocarcinoma, scar, and absence of erythema of the surface were associated with a high risk of local recurrence.

Conclusion: Predicting local recurrence during regular endoscopic surveillance after ESD is important, especially in patients with a larger lesion size (≥15 mm), incomplete histologic resection, surface changes of scars, and no erythema of the surface.

Disclosure: We have no conflicts of interest or financial ties to disclose.

P0101

INVESTIGATING IDA: LARGE-SCALE DATA SHOWING PERSISTENT GAPS AT THE FRONT DOOR

G. Howell¹, A. Thumbe², M.N. Quraishi¹, N. Adderley³, D. Lasserson⁴, K. Nirantharakumar⁵, E. Sapey⁶, N. Sharma¹, T. Iqbal¹, N. Bhala¹

¹University Hospitals Birmingham NHS Foundation Trust, Gastroenterology, Birmingham, United Kingdom, ²Liverpool University Hospitals Foundation Trust, Liverpool, United Kingdom, ³University of Birmingham, Public Health, Epidemiology & Biostatistics Institute of Applied Health Research, Birmingham, United Kingdom, ⁴University of Warwick, Coventry, United Kingdom, ⁵University of Birmingham, Institute of Applied Health Research, Birmingham, United Kingdom, ⁶University of Birmingham, Institute of Inflammation and Ageing, Birmingham, United Kingdom

Contact E-Mail Address: ghowell6@doctors.org.uk

Introduction: Iron deficiency anaemia (IDA) can be a sign of serious underlying disease but is often overlooked. Recently updated guidelines of the British Society of Gastroenterology (BSG) recommend male and post-menopausal female patients with IDA should be screened for coeliac disease and undergo dual endoscopy (or CT).

Aims & Methods: This project looked to assess current adherence to these guidelines at the Queen Elizabeth Hospital in Birmingham, England.

A retrospective audit was performed using health informatics for patients who attended AMU/CDU from April 2018 to March 2021. The number of patients with IDA in this time frame was identified.

A further analysis of this group was made to determine the proportion of patients with IDA who had IgA TTG measured as well as those who had OGD and colonoscopy/CT colonoscopy requested.

Results: There were 67797 patients in this study period. 32422 (47.8%) were anaemic (Hb < 120g/dl for women, <130g/dl for men as per WHO guidelines) of which 6357 (19.6%; 9.38% of total) had a microcytic anaemia (MCV <83 as per University Hospitals Birmingham laboratory reference range). Ferritin was tested in 3337 (52.5%) of this group, and of those, 1041 (31.2%) were found to have overt IDA (ferritin <30 µg/mL).

Rate of investigation.

The patient cohort with confirmed IDA comprised 334 males (32.0%), 556 post-menopausal females (53.4%, defined as age ≥45) and 151 pre-menopausal females (14.5%). A further analysis was made to explore how male and post-menopausal female cases were investigated, and if the rate of investigation was affected by the COVID-19 pandemic from 1st March 2020 onwards in this subgroup.

Results are shown in the table below. In general, only a minority of patients underwent further investigation with males more likely to undergo OGD than females. Surprisingly, apart from increased TTG check latterly, little difference was seen after onset of the COVID-19 pandemic.

	Total patients in study		Effect of COVID-19 pandemic	
Patients with confirmed IDA	Male	Post-menopausal females	1 st April 2018 – February 28 th 2020 (pre-pandemic) ¹	1 st March 2020 – 31 st March 2021 (during pandemic) ¹
Number	334	556	488	432
TTG screened	23 (6.89%)	34 (6.12%)	12 (2.46%)	45 (10.4%)
OGD	144 (43.1%)	150 (27.0%)	167 (34.2%)	130 (30.1%)
Colonoscopy/CT colon	61 (18.3%)	77 (13.8%)	73 (15.0%)	65 (11.9%)

¹ = 30 patients had admissions during both time periods so counted in both columns

Table.

Conclusion: This large-scale study found that only a small minority of patients with IDA underwent further investigation. Whilst the study period includes the pandemic era, our results don't suggest this made a significant impact on practice. Nevertheless, these findings indicate a strong need for increased awareness and quality improvement about optimising IDA investigation according to BSG guidelines.

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Disclosure: None.

P0102

GASTRIC XANTHOMA: YELLOW TRAFFIC LIGHT ALSO IN THE WESTERN WORLD

S. Molina Tejedor¹, V. Roales Gómez¹, E. Velasco Martínez¹, I. Blanco Nodal¹, M. Machín Delgado¹, I. Cacho Soblecherro¹, C. López Martínez¹, E. Rey Díaz-Rubio¹

¹Hospital Clínico San Carlos, Gastroenterology, Madrid, Spain

Contact E-Mail Address: smolinat@salud.madrid.org

Introduction: Gastric xanthomas (GX) are benign lesions with a whitish and granular appearance, characterized by the accumulation of lipids in foamy macrophages. Its presence is usually an incidental finding during upper endoscopies and its prevalence varies between 0.23-7%. It is most common in the antral and prepyloric areas.

In recent years, gastric xanthomas have been associated with atrophy, intestinal metaplasia (IM) and early gastric cancer located in the perixanthomatous region. This suggests that GX could be a useful marker to predict advanced gastric lesions.

Previous studies mostly have focused on Asian populations, and evidence in Western populations is very limited.

Aims & Methods: The aim of this study is to evaluate in a sample of western subjects whether gastric xanthoma is associated with a higher prevalence of IM, dysplasia, atrophy or adenocarcinoma relative to the general dyspeptic population.

It is a retrospective, observational and descriptive study.

The sample includes 116 cases of patients in whom a gastric xanthoma was clearly identified during an endoscopy. We also include 116 controls, defined as dyspeptic patients who went through a gastroscopy, with no identification of GX.

The following variables were analyzed: age, sex, diabetes mellitus, Helicobacter Pylori (Hp) and the presence of advanced lesions (AL) like atrophy, IM, dysplasia or adenocarcinoma.

Controls were randomly matched by age and sex in a 1:1 proportion with cases using a random number generator based on the "Mersenne twister" algorithm.

To evaluate variables associated with the presence of xanthomas, we ran a conditional logistic regression model in which statistically significant or trend variables in univariate analysis were included in multivariate analysis. Data were analyzed using STATA v. 14.

Results: We identified AL in 85 patients, of which gastric xanthoma was present in 76.5% (65), while 23.5% (20) belonged to the control group. This difference was statistically significant ($p < 0.001$), finding a positive correlation between the presence of gastric xanthoma and the probability of having AL (OR 6.7 [3.2-14.1], $p < 0.001$).

When we reviewed the lesions one-by-one, we found that there is a significantly higher percentage of patients with intestinal metaplasia and atrophy in the case group (OR 5.9 [2.8-12.4], $p < 0.001$ and OR 6 [1.3-26.8], $p = 0.019$ respectively). Due to the low incidence of gastric dysplasia and

adenocarcinoma in our sample, we found no significant differences between the case and the control group. No significant differences were found regarding DM or Hp.

Table 1 summarizes these results.

		Univariable analysis		Multivariable analysis		
		Xantoma (N=116)	Control (n=116)	p	mAOR (95% CI)*	p
Sex	Male, n (%)	41/82 (50.0%)	41/82 (50.0%)	>0.999		
	Female, n (%)	75/150 (50.0%)	75/150 (50.0%)			
Age, mean (SD)		63.3 (13.5)	63.1 (13.2)	0.202	1.1 (0.9-1.4)	0.232
H.Pylori, n (%)		29/59 (49.2%)	30/59 (50.8%)	0.873		
Diabetes, n (%)		23/47 (48.9%)	24/47 (51.1%)	0.873		
Lesion**, n (%)		65/85 (76.5%)	20/85 (23.5%)	<0.001	6.7 (3.2-14.1)	<0.001
Metaplasia, n (%)		63/83 (75.9%)	20/83 (24.1%)	<0.001	5.9 (2.8-12.4)	
Atrophy, n (%)		12/14 (85.7%)	2/14 (14.3%)	0.019	6 (1.3-26.8)	

*Matched adjusted Odds Ratio (95% Confidence Interval)

**Presence of metaplasia, atrophy, dysplasia and/or adenocarcinoma

Table 1. Univariable and multivariable analysis of factors associated with the finding of xanthomas.

Conclusion: We concluded that the presence of GX strongly recommends performing biopsy mapping, because we find a strong association between GX and AL (almost 7 times higher than in the dyspeptic population) independent of the endoscopy indication. In populations with a low incidence of gastric cancer, such Spanish and European Caucasian populations, we believe that being aware of indirect signs of AL is particularly relevant. GX are easy to detect even for unexpert endoscopists without needing any advanced equipment.

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P0103

GASTRIC CANCER MISSED IN A WELL-DEFINED SPANISH POPULATION

R.M. Saiz Chumillas¹, C. Pachón Martínez¹, L. Andrés Pascual¹, L. Alba Hernández¹, I. Chivato Martín-Falquina¹, G. Hontoria Bautista¹, A.C. Moncada Urdaneta¹, M.A. Jiménez Moreno¹, B. Sicilia Aladren¹

¹Hospital Universitario de Burgos, Gastroenterology, Burgos, Spain

Contact E-Mail Address: rosasachu@gmail.com

Introduction: Gastric cancer (GC) is the second most common gastrointestinal neoplasm and the sixth highest incident and fatality rates in Spain (less than 30% of 5-year survival). In 2019, one Spanish study investigated the missed rate of GC for the first time and reported a 9.1% (similar that data from Western countries).

Aims & Methods: To determine the frequency and characteristics of missed gastric cancer (MGC) in a determined population in Spain. To compare MGC and non-MGC tumors.

Retrospective observational study of all patients diagnosed with gastric adenocarcinoma between January-2012 and December-2021 in a defined geographic area (Burgos, Spain). Missed GC was defined as a case diagnosed with a negative esophagogastroduodenoscopy (EGD) in the previous 3 years.

Results: From 767 cases of GC, 29 cases were excluded (non-data). The overall rate of MGC was 6.8% (50/738). Mean total age was 73.8 ± 12.08. 62.5% (461/738) was male (68% MGC). The most frequent symptom was anaemia (23.3%), except in the group of MGC that was the acute gastrointestinal haemorrhage (24%). One third of all patients were in stage I and II, nevertheless this rate was higher in patients with MGC (54%). Stage III patients were found in 25.9% (16% MGC) and stage IV in 34.6% (28% MGC). Survival rate was not significantly different between both groups of patients. However, it seems that the survival of patients with previous EGD was some higher.

	Total 738 (100)	Without prior EGD 688 (93.2)	With prior EGD 50 (6.8)	P
Familial history of GC	109 (14.8)	103 (15)	6 (12)	0.336
<i>H. pylori</i> infection	84 (11.4)	74 (10.8)	10 (20)	0.108
Alarm symptoms	650 (88.1)	614 (89.2)	36 (72)	-
Prior gastrectomy*	23 (3.1)	20 (2.9)	3 (6)	0.200
Location				
Proximal (fundus/cardia)	109 (14.8)	97 (14.1)	12 (24)	0.060
Medial (corpus)	153 (20.7)	146 (21.2)	7 (14)	0.215
Distal (antrum/angular incisura)	311 (42.1)	287 (41.7)	24 (48)	0.409
Stump	19 (2.6)	16 (2.3)	3 (6)	0.116
Multifocal (≥2 parts)	141 (19.1)	137 (19.9)	4 (8)	0.037
Histology				
Intestinal	467 (63.3)	432 (62.8)	35 (70)	0.683
Diffuse	139 (18.8)	127 (18.5)	12 (24)	0.470
Mixed	36 (4.9)	35 (5.1)	1 (2)	0.291
Undifferentiated	51 (6.9)	49 (7.1)	2 (4)	0.345
Treatment				
Curative	101 (13.7)	97 (14.1)	4 (8)	0.385
Palliative	387 (52.4)	357 (51.9)	30 (60)	-
Comfort	250 (33.9)	234 (34)	16 (32)	-
ECOG scale (grouped)				
0/1	471 (63.8)	440 (64)	31 (62)	0.446
2	207 (28)	190 (27.6)	17 (34)	0.196
3/4	60 (8.1)	58 (8.4)	2 (4)	-

EGD: Esophagogastroduodenoscopy. GC: Gastric cancer; *Operated on for peptic ulcer. TNM (American Joint Committee on Cancer; AJCC), 8th edition.

Table 1. Characteristics of all patients and the groups of patients with or without a prior EGD in the 3 years before a diagnosis of GC. Data expressed in absolute value (n) and %.

Conclusion: Missing GC in a prior EGD is not uncommon. In our area we found a rate less than other series and half of patients with MGC were in stages non-advanced. Maybe the improvement in quality of EGD will facilitate their detection in the future.

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P0104

MALT LYMPHOMA A LONG-TERM FOLLOW-UP FROM A SINGLE CENTER EXPERIENCE

L. Correia Gomes¹, M. Rajão Saraiva¹, J. Moleiro¹, I. Claro¹

¹Instituto Portugues de Oncologia de Lisboa, Gastroenterology, Lisboa, Portugal

Contact E-Mail Address: luisfilipe.gomes@outlook.com

Introduction: Gastric mucosa-associated lymphoid tissue B-cell lymphoma (GML) is the most frequent site of extranodal marginal-zone B-cell lymphoma. Synchronous or metachronous malignancies have been reported in patients with GML with inconsistent results. We aimed to characterize the prevalence and development of gastric premalignant and malignant conditions during follow-up of these patients.

Aims & Methods: We retrospectively analysed 156 GML patients (1993 – 2020) with a mean follow-up time of 95 months (8 years) and a mean of 10 endoscopies per patient.

Results: Of 156 patients, 79 (51%) were male, mean age at diagnosis of 56-years-old. At diagnosis, endoscopic appearance was, predominantly, ulcer (26.4%), erosions (25%) or erythema (20.8%). The histology at diagnosis revealed gastric atrophy in 31 (21.5%) and intestinal metaplasia in 19 (13.2%), mainly in the antrum.

Most of the patients (88.16%) performed only eradication of *H. pylori* infection; others also needed chemotherapy (3.29%) or radiotherapy (1.97%). Patients' follow-up revealed that 54 patients (39.71%) developed intestinal metaplasia between 4 and 192 months of follow-up.

From the total of 73 patients with intestinal metaplasia, 1 evolved to high grade dysplasia and 1, exposed to radiotherapy, to gastric adenocarcinoma at 24 and 46 months of follow-up, respectively, both in the antrum. Besides, 2 patients developed large B cell Lymphoma, one 8 months after the diagnosis and the other after 108 months.

Conclusion: Despite some limitations, our data showed frequent progression to precancerous lesions of gastric mucosa in GML patients. However, only two patients developed dysplasia and adenocarcinoma, diagnosed within 5 years of follow-up and from the 2 identified diffuse large B-cell lymphoma, only 1 was developed after the 5 years period.

So, despite most literature report increased risk of secondary primary malignancies in these patients, more information is needed to stratify the patients according to risk factors and personalise long-term follow-up.

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P0105

VALIDATION OF A DSC SCORE AS SCREENING TEST FOR GASTRIC PRECANCEROUS LESIONS IN A NON-HIGH-INCIDENCE AREA

V. De Re¹, S. Maiero², P. Pelizzo³, A. Vitiello³, S. Realdon³, M. Fornasarig³, L. Rebuzzi³, F. Dottor³, R. Vettori⁴, O. Repetto¹, M. De Zorzi¹, V. Canzonieri⁵, A. Steffan⁴, R. Cannizzaro³

¹Centro di Riferimento Oncologico di Aviano, Immunopatologia e Biomarcatori Oncologi, Bio-Proteomica Facility, Aviano, Italy, ²Centro Riferimento Oncologico SOC Gastroenterology, Oncological Gastroenterology, Aviano, Italy, ³Centro di Riferimento Oncologico (CRO) Aviano IRCCS, Oncological Gastroenterology, Aviano, Italy, ⁴Centro di Riferimento Oncologico di Aviano, Immunopatologia e Biomarcatori Oncologi, Aviano, Italy, ⁵Centro di Riferimento Oncologico (CRO) Aviano IRCCS, Pathology, Aviano, Italy

Contact E-Mail Address: vdere@cro.it

Introduction: Gastroscopy is the standard procedure for gastric cancer (GC) diagnosis and its use for GC screening in some countries has demonstrated a 30% reduction in GC mortality. Early GC diagnosis improves clinical outcomes and may be cured by endoscopic resection. In Italy, with an intermediate risk for GC incidence, mass gastroscopy screening is not feasible due to costs and invasiveness.

Currently, the available pepsinogen (PG) test (PG-test) based on the combination of serum PG-I level and PG-I/PG-II ratio is considered a good predictor for GC in populations with high GC incidences. In our experience as well as in other studies reported in regions at high/intermediate risk of GC, with a widely accepted cut-off point of PGI <70ng/ml and PGI/PGII <3.0, the sensitivity for GC is satisfactory (≥80%), but the specificity (< 75%) needs to be improved.

We previously developed a model based on coefficient for PG-test combining with patient's age, sex, anti-*Helicobacter pylori* (*H. Pylori*) immunoglobulin level (IgG), and serum gastrin G17 level to discriminate patients at high risk for gastric adenocarcinoma and neuroendocrine tumors, DSC test (1,2).

Aims & Methods: This is the first report of prediction of high-risk gastric lesions using this model and with an acceptable ability to find participants at risk for high gastric lesions.

88 consecutive Caucasian individuals who presented to the Oncological Gastroenterology Unit of the Centro di Riferimento Oncologico in Aviano, Italy, for dyspepsia and/or suspected GC were involved in a prospective

monocenter study. Data of patients' age and sex were collected; expression profiles of serum PG, Gastrin G17, and *H. Pylori* IgG were performed and analyzed to group patients in risk classes for low, medium, and high gastric lesions, respectively. The accuracy of the model was established with gastroscopy and histological diagnosis of the gastric biopsies performed in the near time.

Results: Since June 2020, we enrolled 88 participants for DSC risk classification. Individuals with $y1 > 0.385$ and $y2 > 0.294$ were classified as DSC-high risk (21.6%), those with only $y1$ or $y2$ positive criteria as DSC-medium risk (6.8%), the remaining individuals as DSC-low risk (71.6%). 5 were found to have a high-grade lesion histologically confirmed (68%), 13 (14.77%) showed moderate atrophy and 57 (71.6%) did not show evident lesion or gastric atrophy and were excluded from secondary endoscopic follow-up.

The percentage of correctly diagnosed individuals with high-grade lesions was 4 (80%) and those correctly diagnosed as low/negative risk was 57 (81.4%). Of the 13 patients with a moderate lesion at the endoscopic examination, 6 (46.2%) were classified in the high-risk, 2 (15.4%) in the medium, and 5 (38.5%) in the low-risk DSC-risk group.

In total, the global DSC-test reaches 80.0% sensitivity, 86.36% of specificity, and an accuracy of 86.0% (100% in younger, 80.45% in older patients). PG-II level, but no PG-I, increased in patients with *H. pylori* infection, but proportionally increase with aging independently of *H. pylori* infection. Accordingly in *H. pylori*-negative individuals the range of PGI/PGII ratio shows the highest variability in the elderly.

Conclusion: We demonstrated the accuracy of the DSC-test in a prospective study including 88 participants with confirmed endoscopic and histological diagnoses. Whether DSC-test is effective in the follow-up remains to be seen, since high gastric lesions may be developed later.

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P0106

A STUDY ON THE USEFULNESS OF LINKED COLOR IMAGING DEPENDING ON DOCTORS AND LESIONS USING EYE TRACKING

M. Higashino¹, S. Ono², T. Sone¹, S. Matsumoto¹, Y. Nishimura¹, M. Kubo¹, M. Ono¹, K. Yamamoto², N. Sakamoto¹

¹Hokkaido University Graduate School of Medicine, Department of Gastroenterology and Hepatology, Sapporo, Japan, ²Hokkaido University Hospital, Division of Endoscopy, Sapporo, Japan

Contact E-Mail Address: masatare57@gmail.com

Introduction: Image-enhanced endoscopy (IEE) has advanced to become a mandatory modality in clinical practice, especially for surveillance of neoplastic lesions^{1,2}. Linked color imaging (LCI) (Fujifilm Medicals, Japan) is a unique IEE and it provides images similar to those provided by white light imaging (WLI).

A multicenter randomized study showed that LCI was superior to WLI for surveillance of neoplasia in the upper gastrointestinal (GI) tract. However, the doctors and lesions for which IEE is clinically useful have not been clarified.

Aims & Methods: The aim of this study was to determine the clinical advantage of LCI in endoscopic diagnosis of epithelial neoplasia using eye tracking. Nine doctors (3 experts, 3 trainees and 3 novices) who did not have information on the prepared endoscopic images participated in this study. Sixty cases including 30 epithelial tumors (8 cases of esophageal cancer and 22 cases of gastric cancer) and 30 normal cases or cases with no tumors were selected. A total of 120 images including 60 images of WLI and 60 images of LCI taken at the same position were randomly and anonymously set. The opt-out method to obtain consent for participants in this study was applied and this study was performed in accordance with the ethical standards detailed in the Declaration of Helsinki.

The authors' institutional ethics committee approved this study on October 27, 2021 (021-0081). EMRACTUS (nac Image Technology Inc., Japan) was used for eye tracking, and endoscopic images were displayed for 10 seconds followed by a black screen for 2 seconds. 'Correct answer' was defined as gazing at the lesion and pressing the button within 5 seconds from the start of display of images. Entry time was defined as time to the first gaze of the lesions from the display of images.

The primary endpoint was sensitivity for diagnosis of epithelial neoplasia in WLI and LCI, and secondary endpoints were specificity, positive predictive value (PPV), negative predictive value (NPV) and entry time.

Results: Sensitivities were 68.1% (95%CI: 64.8-70.8) in LCI and 51.9% (48.3-54.9) in WLI, and sensitivity in LCI was significantly higher than that in WLI ($P=0.002$). Also, NPV in LCI was significantly higher than that in WLI (73.9% vs 64.3%, $P=0.007$), but there was no significant difference in specificity or PPV between LCI and WLI.

Sub-analysis is showed that sensitivity in LCI was significantly higher than that in WLI in trainees (70.0% vs 54.4%, $P=0.045$), novices (65.6% vs 42.2%, $P=0.003$) and esophageal cancer (73.6% vs 45.8%, $P=0.007$). Entry times were 0.74 ± 0.6 in LCI and 0.74 ± 0.73 in WLI ($n.s.$)

Conclusion: LCI is an effective modality for diagnosis of epithelial tumors in the upper GI tract, especially for trainees and novices. It is necessary to consider effective use of IEE according to endoscopists and target patients and lesions.

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P0107

CONFOCAL LASER ENDOMICROSCOPY (PCLE) DETECTS MUCOSAL NEOPLASTIC VASCULAR PATTERN IN GASTRIC LINITIS PLASTICA

P. Spessotto¹, A. Capuano², S. Maiero³, A. Vitiello³, P. Pelizzo³, S. Realdon³, L. Rebuzzi³, F. Dottor³, E. Pivetta¹, V. Canzonieri⁴, C. Belluco⁵, M. Mongiat¹, M. Fornasarig³, R. Cannizzaro³

¹Centro di Riferimento Oncologico (CRO) Aviano IRCCS, Molecular Oncology, Aviano, Italy, ²Centro di Riferimento Oncologico di Aviano (CRO) IRCCS, Molecular Oncology, Aviano, Italy, ³Centro di Riferimento Oncologico (CRO) Aviano IRCCS, Oncological Gastroenterology, Aviano, Italy, ⁴Centro di Riferimento Oncologico (CRO) Aviano IRCCS, Pathology Dept., Aviano, Italy, ⁵Centro di Riferimento Oncologico (CRO) Aviano IRCCS, Surgical Oncology, Aviano, Italy

Contact E-Mail Address: pspessotto@cro.it

Introduction: Linitis plastica (LP) is a very aggressive and rare carcinoma with a scirrhous stroma that affects the submucosal and muscular layers of the stomach even without mucosal alterations. Lack of timely diagnosis is a crucial problem related to its prognosis and treatment.

The probe-based Confocal Laser Endomicroscopy (pCLE) enables *in vivo* analysis of tissue microarchitecture and precise identification of areas suitable for biopsy sampling by enhancing contrast and magnification of the diseased tissues at the cellular level. This technique has also been used in a few studies to objectively assess microvessel density at different neoplastic stages and angiogenic status of gastrointestinal cancers. pCLE has been shown not only to be a useful tool but also a valid technique for the evaluation of vascular changes in gastric cancer [1-2].

Aims & Methods: With the aim of developing new approaches to improve LP diagnosis, in this study we used the pCLE technique for the first time to determine whether these lesions, with negative histological samples, are also characterized by aberrant vasculature similar to gastric cancer.

During standard endoscopy, mucosal architecture, tortuosity and enlargement of vessels, as well as the presence of vascular leakage and efficiency of the blood flow were assessed in six LP consecutive patients using probe-based Confocal Laser Endomicroscopy (pCLE).

Results: In all LP patients, we detected abnormal changes in vasculature. The aberrant features of the vascular network were common to all LP patients examined and consisted of vessel enlargement, tortuosity, and leakage associated with the affected submucosal layer.

Conclusion: This is the first study to highlight the presence of marked vascularization associated with LP, characterized by the presence of abnormal and non-functional vessels, similar to what is observed in neoplastic tissues. Therefore, the analysis of LP by pCLE may provide a new endoscopic approach and strategy to better define these patients.

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P0108

ENDOSCOPIC TREATMENT OUTCOMES FOR DUODENAL NEUROENDOCRINE TUMOR

J.H. Noh¹, D.H. Kim¹, H.-K. Na¹, J.Y. Ahn¹, J.H. Lee¹, K.W. Jung¹, K.D. Choi¹, H.J. Song¹, G.H. Lee¹, H.-Y. Jung¹

¹Asan Medical Center, University of Ulsan College of Medicine, Gastroenterology, Seoul, Korea (Republic of)

Contact E-Mail Address: mdjh1432@gmail.com

Introduction: As the incidence of duodenal neuroendocrine tumors (DNETs) is steadily increasing, the role of endoscopic treatment for small and low-grade lesions is also raised. We aimed to investigate the efficacy and safety of endoscopic treatment for DNETs.

Aims & Methods: Patients who underwent endoscopic treatment for DNETs between 2000 and 2019 were included. The clinical features, treatment modalities, recurrence rate, and endoscopic outcomes according to tumor size were analyzed retrospectively.

Results: Overall, 125 patients underwent endoscopic treatment including forceps biopsy (n=18), endoscopic mucosal resection (EMR, n=98), endoscopic submucosal dissection (ESD, n=6), and argon plasma coagulation (n=3). Of patients who underwent EMR or ESD, En bloc resection rates were 98.1% (n=102), and complete resection rates were 64.4% (n=67). Complete resection rates were significantly higher in <1 cm small-sized lesions than in 1-2 cm large-sized lesions (69.8% vs. 38.9%, $p=0.013$). The rates of lateral and vertical margin involvements were 7.7% (n=8) and 34.0% (n=35), respectively. The 4 cases of perforation required surgical intervention, and no procedure-related mortality occurred. The tumor recurrence rates were 5.6% (n=7), and no tumor-related mortality occurred during median follow-up period of 50 months (interquartile range 18-79).

Conclusion: Based on our favorable long-term outcome, endoscopic treatment for DNETs less than 1 cm in diameter and confined to mucosal and submucosal layers could be an effective and safe treatment strategy.

Disclosure: All authors have no conflicts of interest or financial ties to disclose.

P0109

GASTRIC NEOPLASTIC LESIONS IN AUTOIMMUNE ATROPHIC GASTRITIS: OCCURRENCE AND PREDICTORS

E. Dilaghi¹, G. Pivetta¹, M. Dalla Bella¹, L. Dottori¹, G. Esposito², E. Pilozzi², B. Annibale¹, E. Lahner¹

¹Sant'Andrea Hospital-Sapienza University of Rome, Department of Medical-Surgical Sciences and Translational Medicine, Rome, Italy,

²Sant'Andrea Hospital-Sapienza University of Rome, Department of Clinical and Molecular Medicine, Sant'Andrea Hospital, University Sapienza, Rome, Italy

Contact E-Mail Address: emanuele.dilaghi@uniroma1.it

Introduction: Autoimmune atrophic gastritis (AAG) is a chronic inflammatory disorder affecting the oxyntic mucosa, leading to mucosal atrophy, intestinal metaplasia (IM), up to possible development of type I neuroendocrine tumors (T1gNET), dysplasia, and intestinal-type gastric cancer (GC). The occurrence of epithelial and neuroendocrine lesions in AAG patients at long-term follow-up was not assessed so far.

Aims & Methods: The aim of this study was to assess the occurrence of gastric neoplastic lesions (GNL) at long-term follow-up (FU), in a prospective cohort of AAG patients (diagnosed 1996-2020) adhering to endoscopic-histological surveillance. FU gastroscopies were scheduled at 4 years before 2011 and then every 3 years, according to MAPS guidelines. In case of new symptoms not reported during baseline evaluation, worsening of known symptoms, or onset of anemia, gastroscopy was anticipated. The

main features of patients with and without GNL were compared at univariate and multivariate analyses to assess for eventual predictive features. Kaplan-Meier survival curves were obtained.

Results: A total of 275 AAG patients [72.0% female, median age 61 (23-84) years] were included with a median FU of 5 (1-17) years. Overall, 58 gastric neoplastic lesions were detected (crude incidence 21.1%). At FU, GC/high grade dysplasia (HGD) was diagnosed in 7 patients (crude incidence 2.5%), low grade dysplasia (LGD) in 9 patients (crude incidence 3.3%), and 42 T1gNET in 28 patients (13 patients with recurrent T1gNET) (crude incidence 15.3%). The annual incidence rate person-year was 3.9% for all GNL (0.5%, 0.6%, and 2.8% for GC/HGD, LGD, and T1gNET, respectively). All GNL showed at baseline endoscopic-histological evaluation OLGA score 2, except 2 patients with LGD and 1 patient with T1gNET that presented OLGA 1 at baseline evaluation. At logistic regression, considering as dependent variable the presence of epithelial GNL (GC, HGD, LGD) at FU, a positive association was found for age ≥ 60 years (OR 6.6, 95%CI 1.45-31.5) and the presence of baseline IM without PPM (OR 5.4, 95%CI 1.4-21.0); considering as dependent variable the presence of T1gNET at long term FU, a positive association was found for the presence of baseline severe corpus atrophy (OR 3.3, 95%CI 1.1-9.9).

In AAG patients presenting IM without PPM at baseline, a shorter mean overall survival time (95%CI for the mean) free of epithelial GNL was observed [15.4 (14.4-16.4) years vs 13.3 (11.0-15.7) years ($p=0.02$). In AAG patients with severe corpus atrophy at baseline, a shorter mean overall survival time free of T1gNET [15.9 (15.0-16.8) years vs 13.0 (11.8-14.3) years ($p=0.04$)] was shown.

Conclusion: The current study provides data to confirm the higher risk of developing GNL in AAG patients, despite the low-risk OLGA scores, quantified by an annual incidence rate of 3.9%-person year. Regular endoscopic-histological surveillance should be proposed in AAG patients for early diagnosis of GNL, in particular in those over 60 years of age, presenting with IM without PPM and/or with severe corpus atrophy at diagnosis, possibly optimizing surveillance strategies.

Disclosure: Nothing to disclose.

P0110

USEFULNESS OF LINKED COLOR IMAGING FOR DETECTION AND CHARACTERIZATION OF EARLY UNDIFFERENTIATED-TYPE GASTRIC CANCER

W. Lee¹

¹Chonnam University Hwasun Hospital, Internal Medicine, Gastroenterology, Jeollanam-do, Korea (Republic of)

Contact E-Mail Address: jadelook@hanmail.net

Introduction: Linked color imaging (LCI) is based on the bioluminescent imaging technique, which enhances slight differences in mucosal color allowing for the reddish mucosa to appear redder. Small number of studies have reported the usefulness of LCI for assessing differences in early gastric cancer (EGC) cases, however, the results were mostly about differentiated EGC.

This study aimed to analyze the color difference between cancerous and non-cancerous areas to compare LCI with conventional white light image (WLI) in a cohort of undifferentiated-type EGC patients.

Aims & Methods: We prospectively enrolled 46 patients with undifferentiated-type EGC from three national based hospitals between September 2020 and October 2021. All lesions were observed first by WLI, followed by LCI. Additional biopsy was taken from surrounding mucosa to check for intestinal metaplasia, and test for *Helicobacter pylori* were performed. Color difference was measured in accordance with the International Commission on Illumination (CIE) details.

Results: Color difference value with LCI was significantly higher and approximately twice that of WLI, while this difference did not appear to be higher in the cases of accompanying *H. pylori* infection or intestinal metaplasia. In subgroup analysis, color difference of poorly-differentiated EGC was marked in LCI compare to WLI, but in signet ring cell type or mixed type EGC, the difference was not statistically significant.

Conclusion: LCI appears to be effective for detection of undifferentiated type EGC than WLI in endoscopic screening. Moreover, LCI may discriminate pathologic subgroup of undifferentiated type EGC possibly due to characteristic cellular growth pattern.

Disclosure: Nothing to disclose.

P0111

CLINICOPATHOLOGICAL AND ENDOSCOPIC FEATURES OF GASTRIC ADENOCARCINOMA OF THE FUNDIC GLAND TYPE

J. Cao¹, D. Zhuang², Y. Yang¹, L. Zhang³, Q. Xu¹, M. Xu¹

¹Shanghai East Hospital, Tongji University School of Medicine, Endoscopy Center, Department of Gastroenterology, Shanghai, China, ²Zhejiang Zhoushan Hospital, Department of Gastroenterology, Zhoushan, China, ³Shanghai East Hospital, Tongji University School of Medicine, Department of Pathology, Shanghai, China

Contact E-Mail Address: jia_cao@yeah.net

Introduction: Gastric adenocarcinoma of the fundic gland type (GA-FG) is a new type of gastric cancer discovered in recent years, and its histopathological features are similar to fundic gland cells. It can be accompanied with other epithelial tumors with or without *H. pylori* infection. Besides, GA-FG can sometimes occurred among younger patients. Most GA-FG cases turn out to have good prognosis.

However, it can also be combined with other well differentiated or even poorly-differentiated epithelial tumors, so that its ability to invade or metastasize needs further research.

Aims & Methods: To retrospectively observe and compare the clinicopathological features of gastric adenocarcinoma of the fundic gland type (GA-FG).

The clinicopathological features of 19 cases of GA-FG diagnosed in our center from April 2019 to March 2022 were retrospectively analyzed, including age, sex, tumor location, shape, diameter, surrounding mucosa and the status of *Helicobacter pylori* infection. The depth of tumor invasion and immunohistochemical results were analyzed in 15 cases treated with EMR/ESD.

Results: Most of the patients were middle-aged or elderly, among whom the youngest was 37 years, and the average age was 55.5±11.6 years, the sex ratio was 8 male: 11 female. Most of the lesions were type 0-IIa with irregular microsurface pattern (IMSP) and irregular microvascular pattern (IMVP) (14/19), which originated from the non-atrophic mucosa in the upper or middle part of the stomach. The average diameter of the tumors was ≤1.0 cm (0.7±0.2cm), and the their phenotypes were chief cell predominant type. In 15 cases (15/19) treated with EMR/ESD, the lesions invaded into submucosa, but no lymphovascular invasion was found. The Ki-67 index of all lesions was ≤10%.

Conclusion: GA-FG is a rare and low-malignant tumor. It occurs on the non-atrophic mucosa of the upper or middle third of the stomach, most of GA-FGs are superficial elevated lesions. GA-FG can occur in younger patients, and it can also be accompanied with other epithelial tumors. Pathology and immunohistochemistry are helpful with the diagnosis.

Disclosure: AUTHORS DECLARE NO conflicts of interest for this article.

P0112

A 10-YEAR EXPERIENCE WITH TYPE I GASTRIC NEUROENDOCRINE TUMOURS

R. Ortigão¹, C. Pinto¹, J. Chaves¹, L.P. Afonso¹, P. Pimentel-Nunes², M. Dinis-Ribeiro³, D. Libânio⁴

¹Oncology Institute of Porto, Gastroenterology, Porto, Portugal,

²Oncology Portuguese Institute of Porto, Gastroenterology

Department, Porto, Portugal, ³IPO Porto, Dept. of

Gastroenterology, Porto, Portugal, ⁴Instituto Português de

Oncologia do Porto, Gastroenterology Department, Porto, Portugal

Contact E-Mail Address: raquel.ortigao@hotmail.com

Introduction: Type I Gastric Neuroendocrine Tumors (GNETs) have an increasing incidence, but data on the most appropriate management is scarce.

Aims & Methods: The aim of the study was to evaluate the outcomes of different therapeutic strategies (polypectomy/surgery, mucosectomy [EMR], endoscopic submucosal dissection [ESD], surgery and somatostatin analogues) in patients with type I GNET.

Retrospective study including consecutive patients admitted for type I GNETs between January 2010 and December 2019 was performed.

Results: 113 patients with type I GNET were included, 62% were women, with a mean age of 60 years. At diagnosis, 18% of patients had anemia and 16% vitamin B12 deficiency. Anti-parietal cell and intrinsic factor antibodies were present in 76% and 4% of patients with autoimmune gastritis, respectively.

At diagnosis, the surveillance/polypectomy strategy was adopted in 77 patients. Twenty-four patients underwent EMR, 6 underwent ESD, 3 underwent surgery (2 for evidence of lymph node metastases) and 3 started somatostatin analogues.

Patients undergoing EMR and ESD had no statistically significant differences in maximum lesion diameter (16 vs 13mm, p=0.515), Ki67 index (p=0.745) and grade (p=0.855). The rate of complete histological resection (78 vs 60%, p=0.255) and the presence of negative horizontal and vertical margins (89 vs 100%, p=0.597; 77 vs 60%, p=0.470, respectively) were similar in both groups. Lesions removed by ESD had more frequently lymphovascular invasion (40 vs 6%, p=0.120).

The development of metachronous lesions was similar in the group undergoing EMR, ESD and surgery (38 vs 40% vs 33%, p=0.876). Overall survival was 100%.

Conclusion: Regardless of disease stage, the overall survival of patients with type I GNET is excellent. ESD and EMR achieved similar short- and long-term results in this group of patients.

Disclosure: Nothing to disclose.

P0113

CLINICAL COMPARISON OF ENDOSCOPIC RESECTION VERSUS SURGICAL TREATMENT AMONG PRIMARY DUODENAL GASTROINTESTINAL STROMAL TUMORS (D-GISTS)

X.-Q. Li¹, Z.-Q. Liu¹, Q.-L. Li¹, P.-H. Zhou¹

¹Zhongshan Hospital, Endoscopy Center and Endoscopy Research Institute, Shanghai, China

Contact E-Mail Address: li.quanlin@zs-hospital.sh.cn

Introduction: Duodenal gastrointestinal stromal tumors (D-GISTs) are relatively rare. Due to small numbers in reported cohorts, the prognostic characteristics and therapeutic efficacy of duodenal GISTs remain uncertain. There are few studies focused on the safety and efficacy of endoscopic resection (ER) compared with surgical resection (SR).

Aims & Methods: We aimed to compare the safety and efficacy of endoscopic resection (ER) with surgical resection (SR) of D-GISTs in Zhongshan hospital. The study included 88 patients with D-GISTs between January 2014 and December 2021, among them 28 patients undergoing ER and 60 patients undergoing SR. Clinicopathological characteristics, intraoperative and postoperative complications, and long-term follow-up were compared between the 2 groups. Disease-free survival (DFS) was calculated using Kaplan-Meier analysis.

Results: The mean age (56.0±8.9years vs. 57.7±11.3years, $p = 0.214$) and man ratio (19/28, 67.9% vs. 33/60, 55%, $p = 0.253$) between the two groups were not significantly different. The most common location of D-GISTs was the descending portion (16/28, 57.1% vs. 41/60, 68.3%). Patients undergoing ER had significantly smaller tumor size (1.83 vs. 4.72 cm, $p < 0.001$), shorter procedure time (73.58 vs. 168.80 min, $p < 0.001$), and shorter hospital stay (2.64 vs. 14.83 days, $p < 0.001$) compared with those undergoing SR. The en bloc resection rate was achieved in 96.4% ($n = 27/28$) of patients in the ER group, whereas 100% ($n = 60/60$) in surgical group ($p = 0.318$). However, during long-term follow-up (50.34±27.7 months), recurrence occurred in one patient in the ER group (occurring at 12 months postoperatively) and one in the SR group (occurring at 30 months postoperatively). the three-year recurrence rate (3.5% vs. 1.7%, $p = 0.5$) was not significantly different between the two groups. One patient in the SR group died two years after surgery.

Conclusion: Endoscopic resection might be an alternative therapeutic method for GISTs in the duodenum in selective cases.

Disclosure: Nothing to disclose.

P0114

PREVALENCE AND PREDICTORS OF MALNUTRITION IN PATIENTS WITH GASTRIC CANCER – A SINGLE CENTRE PROSPECTIVE STUDY

P. Patil¹, A.K. Jain¹, S. Mehta¹, S. Sundaram¹, O. Salvi², S. Khan¹, A.M. Khan¹

¹Tata Memorial Hospital, Homi Bhabha National Institute (HBNI), Department of Digestive Diseases and Clinical Nutrition, Mumbai, India, ²Tata Memorial Hospital, Homi Bhabha National Institute (HBNI), Mumbai, India

Contact E-Mail Address: prachipatil@gmail.com

Introduction: Malnutrition is seen in 60-90% of patients with gastric cancer (GC). Both the malignancy and adverse effects of multimodality treatments can lead to malnutrition. Malnutrition can result in increased treatment toxicity, decreased response rates, and increased length of stay in patients with Gastric cancer (GC) and may also impact outcomes. Various nutrition assessment tools such as Subjective Global Assessment (SGA), Malnutrition Universal Screening Tool (MUST), Mini Nutritional Assessment (MNA), and the Nutrition Risk Screening (NRS) 2002 are used in practice to assess for malnutrition in addition to the standard anthropometric measurements.

Aims & Methods: We conducted a prospective IRB-approved observational study with the primary aim of studying the prevalence of malnutrition in GC and secondary aims of studying the concordance between SGA and other screening tools and assessing the predictors of malnutrition in GC. 1000 consecutive untreated patients with biopsy-proven GC (adenocarcinoma) registered at Tata Memorial Hospital, a referral cancer center were recruited over 3 years. Demographic details and baseline disease status were noted. Nutritional assessments were done by a trained dietician at baseline and at predefined intervals. We present the baseline data here.

Results: The mean age was 53.4 years (range 18-86 years) and 71.5% were males. 15.2% were ≤ 40 years of age (young GC). 770 (77%) patients had an ECOG-Performance Status of 0/1 at baseline. 2.5% of patients were from

Upper socioeconomic status (SES), 38.6% from middle SES and 58.9% were from lower SES. 9% each had a previous history of gastric surgery and a family history of malignancy. Features suggestive of gastric outlet obstruction (GOO) were present in 36.5% of patients with GC (42.9% amongst malnourished and 15.7% amongst well-nourished).

The prevalence of malnutrition using the SGA was 76.5%. 524 (52.4%) were SGA B (moderately malnourished) and 241 (24.1%) patients were SGA C (severely malnourished). Using MUST, MNA, and NRS 2002, 82.3%, 91.2%, and 58.3 % of the patients respectively were malnourished or at risk.

The kappa coefficient analysis to study concordance between the MUST, MNA, NRS 2002, and the gold standard SGA showed the best agreement between the SGA and MUST (0.617). There was moderate agreement between the SGA and MNA (0.450) and SGA with NRS 2002 (0.425). Sensitivity with MUST, MNA, and NRS 2002 was 95.56%, 99.48%, and 70.98% respectively in detecting malnourishment, but the specificity was lower (60.85%, 35.74%, and 82.98%, respectively).

Body mass index <18.5 Kg/m², low calf circumference, and low mid-upper arm circumference suggestive of malnutrition were seen in 34.7%, 86.1%, and 28.5% patients respectively.

On multivariate logistical regression analysis, symptoms of nausea/vomiting, weight loss, anorexia, pain, and the presence of gastric outlet obstruction increased the likelihood of malnutrition with an Odds ratio of 3.8, 9.9, 2.5, 1.35, and 2.5 respectively as compared to those who did not have those symptoms.

Conclusion: Malnutrition was seen in 76.5% of Gastric Cancer patients at diagnosis. MUST had a better concordance with SGA as compared to MNA or NRS 2002. BMI and anthropometry underestimated the prevalence of malnutrition hence standard validated screening tools should be preferred. Symptoms of weight loss, nausea or vomiting, anorexia, and pain predicted malnutrition in patients with GC. Nutritional assessment and appropriate intervention should be an integral part of GC care pathways.

Disclosure: Nothing to disclose.

P0115

PIECEMEAL COLD SNARE POLYPECTOMY FOR THE REMOVAL OF LARGE DUODENAL ADENOMAS

H. Wang¹, M. Sidhu¹, S. Gupta¹, P. Kumar^{1,2}, O. Cronin¹, A. Whitfield¹, T. O'Sullivan¹, S. Williams¹, E. Lee¹, N.G. Burgess¹, M.J. Bourke¹

¹Westmead Hospital, Department of Gastroenterology and Hepatology, Westmead, Australia, ²University of Calgary, Division of Gastroenterology and Hepatology, Calgary, Canada

Contact E-Mail Address: olivergcronin@gmail.com

Introduction: Large (≥15mm) duodenal adenomas (DA) are premalignant and require removal. Existing endoscopic resection techniques are compromised by adverse events, most notably post procedural bleeding (PPB) or recurrence. To ameliorate these problems we sought to evaluate the novel technique of piecemeal cold snare polypectomy (P-CSP) against the emerging standard of conventional EMR with thermal ablation of the post resection margin (EMR-T) for the safe and effective removal of DA.

Aims & Methods: Consecutive patients were enrolled in a single expert Western endoscopy centre for P-CSP and prospectively analysed against a previously reported cohort of EMR-T from the same centre. The primary outcome was rate of adverse events. Patient and lesion characteristics, technical success and recurrence at the first surveillance endoscopy (SE1) were collected.

Results: Between July 2017 until April 2022, 48 DA were removed via P-CSP (median size 30mm, range 10mm – 100mm, mean age 68 years old) compared with 54 DA EMR-T (median size 30mm, range 10mm – 70mm,

mean age 67 years old). P-CSP had a significantly lower rate of intra-procedural bleeding (4.1% vs 31%, $P < 0.00006$) and PPB (4.1% vs 16.7%, $P = 0.04$). 3 cases (6.3%) of immediate perforation occurred in P-CSP. In all 3 cases, perforation occurred due to amputation of ensnared tissue against the tip of the endoscope in the second part of the duodenum. These were recognised intraprocedurally and closed with clips without sequelae. Overall serious adverse events (15% vs 16.7%, $P = 0.77$), hospital admission rate (32.7% vs 42.6%, $P = 0.46$), technical success (98% vs 100% $P = 0.47$), and procedural time (33mins vs 30mins, $P = 0.95$) were similar. Recurrence at SE1 was significantly lower in EMR-T (2.3% vs 15.8%, $P = 0.048$).

	P-CSP (n = 48)	EMR-T (n = 54)	P-value
Duration (minutes), median (IQR)	33 (20 – 50)	30 (20-60)	0.95
Technical success	47 (98)	54 (100)	0.47
En bloc resection	0 (0)	9 (16.7)	0.003
Hospital admission	17 (32.7)	23 (42.6)	0.46
IPB	2 (4.1)	20 (37)	0.00006
SAE*	7 (15)	9 (16.7)	0.77
Immediate perforation	3 (6.1)	0 (0.0)	0.10
PPB	2 (4.1)	9 (16.7)	0.04
Recurrence at SE1	6 (15.8)	1 (2.3)	0.048

Values are number (%) except where indicated otherwise.
 *other SAE included pancreatitis (1 patient), duodenal stenosis requiring dilation (1 patient) in P-CSP group
 P-CSP, piecemeal cold snare polypectomy; EMR-T, thermal ablation of the post resection margin after endoscopic mucosal resection; IQR, Interquartile range; IPB, intraprocedural bleeding; SAE, serious adverse events; PPB, post procedural bleeding; SE1, first surveillance endoscopy

Table 1. Procedural outcomes

Conclusion: P-CSP reduces IPB and PPB however it may increase the risk of immediate perforation and is associated with significantly higher rate of recurrence at SE1. Further technical refinements are required to optimise endoscopic resection techniques for DA.

Disclosure: Nothing to disclose.

P1028

THE EFFECT OF DATA DIVERSITY ON THE PERFORMANCE OF DEEP LEARNING MODELS FOR PREDICTING EARLY GASTRIC CANCER UNDER ENDOSCOPY

C. Shi¹, J. Li¹, L. Wu², H. Yu²
¹Renmin Hospital of Wuhan University, Wuhan, China, ²Renmin Hospital of Wuhan University, Gastroenterology, Wuhan, China

Contact E-Mail Address: 914091879@qq.com

Introduction: Gastric cancer is the second leading cause of cancer-related death worldwide and one of the most common cancers in East Asia. Improving the detection rate of early gastric cancer (EGC) can greatly improve the survival rate of gastric cancer patients. It has been demonstrated that magnifying narrow-band imaging (ME-NBI) and magnifying blue laser imaging (ME-BLI) diagnosis accuracy of early gastric cancer is higher than white light endoscopy, and both techniques have been widely applied in clinical practice.

With the rapid development of artificial intelligence (AI), deep learning technologies have been widely researched in the field of digestive endoscopy. In clinical practice, we can use different brands or types of equipment to do a same examination for patients. Different devices have some different characteristics, such as color, imaging resolution, shape and so

on. Although these differences in details rarely affect doctor's diagnosis, they may interfere with the performance of AI models. Should we extensively collect highly heterogeneous images for training, or should we train different deep learning models for different patterns of images? There is no satisfactory answer to this question.

Aims & Methods: To explore the effect of training set diversity on the performance of deep learning models for predicting early gastric cancer (EGC) under endoscopy.

Images of EGC and non-cancerous lesions under narrow-band imaging (ME-NBI) and magnifying blue laser imaging (ME-BLI) were retrospectively collected. Training set 1 was composed of 1505 noncancerous and 309 EGC ME-NBI images, training set 2 was composed of 1505 non-cancerous and 309 EGC ME-BLI images, and training set 3 was the combination of training set 1 and 2. Test set 1 was composed of 376 non-cancerous and 1052 EGC ME-NBI images, test set 2 was composed of 529 non-cancerous and 71 EGC ME-BLI images, and test set 3 was the combination of test set 1 and test set 2.

Three deep learning models were constructed, which were respectively CNN1, CNN2 and CNN3 (CNN1, CNN2 and CNN3 were independently trained using training set 1, training set 2 and training set 3 respectively), and their performance on each test set was respectively evaluated. 138 ME-NB videos and 17 ME-BLI videos were further collected to evaluate and compare the performance of each model in real time.

Results: The performance of CNN3 was the best in the three test sets. The accuracy, specificity and sensitivity of test set 1 in CNN3 were 87.89% (1255/1428), 90.96% (342/376) and 86.79% (913/1052) respectively. The accuracy, specificity and sensitivity of test set 2 in CNN3 were 95% (570/600), 97.92% (518/529) and 73.24% (52/71) respectively.

The accuracy, specificity and sensitivity of test set 3 in CNN3 were 89.99% (1825/2028), 95.03% (860/905) and 85.93% (965/1123) respectively. The performance of CNN3 was also the best in videos test set.

The accuracy, specificity and sensitivity of videos test set in CNN3 were 91.03% (142/156), 90.58% (125/138) and 94.44% (17/18) respectively. In clinical practice, we can use different brands or types of equipment to do a same examination for patients.

Different devices have some different characteristics, such as color, imaging resolution, shape and so on. Although these differences in details rarely affect doctor's diagnosis, they may interfere with the performance of AI models.

Conclusion: The deep learning model with the most diverse training data has the best diagnostic effect.

Disclosure: Nothing to disclose.

P1029

REALTIME ARTIFICIAL INTELLIGENCE ASSISTED DEVICE CAN EFFECTIVELY IMPROVE EARLY GASTRIC CANCER DETECTION: A HISTORICAL MULTICENTER CONTROLLED TRIAL

L. Huang¹, L. Wu¹, Z. Lu¹, H. Yu²
¹Renmin Hospital of Wuhan University, Wuhan, China, ²Renmin Hospital of Wuhan University, Gastroenterology, Wuhan, China

Contact E-Mail Address: huangli9707@163.com

Introduction: Artificial intelligence assisted devices (AIAD) have been widely applied in endoscopy in recent years [1-3], some of which have been utilized in clinical environment. We have developed an AIAD for gastroscopy which could monitor the blind spot and detect the early gastric cancer (EGC) in real time [3].

The AIAD was applied in several health centers for some time and we retrospectively collected the data of gastroscopy cases before and after the utilization of AIAD to explore the efficacy of AIAD in clinical practice.

Aims & Methods: This is a historical multicenter controlled trial and conducted in 7 hospitals in China to explore the difference between the AIAD group and the control group to evaluate the AIAD in clinical environment, which are closer to the real clinical treatment procedures and related with less intervention like the prospective controlled study. The AIAD was designed and aimed to adopted in daily endoscopy process. So, except the clinical trials, the historical without the supervision of researcher may truly presented the efficacy of artificial intelligence assisted device.

A total of 220,498 patients who underwent the gastroscopy were included from January 1 2017 to February 28 2022 and divided into the AIAD group (after the use of AIAD) and control group (before the use of AIAD). The EGC detection rates were compared using a two tailed Chi-squared test. And the EGC detection rate was defined as the number of EGC divided by the sum number of EGC and gastric developed cancer.

Results: The control group and AIAD group were included 101696 and 118802 patients respectively. 144 EGC and 1007 gastric developed cancer were found in the control group as well as 431 EGC and 825 gastric developed cancer were found in the AIAD group. The AIAD group presented a higher EGC detection rate (11.61% vs. 34.42%, $P < 0.0001$).

Conclusion: The use of the AIAD during upper gastrointestinal endoscopy significantly increased the EGC detection rate in clinical practice without intervention. AIAD-assisted gastroscopy has the potential to improve the detection of EGC.

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Disclosure: Nothing to disclose.

P0116

HP INFECTION IN GASTRIC DIFFUSE LARGE B CELL LYMPHOMA: FREQUENCY, RESPONSE TO TREATMENT AND IMPACT ON LYMPHOMA PROGRESSION

G. Gharbi¹, A. Khsiba¹, M. Moufida¹, A. Ben Mohamed¹, E. Chelbi², H. Belfkih³, M. Yakoubi¹, M. Medhioub¹, M.L. Hamzaoui⁴, M. Azouz¹

¹University of Medicine Tunis El Manar / Mohamed Taher Maamouri Hospital, Gastroenterology and Hepatology, Nabeul, Tunisia,

²University of Medicine Tunis El Manar / Mohamed Taher Maamouri Hospital, Pathology, Nabeul, Tunisia, ³University of Medicine Tunis El Manar / Mohamed Taher Maamouri Hospital, Oncology, Nabeul, Tunisia, ⁴University of Medecine Tunis El Manar / Mohamed Taher Maamouri Hospital, Gastroenterology and Hepatology, Nabeul, Tunisia

Contact E-Mail Address: gharbighada1801@gmail.com

Introduction: The role of *Helicobacter Pylori* (HP) infection has been well demonstrated in the genesis of gastric MALT lymphoma. Its involvement in Gastric Diffuse Large B Cell Lymphoma (GDBCL) is less clear. However, improved prognosis and even complete regression of the tumour have been reported after HP eradication therapy.

Aims & Methods: The aim was to study the frequency of HP infection during GDBCL and evaluate the response to HP eradication therapy.

This is a retrospective study investigating patients with GDBCL managed in our gastroenterology department between January 2009 and December 2020.

Patients were divided into 2 groups:

G1 : patients diagnosed with GDBCL and HP infection

G2 : patients diagnosed with GDBCL without HP infection

Results: Forty-five patients were included with a mean age at diagnosis of 59 years old and a M/F sex ratio of 2. HP infection was found in 32 patients (71.1%). GDBCL was mainly de novo in both groups (G1: 68.8%, G2: 28.1%), whereas transformation from a MALT lymphoma was only observed in 28.1% in G1 and 30.8% in G2.

The presence of atrophy (G1: 9.4% vs G2: 7.7%) and intestinal metaplasia (G1: 28.1% vs G2: 15.4%) were more frequent in G1 with no statistically significant difference ($p = 0.86$ and 0.37 respectively).

The NGC (Non-Germinal Center) subtype was the most frequent in both groups (G1: 40.6% vs G2: 46.2%).

Advanced GDBCL (stage III or VI) was more frequent in G2 (G1: 25%, G2: 38.5%) with no statistically significant difference ($p = 0.37$).

More complications such as bleeding, perforation and tumour lysis syndrome were observed in G1 with no statistically significant difference ($p = 0.48$).

In G1, 20 patients (62.5%) received HP eradication therapy and this eradication was controlled in only 9 patients with 2 patients failing.

The evolution was more negative in G2 with tumour progression in 35.8% of patients, while it was only 6.3% in G1 with no statistically significant difference ($p = 0.6$).

Conclusion: A negative HP status appears to be associated with a more advanced GDBCL with a worse outcome and prognosis.

Disclosure: Nothing to disclose.

P0117 WITHDRAWN

P0118

USE OF MUCOLYTIC SOLUTION BEFORE GASTROSCOPY – A DOUBLE-BLIND, RANDOMIZED STUDY

M. Stepan^{1,2,3}, P. Falt^{4,1}, B. Pipek^{4,2,1,3}, R. Psar^{1,2}, P. Fojtík^{2,3}, O. Urban^{4,1}

¹Faculty of Medicine, Palacky University, Olomouc, Czech Republic,

²AGEL Hospital Ostrava-Vítkovice, Ostrava-Vítkovice, Czech Republic, ³Faculty of Medicine, University of Ostrava, Ostrava, Czech Republic, ⁴University Hospital and Faculty of Medicine, Palacky University, 2nd Department of Internal Medicine, Olomouc, Czech Republic

Contact E-Mail Address: michal.stepan@vtn.agel.cz

Introduction: Sufficiently clear mucosa during upper endoscopy is essential for proper diagnosis in the upper gastrointestinal tract. Still discussed, especially in terms of effect and effective dose, is the use of simethicone and N acetylcysteine, substances with antifoam and mucolytic effects, to increase the clarity of the mucosa in the upper gastrointestinal tract.

Aims & Methods: The primary objective was to demonstrate that a higher, maximum dose of mucolytic administered 20-30 minutes before gastroscopy increased the upper gastrointestinal visibility score compared to D arm, without mucolytic solution and water.

The secondary objective was to demonstrate that the visibility score after administration of the maximum dose of mucolytic administered to arm A is higher than the visibility score in the upper gastrointestinal tract after administration of the lower mucolytic dose in arm B.

The primary endpoint was the visibility score evaluated by the examining blinded endoscopist, given by the sum of 5 scores 0-5 in the esophagus, fundus, body and antrum of the stomach and in the duodenum, for a total of 0-25.

The secondary endpoint was the visibility score evaluated according to 10 photos taken according to ESGE recommendations and blinded endoscopists, given again by the sum of 5 scores 0-5.

The study was double-blind, randomized and conducted from May to September 2021, at the Digestive Diseases Center, Vitkovice Hospital, Ostrava, Czech Republic. The study protocol was approved by the local ethics committee, the State Institute for Drug Control of the Czech Republic and was registered in the Clinical Studies Registry at ClinicalTrials.gov (NCT04641455).

Patients were randomized into four arms, with administration of the maximum dose of mucolytic solution (arm A, 100 ml water + 600 mg N-acetylcysteine + 400 mg simethicone), with administration of a lower dose of mucolytic solution (100 ml water + 400 mg N-acetylcysteine + 20 mg simethicone), with administration of 100 ml water (arm C), and without administration of water and mucolytic solution (arm D). During the examination, a total of 10 photographs were taken in the defined areas.

The overall visibility score was given by the sum of the 0-5 scores of the five areas and was assessed by the endoscopist performing the procedure and then by two blinded endoscopists who assessed this from the photodocumentation taken. Other parameters monitored were the time of the examination and the amount of residual fluid in the stomach.

Results: A total of 129 patients who met the inclusion criteria were enrolled in the study. 9 patients were subsequently excluded. Patients did not differ significantly in age or gender distribution between arms.

Overall visibility score as assessed by the performing endoscopist, was similar between arms A, B and C (18.9±2.9 vs. 18.6±3.0, p=1.000); however, when comparing the total visibility scores of arms A, B, and C with arm D, only arm A demonstrated significantly higher visibility scores compared with arm D (18.9±2.9 vs. 16.6±3.3, p=0.023).

The secondary endpoint was different between the two blinded endoscopists. The total amount of residual fluid in the stomach and the time of examination were comparable between the different arms.

Conclusion: Administration of mucolytic solution with maximum dose of N-acetylcysteine and simethicone before gastroscopy improves mucosal clarity in the upper gastrointestinal tract during the examination compared without fluid or mucolytic solution when evaluated by the performing endoscopist.

Disclosure: No Conflict of Interest.

P0119

ONE TIME SCREENING GASTROSCOPY IN LOW TO MODERATE UPPER GASTROINTESTINAL CANCERS PREVALENCE POPULATION – IS IT WORTH?

M. Romańczyk^{1,2}, B. Ostrowski¹, K. Barański³, T. Romańczyk^{2,4}, M. Błaszczyszka⁵, K. Budzyń^{1,2}, J. Didkowska⁶, U. Wojciechowska⁶, M. Hartleb¹

¹Medical University of Silesia, School of Medicine in Katowice, Department of Gastroenterology and Hepatology, Katowice, Poland, ²H-T. Centrum Medyczne, Endoterapia, Tychy, Poland, ³Medical University of Silesia, School of Medicine in Katowice, Department of Epidemiology, Katowice, Poland, ⁴Wyższa Szkoła Techniczna, Department of Gastroenterology, Katowice, Poland, ⁵District Hospitals of Chorzów Trust, Endoscopy Unit, Chorzów, Poland, ⁶The Maria Skłodowska-Curie National Research Institute of Oncology, National Cancer Registry of Poland, Warsaw, Poland

Contact E-Mail Address: krzysztof.budzyn96@gmail.com

Introduction: The prognosis of survival in gastric and esophageal cancers is related to the disease stage. Screening esophagogastroduodenoscopy (EGD) has proven beneficial in populations at high risk of gastric cancer. Esophageal (EA) and gastric adenocarcinoma (GA) develop in multistep processes from atrophic gastritis (AG) and Barrett's esophagus (BE), respectively. Surveillance of the conditions mentioned above is a recognized method in diagnosing early lesions that can be treated endoscopically.

Aims & Methods: The main aim of the study was to assess if population-based one-time screening EGD would be suitable for a population at low to moderate risk of upper gastrointestinal cancer. Two databases were analyzed – 23864 patients with esophageal and gastric malignant neoplasm in the national cancer registry (KRN) diagnosed between 2014 and 2017 and another 5984 patients who underwent diagnostic EGD in three endoscopic units (retrospective cohort) from 03.2018 to 10.2019.

A retrospective cohort was analyzed to assess the age of patients diagnosed with precancerous conditions (AG and BE), esophageal and gastric dysplasia (ED and GD, respectively), cancers (EA and GA) and healthy individuals. Also, a retrospective cohort was analyzed to estimate particular histologic types of malignant esophageal and gastric tumors. An Internet questionnaire was provided to 304 individuals to estimate the acceptable ratio of potential benefits and harms of screening EGD.

Variable	Age groups					
	40-44	45-49	50-54	55-59	60-64	65-69
Number of potential cancers to avoid	10480	10074	9386	8164	6488	4697
Number of procedures needed to avoid one cancer	236	235	290	360	394	344
Ratio of potential benefits and harms	47	47	38	31	28	32

Number of potential cancers to avoid – number of esophageal adenocarcinomas and gastric non-cardia adenocarcinomas diagnosed in consecutive age groups (based on national cancer registry - KRN);

Number of procedures needed to avoid one cancer – the proportion of the number of procedures (population in each age group) and number of potential cancers to avoid;

The ratio of potential benefits and harms – the proportion of the 1/ number of procedures needed to avoid one cancer and risk of complications (9/100 000) [1].

Results: In the retrospective cohort, 131 patients were diagnosed with BE, 707 with AG, 26 ED, 102 GD, 5 EA, and 23 non-cardia GA. The mean age was significantly higher in patients with AG and BE (group 1; 62.9 SD 13.9), ED and GD (group 2; 67.2 SD 12.6), EA and GA (group 3; 64.6 SD 12.5) than in healthy controls (54.9 SD 16.6, all of the comparisons p<0.0001) and between group 1 and 2 (p=0.004). The risk of precancerous BE and AG, ED and GD, EA and GA diagnosis has been rising from age groups 40-

44 (OR 1.6; 95%CI 1.04-2.4), 55-59 (OR 3.6; 95%CI 1.3-9.7), and 60-64 (OR 12.1; 95%CI 1.5-98.6) respectively in comparison with patients at age <40 years. 10 480 cases in KRN were identified as EA and non-cardia GA aged 45 years or older. Based on questionnaire acceptable median ratio of potential benefits and harms was 100 for the 40-44 years group and 10 for the other 45-64 years groups. The estimated ratio of potential harms and benefits was higher than expected in screening groups aged 45-69 years and highest in the group 45-49 years.

Conclusion: The implementation of one-time screening EGD could be potentially beneficial and acceptable in groups aged 45 to 69 years, even in a population at low to moderate risk of esophageal and gastric cancer.

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P0120

CYSTIC FIBROSIS-RELATED GI DISEASE: A GROWING BURDEN FOR BOTH SERVICES

C. Mc Closkey¹, T. Nicholson¹, E. McKone¹, S.M. O'Reilly¹

¹St. Vincent's University Hospital, Centre for Colorectal Disease, Dublin, Ireland

Contact E-Mail Address: 10ciaran@gmail.com

Introduction: Ireland has one of the highest incidences of Cystic Fibrosis (CF) in the world, with approximately 1 in 19 Irish people carrying the gene. Much of the morbidity in patients with CF has traditionally related to their respiratory disease. Over time, this patient cohort has seen an increase in GI symptoms due to a number of factors including chronic PPI and laxative use, and increasing life expectancy. Whether CFTR modulators play a role or not has yet to be determined.

Data in recent years has also demonstrated significantly increased risk of GI tract malignancies in this cohort. While there is well established guidance regarding colorectal cancer screening in patients with CF, the link with many other GI tract pathologies remains unclear.

Aims & Methods: To explore the burden of GI disease in the CF population at a National Specialist Centre, on both hospital admissions and the endoscopy department, and to determine the prevalence of GI tract dysplasia in this patient cohort.

Results: From 2015 to 2020, there were 485 patients admitted a total of 11483 times, to the day or inpatient ward. 132 patients (27.2%) had at least one admission with a gastrointestinal issue as either a primary or secondary diagnosis over 6 years. The number of GI related admissions has increased almost threefold over the past 5 years, from 2.9% (55) to 8.4% (165).

The prevalence of diagnoses among this cohort were as follows; GORD (42.4%), CFRLD (40.2%) of which 4.5% had OLT, DIOS (19.7%), PEG/RIG insertion (11.4%), Chronic constipation (7.6%), Pancreatitis (3%) and Barrett's oesophagus (2.3%).

184 of 485 patients (37.9%) had at least one GI endoscopic procedure in our centre. 123 patients (25.3%) had an OGD with a median age of 39. 12 patients (9.8%) had endoscopic evidence of Barrett's oesophagus, 3.3% had histologic metaplasia and 1% had high grade dysplasia. Prevalence of Barrett's in the non-CF population at a comparable age is estimated at between 2 and 8%. Other diagnoses included; 7.3% benign polyps, 23.6% hiatal hernia (5.7% undergoing fundoplication), 8.1% Varices. 54 patients had a colonoscopy with a median age of 35, 20.4% had tubular adenomas with low grade dysplasia, 5.6% had tubulovillous adenomas and 1.9% had adenocarcinoma.

Conclusion: There is a rising prevalence of GI disease among the CF patient cohort, which is likely attributable at least in part to the introduction of CFTR modulators. Our study found significantly higher rates of GI tract dysplasia in this population, both upper and lower GI. It is possible that the increase in Barrett's is due to chronic oesophagitis and gastritis as opposed to being attributable to the genetic mutation.

Despite established colonoscopy screening guidelines, there are no upper endoscopy guidelines for this cohort, with more work needed to be done in this area. As life expectancy continues to improve, it is likely we will see an increasing burden on endoscopy services in years to come. Use of non-invasive methods for screening should be evaluated in this population.

Disclosure: Nothing to disclose.

Poster presentations *H. pylori*

Poster Presentations

H. pylori

H. pylori

P0121

PREVALENCE OF *HELICOBACTER PYLORI* IN OBESE PATIENTS UNDERGOING PREOPERATIVE ENDOSCOPIC EVALUATION FOR BARIATRIC SURGERY: EXPERIENCE FROM A SINGLE CENTER IN NORTHERN ITALY

N. Mezzina¹, C. Gentile¹, A. Dell'Era², R. Salerno¹, S. Carmagnola¹, M.P. Giusti³, M.A. Zappa³, S. Ardizzone²

¹ASST Fatebenefratelli Sacco, Gastroenterology and Digestive Endoscopy Unit, Milano, Italy, ²Università degli Studi di Milano, Department of Biomedical and Clinical Sciences "Luigi Sacco", Milano, Italy, ³ASST Fatebenefratelli Sacco, General Surgery, Milano, Italy

Contact E-Mail Address: nikmez@gmail.com

Introduction: *Helicobacter pylori* (Hp) infection still represents an important public health issue worldwide. The most recent large meta-analysis reported an estimated prevalence of Hp infection in Europe of 47% (56% in Italy)¹.

With regard to morbidly obese patients, the prevalence and role of Hp infection is still controversial, with limited data available, especially from western countries. Routine upper gastrointestinal endoscopy before bariatric surgery is generally recommended, to rule out pathological abnormalities, including Hp infection.

Aims & Methods: Data from all consecutive patients undergoing preoperative endoscopic evaluation for bariatric surgery at our institution (Fatebenefratelli Hospital, Milan, Italy) between January 2019 and December 2021 were retrospectively analyzed. Hp infection was evaluated with histology from biopsy samples, which are part of the preoperative evaluation protocol.

Results: 123 patients (96 females, median age 44 years) were included (Table 1). The median BMI was 40.5, with most patients suffering from grade III obesity (58.5%). Half of patients (n=59) were non-smokers.

Diabetes was present in 11% of patients, hypertension in 35%, OSAS 11%, and hypothyroidism in 13%. Hp infection was present in 29% of patients. There was no statistically significant association between Hp status and demographic or clinical characteristics; interestingly, Hp positive patients were less frequently affected by diabetes compared to Hp negative patients, although this trend was not statistically significant (3% vs 14%, p=0.1).

Regarding endoscopic findings, overall, 24% of patients presented no abnormalities; 11% had esophagitis, 73% hiatal hernia, 44% hyperemic gastritis, 15% erosive gastritis, 13% duodenitis: these endoscopic findings did not differ between Hp positive and negative patients.

Regarding histologic findings, acute and/or chronic gastritis was significantly more common among Hp positive patients (100% vs 73%, p<0.001), while atrophy didn't depend on Hp status.

Surprisingly, there was a trend toward a higher frequency of intestinal metaplasia in Hp negative patients, although not statistically significant (8% vs 0% in Hp positive, p=0.1).

Conclusion: In our cohort of morbidly obese patients, the prevalence of Hp infection – diagnosed by histology – was 29%, which resulted slightly lower compared to what has been reported in the literature in the overall population. Hp positive patients didn't appear to have worse endoscopic

findings compared with Hp negative patients, but histologically proven gastritis was significantly more frequent among Hp positive patients. Finally, diabetes was more frequent in Hp negative patients, but this latter evidence, as well as the others, must be interpreted with caution, and are needed to be confirmed in a larger cohort.

	Hp positive	Hp negative	p value
Age (median, range)	46.5 (28-67)	43.2 (20-65)	n.s.
Male (%)	25	21	n.s.
BMI (median, range)	40.1 (32.8-58.1)	41 (32-61.2)	n.s.
Obesity (%)			
class I	8	4	n.s.
class II	36	36	
class III	56	60	
Smoking (%)			
Never	47	52	n.s.
Active	35	37	
Former	17	11	
Comorbidities (%)			
Diabetes	3	14	0.1
Hypertension	28	38	n.s.
Osas	17	8	n.s.
Hypothyroidism	11	15	n.s.
Previous cholecystectomy	11	10	n.s.
PPI use	14	15	n.s.
Endoscopy (%)			
Normal	25	24	n.s.
Gastritis	64	60	n.s.
Duodenitis	20	10	n.s.
Esophagitis	8	12	n.s.
Hiatal hernia	19	30	n.s.
Histology (%)			
Gastritis	100	73	< 0.001
Atrophy	11	5	n.s.
Intestinal metaplasia	0	8	0.1

Table 1.

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Disclosure: Nothing to disclose.

P0122

REFRACTORY *H. PYLORI* INFECTION AND GASTRIC MICROBIOTA

J. Wang¹, Y. Xie¹

¹The First Affiliated Hospital of Nanchang University, Department of Gastroenterology, Nanchang, China

Contact E-Mail Address: dnk63006@163.com

Introduction: Since Marshall and Warren discovered *Helicobacter pylori* in 1983(1), the international digestive community has made a breakthrough progress in the etiology research and treatment of chronic gastritis, peptic ulcer disease and gastric cancer. Over 50% of people were infected with *H.pylori*(2).

At present, the World Health Organization (WHO) has regarded *H.pylori* as the class I carcinogen of gastric cancer(3). However, In recent years, with the application of high-throughput sequencing technology, people have

made great progress in the cognition of gastric flora. Many previous studies mainly focused on the role of changes in gastric flora in the occurrence and development of gastric diseases(4-7). However, the diversity, composition and function of gastric flora after *H.pylori* colonization and eradication treatment are not clear. There are many subjects who fail to eradicate *H.pylori* for many times in clinic, and the eradication is still unsuccessful after multiple replacements of antibiotics. Therefore, the related gastric microecology research is particularly important. At present, there is no research on the influence of multiple *H.pylori* eradication history on gastric flora.

Aims & Methods: To investigate the effect of refractory *Helicobacter pylori* infection on the diversity, composition and function of gastric flora. We designed a clinical study involved with 32 subjects who were divided into three groups: 1. nAGHp. a group: *H.pylori* positive was first found in non-atrophic gastritis; 2. nAGHp. b group: *H.pylori* negative in non-atrophic gastritis; 3. EFHp. a group: Refractory *H.pylori* infection. Gastric mucosa samples were collected for 16S rRNA sequencing analysis.

Results: There are significant differences between *H.pylori* positive group and *H.pylori* negative group in species diversity, gastric flora structure and bacterial function. The results of LEfSe analysis suggested that the beneficial *Lactobacillus* in *H.pylori* positive group was significantly enriched than that in refractory *H.pylori* infection group. The bacterial interaction network diagram suggested that the interaction between bacteria in refractory *H.pylori* infection group decreased. We found that the refractory *H.pylori* infection group gastric microbiota was enriched in energy metabolism, bacteria secretion system, glutathione metabolism, protein folding and associated processing, surficial metabolism, membrane and intracellular structural molecules, lipopolysaccharide biosynthesis, ubiquinone and other terpenoid-quinone biosynthesis, inorganic ion transport and metabolism as well as metabolism of cofactors and vitamins compared with *H.pylori* positive group by PICRUST2 analysis.

Conclusion: *H.pylori* infection is an important factor affecting the diversity, composition and function of normal gastric flora. Multiple *H.pylori* eradication history can lead to imbalance of gastric mucosal flora to a certain extent, which is mainly reflected in inhibiting the growth of beneficial *Lactobacillus* in the stomach, and multiple *H.pylori* eradication history can change some functions of gastric flora.

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P0123

EFFECT OF HELICOBACTER PYLORI VIRULENCE FACTORS ON THE MORPHOLOGICAL CHANGES OF GASTRIC MUCOSA IN PATIENTS WITH CHRONIC GASTRITIS AND THEIR ROLE IN CLARITHROMYCIN PRIMARY RESISTANCE

L. Nikulina¹, G. Solovyova^{1,2}

¹Bogomolets National Medical University, Kyiv, Ukraine, ²Gastro Center of the Clinic «Oberig», Kyiv, Ukraine

Contact E-Mail Address: Lilinika95@gmail.com

Introduction: Helicobacter pylori is recognized as the main etiological factor in the development of gastric cancer. The virulence factors of CagA and VacA have demonstrated their genetic differences among other HP strains, making them of clinical interest as possible predictors of gastric cancer. Some studies also have found an association between virulent strains of *H. pylori* and the presence of antibiotic resistance, however these data are controversial.

Aims & Methods: The aim of this study was to evaluate the effect of HP virulence factors (CagA + VacA +) on morphological changes of the gastric mucosa and to determine their relationship with clarithromycin resistance. This study was conducted as a cross-sectional study in adult subjects with HP chronic gastritis. EGD with chromoscopy and NBI and biopsy with gastritis evaluation by OLGA and OLGIM was used for the detection of chronic gastritis.

We compare the degree of inflammation, activity of gastritis, presence and degree of atrophy, metaplasia and dysplasia in patients with HP virulence factors and without virulence factors (control group). Genotyping for virulence factors and Hp gene mutations in the V 23S rRNA domain associated with clarithromycin resistance were determined by PCR. The 23S rRNA gene was analyzed with three-point mutations (A2142G/C, A2143G, T2182C) for clarithromycin. Patients who had received macrolides antibiotics within the last 6 months were excluded from the study.

Results: The study included 64 patients with chronic HP-associated gastritis, aged 25-70 years (mean age 46.0 ± 11.8 years). Among the patients, 38 (59,4%) were men and 26 (40,6%) women. Highly pathogenic CagA + VacA + Hp strains were detected in 38 patients (59,4%).

The level of both gastric and antral body inflammation was higher in patients with CagA+VacA+ strains. The level of antral inflammation was I-st degree in 13,1%; II-nd in 71,1%; III-d in 15,8% in examined patients and I-st degree in 61,5%; II-nd in 38,5%; III-d in 0% in control group ($\chi^2 = 17.9$, $p < 0.0001$).

The level of body inflammation was I-st degree in 31,6%; II-nd in 15,8%; III-d in 52,6% in examined patients and I-st degree in 100% of the control group ($\chi^2 = 29.9$, $p < 0.0001$). The grade of antral atrophy was significantly higher in patients with CagA+VacA+ strains (63,1% vs 42,3%; $\chi^2 = 2.7$, $p < 0.05$). An inflammatory activity degree and metaplasia were observed at the same frequency in both groups ($p > 0.05$).

The level of primary resistance to clarithromycin was 31.2%. Clarithromycin resistance was significantly lower in CagA+VacA+ than CagA-VacA- strains (13,1% vs 57,7%; $\chi^2 = 14.25$, $p < 0.0001$). The most observed resistance mutation was A2143G (75%).

Conclusion: Our study shows that patients infected with highly pathogenic strains of Hp (CagA+VacA+) tended to have more pronounced morphological changes of the gastric mucous, namely inflammation and atrophy. Nevertheless, primary clarithromycin resistance is more common in patients infected with non-pathogenic CagA-VacA- strains of Helicobacter pylori.

Disclosure: All authors have declared no conflict of interest.

P0124

EVALUATION OF IL-17F A7488G POLYMORPHISM IN *HELICOBACTER PYLORI*-INFECTED PATIENTS IN QOM-IRAN

F.S. Mirtalebi Roknabadi¹, A. Hormati², S. Shams³, M. Aghaali⁴

¹Islamic Azad University Qom Branch, Department of Genetics, Qom, Iran (Islamic Republic of), ²Qom University of Medical Sciences, Gastroenterology and Hepatology Disease Research Center, Qom, Iran (Islamic Republic of), ³Qom University of Medical Sciences, Cellular and Molecular Research Center, Qom, Iran (Islamic Republic of), ⁴Qom University of Medical Sciences, Department of Epidemiology, School of Medicine, Qom, Iran (Islamic Republic of)

Contact E-Mail Address: sshamsmed@gmail.com

Introduction: *Helicobacter pylori* is a gram-negative gram, microaerophilic, and spiral bacteria. The prevalence of infection varies from country to country and from population to population and is closely related to the socioeconomic status of the people. There are no specific symptoms in most colonized patients, but clinical complications can range from gastritis and duodenal ulcer to cancer and mucosa-associated lymphoid tissue (MALT) lymphoma. *H. pylori* infection and its progression are influenced by the heterogeneity of virulence factors, environmental factors, host genetic predisposition, and gene regulation. Among the virulence factors, the CagA (cytotoxin-associated gene A) is a known oncoprotein, encoded by the *cagA* gene localized in the *H. pylori* pathogenicity island. IL-17, as an inflammatory cytokine, plays an important role in the severity of gastric mucosal inflammation and gastric cancer development.

Aims & Methods: Our aim was to evaluate the IL-17 A7488G polymorphism in *H. pylori*-infected patients and its association with the *cagA* virulence gene in Qom, Iran, for the first time. In this case-control study, 86 samples of the gastric biopsy were collected from patients with gastrointestinal problems referred to the endoscopy ward of Shahid-Beheshti hospital. Rapid urease test (for initial screening) and PCR of 16S rRNA gene (to confirm infection) were performed to identify positive and negative cases of *H. pylori*. The *cagA* gene was also evaluated as a pathogenic bacterial factor. PCR-RFLP was performed to investigate the IL-17 polymorphism using the *NotI* enzyme.

Results: Among 86 participants, 49 (57.0%) patients were male, and 37 (43.0%) cases were female, with a mean±SD age of 47.13±16.72 years. *H. pylori*-positive ratio in males (30/43, 69.8%) was significantly higher than in females (13/43, 30.2%). The mean±SD of age in the case and control groups was 45.14±14.90 and 49.12±18.54, respectively ($p=0.276$). In the *H. pylori*-positive group, abdominal pain (32 cases-74.4%) and duodenal ulcer (12 cases-27.9%) were the most clinical symptom and endoscopic finding, respectively. Except for abdominal pain ($p=0.015$), no significant relationship was observed between other clinical symptoms and endoscopic features in both groups of patients. There was also no significant difference between the two groups in terms of age, height, weight, BMI, smoking, and education. In addition, in case group, 13 patients (30.2%) were positive for the *cagA* gene. Regarding IL-17 genotypes distribution, the wild genotype (AA) frequency was 96.5% in patients in both groups (40/43, 93.0% in the case group vs. 43/43, 100.0% in the control group). Only three patients had polymorphisms in the IL-17 gene (AG in one patient and GG in two patients), all belonged to the case group. There was no association between infection and even the presence of *cagA* and the IL-17 polymorphism. Interestingly, three patients with GG and AG variants were positive for the *cagA* gene.

Conclusion: This study provides the first data on IL-17F A7488G gene polymorphism among individuals with *H. pylori* infection in Qom. Our results showed no association between polymorphism and infection among patients under study. According to the results of the *cagA* gene, it seems that

the strains evaluated in this study were less pathogenic. Also, no correlation was observed between *cagA*-positive strains and cytokine polymorphism. However, three patients with mutant patterns were positive for the *cagA* gene, which might be an association between pathogenic strains and this polymorphism. However, this finding needs further investigation.

Disclosure: Nothing to disclose

P0125

PERNICIOUS ANEMIA AND *HELICOBACTER PYLORI* INFECTION : AN INTRICATE ASSOCIATION

M. Mtir¹, M. Ayari¹, A. Chehaider¹, Y. Ben Hamadi¹, W. Khemiri¹, I. Abdelaali¹, T. Jomni¹, M.H. Douggui¹

¹Internal Security Forces Hospital of Tunis, Gastroenterology Department, Tunis, Tunisia

Contact E-Mail Address: mtirmaha@gmail.com

Introduction: Pernicious anemia, also known as Biermer's disease, is an autoimmune atrophic gastritis caused by autoantibodies targeting intrinsic factor and/or gastric parietal cells, leading to impaired absorption of vitamin B12. Its association with a colonization by *Helicobacter pylori* (Hp), itself incriminated in the occurrence of atrophic gastritis and vitamin B12 deficiency, may suggest the possibility of an unfavorable outcome of this disease, including a potentiation of the carcinogenic risk.

Aims & Methods: The aim of our study was to determine the prevalence and the impact of Hp in patients diagnosed with Pernicious anemia.

We conducted a retrospective single-center study, including all patients followed for pernicious anemia over a 7-year period [2014 - 2021]. Clinicobiological, endoscopic, histological data and outcomes were collected. Anatomopathological examination was used to assess the severity of gastritis according to the Sydney system as well as the presence of Hp and the patients were classified into two groups:

- G1 (N=17): pernicious anemia Hp +
- G2 (N=50): pernicious anemia Hp -

A descriptive and analytical statistical study using SPSS software was performed to compare the two groups.

Results: In total, we included 67 patients with a mean age of 63 years [38-89] and a sex ratio M/F of 1.68. The prevalence of Hp in patients followed for pernicious anemia was 25.4%. In Hp+ group, severe atrophy was observed in 88.2% of cases versus 64% in Hp- ($p=0.05$). Similarly, the degree of activity was severe in 11.8% of cases in Hp + group versus 2% in the absence of Hp.

However, there was no significant difference in severe intestinal metaplasia lesions in both groups, which were respectively 17.6% in G1 and 26% in G2. All patients received vitamin B12 therapy for a mean duration of 41 months. A significantly better response was observed in the group of patients without Hp infection.

	Group 1			Group 2		
	Before treatment	After treatment	p-value	Before treatment	After treatment	p-value
Mean Hb (g/dl)	11.2	12.6	0.02	9.3	15.2	0.02
Mean MCV(μm3)	84.2	79.3	0.041	92.5	84.1	0.0001
Mean VB12 (pg/ml)	172.5	260.6	0.171	102	565.7	<0.0001

During the follow-up, we observed the occurrence of stomach cancer in 7 patients: 4 cases of gastric carcinoid tumor, 2 cases of gastric adenocarcinoma and one case of gastric MALT lymphoma, which were respectively 11.7% for G1 and 10% for G2 with $p\text{-value}=0.837$, suggesting the absence of an over-risk of carcinogenesis in the presence of Hp.

In univariate study and using the chi-square test, the factors associated with Hp in Biermer's disease were: gender ($p=0.035$), anemia ($p=0.009$) and vitamin B12 deficiency ($p=0.009$).

Conclusion: According to our study, one in four patients with pernicious anemia have Hp infection. Although this association may not present an over-risk of carcinogenesis, it is most likely to cause more severe gastric atrophy, anemia, vitamin B12 deficiency and lower response to treatment. Early systematic screening and eradication of Hp in this context is recommended to improve the course of the disease.

Disclosure: Nothing to disclose.

P1030

HELICOBACTER PYLORI INFECTION PROMOTES CARCINOGENESIS BY UP-REGULATING ACE2 EXPRESSION

H. Wang¹, J. Rong¹, Y. Xie¹

¹The First Affiliated Hospital of Nanchang University, Gastroenterology, Nanchang, China

Contact E-Mail Address: 1099163722@qq.com

Introduction: As a SARS-CoV-2 receptor, ACE2 has attracted much attention in recent years, and studies have shown that ACE2 is widely expressed in human digestive tract. A clinical study showed that *Helicobacter pylori* (*H. pylori*)-positive patients infected with SARS-CoV-2 showed more severe gastrointestinal symptoms. However, the relationship between ACE2 and *H. pylori* infection and its role in the pathogenesis of *H. pylori* infection are unknown.

Aims & Methods: An in vitro coculture system and an in vivo C57BL/6 mouse model of *H. pylori*-infected gastric epithelial cells were established. The effect of *H. pylori* infection in vitro and in vivo on ACE2 expression was detected by western blot, and the changes of ACE2 expression in gastric mucosa tissues of *H. pylori*-infected mice were also detected by IHC. At the same time, 28 pairs of gastric cancer and paracancer tissue specimens were collected in this study, and the expression differences of ACE2 in gastric cancer and paracancer tissues were detected. Finally, overexpression and knockdown ACE2 cell lines were constructed, and the effects of ACE2 on cell biological functions were detected by CCK8, EdU, plate clone formation, cell scratch repair assay and Transwell cell migration and invasion assay.

Results: *H. pylori* infection in vitro and in vivo can significantly up-regulate the expression of ACE2, and the expression of ACE2 in gastric cancer tissues is significantly higher than that in paracancer tissues. Cell biological function experiments showed that ACE2 overexpression significantly promoted the proliferation, migration and invasion of gastric epithelial cells, while knockdown ACE2 expression significantly reduced the proliferation, migration and invasion of gastric epithelial cells.

Conclusion: *H. pylori* infection significantly up-regulated the expression of the oncogene ACE2, suggesting that ACE2 may be involved in the pathogenesis of *H. pylori* infection.

References:

Disclosure: Nothing to disclose.

P0126

EVALUATION OF THE ACCURACY OF THE "LIAISON® MERIDIAN HELICOBACTER PYLORI SA" STOOL ANTIGEN TEST FOR THE DIAGNOSIS OF H. PYLORI INFECTION: A SPANISH MULTICENTRE STUDY

E. Resina Sierra¹, M. G. Donday¹, S.J. Martínez-Domínguez², E.J. Laserna-Mendieta³, A. Lanás², A.J. Lucendo⁴, M. Sánchez-Luengo², N. Alcaide Suárez², V. Bachiller⁵, L. Luisa De La Peña-Negro⁶, L. Bujanda Fernández de Piérola⁷, M. Gómez-Ruiz de Arbulo⁸, J. Alcedo⁹, Á. Pérez-Aísa¹⁰, R. Rodríguez Insa¹¹, S. Hermida¹, Y. Brenes¹, O. P. Nyssen¹, J. P. Gisbert¹

¹Hospital Universitario de La Princesa, Instituto de Investigación Sanitaria Princesa (IIS-Princesa) Universidad Autónoma de Madrid (UAM), and Centro de Investigación Biomédica en Red de Enfermedades Hepáticas y Digestivas (CIBEREHD), Gastroenterology Unit, Madrid, Spain, ²Hospital Clínico Universitario Lozano Blesa, Zaragoza, Spain, ³Laboratory Medicine Department, Hospital Universitario de La Princesa, Instituto de Investigación Sanitaria Princesa (IIS-IP), Research Unit, Hospital General de Tomelloso, Ciudad Real, Tomelloso, Spain, ⁴Hospital General de Tomelloso, Dept. de Gastroenterology, Tomelloso, Spain, ⁵Hospital Clínico Universitario de Valladolid, Gastroenterology Unit, Gerencia Regional de Salud (SACYL), Valladolid, Spain, ⁶Hospital de Viladecans, Viladecans, Spain, ⁷Gastroenterology Unit, Hospital Donostia/Instituto Biodonostia, Universidad del País Vasco (UPV/EHU), Centro de Investigación Biomédica en Red de Enfermedades Hepáticas y Digestivas (CIBEREHD), San Sebastián, Spain, ⁸Hospital Donostia/Instituto Biodonostia, Centro de Investigación Biomédica en Red de Enfermedades Respiratorias (CIBERES), Microbiology Department, Donostia, Spain, ⁹Miguel Servet University Hospital, Digestive Diseases Department, Zaragoza, Spain, ¹⁰Hospital Costa del Sol, Gastroenterology Unit, Marbella, Spain, ¹¹Hospital General Universitario de Castellón, Castellón, Spain

Contact E-Mail Address: elenaresina93@gmail.com

Introduction: Detection of *Helicobacter pylori* by a stool antigen test (SAT) is an attractive non-invasive alternative.

Aims & Methods: The aim of this study was to assess the accuracy of a new SAT, the automated LIAISON® Meridian *H. pylori* SA chemiluminescent immunoassay (CLIA) based on monoclonal antibodies, as compared to the ¹³C-Urea Breath Test (UBT) gold standard. This prospective multicentre study (9 Spanish centres) enrolled patients over 18 years of age with clinical indication to perform UBT, both for initial diagnosis and confirmation of eradication of *H. pylori*.

Patients taking PPIs, antibiotics or prior gastric surgery were excluded. Two UBT methods were used, as available: mass spectrometer (MS), including citric acid in its protocol; and infrared spectrophotometer (IRS), without citric acid.

Results: Three-hundred and seven patients (145 naïve and 162 confirmation of eradication) were included: 67% female, mean age 47 years (range 19-81). When using recommended cut-off values (negative SAT <0.90, positive ≥1.10), the sensitivity, specificity, positive predictive value, negative predictive value and accuracy were 67%, 97%, 86%, 92% and 91% respectively; obtaining an area under the ROC curve (AUC) of 0.85. In total, 28/307 patients, including 7 false positives and 21 false negatives, presented a discordant result between SAT and UBT.

Among the 21 false negatives, 4/6 tested with MS and 11/15 tested with IRS had a borderline UBT delta value (values between 5.2 and 5.8, being the cut-off point of 5‰ with MS, and close to the cut-off point of 2.5‰ with IRS). In 25/28 discordant samples, PCR targeting *H. pylori* DNA was

performed and SAT accuracy was re-analysed: sensitivity, specificity, positive predictive value, negative predictive value, accuracy and AUC were 94%, 97%, 86%, 99%, 97% and 0.96 respectively. Diagnostic accuracy was calculated separately for the naïve and post-treatment groups (Table 1).

Comparison SAT vs UBT	Sensitivity 95% CI	Specificity 95% CI	PPV 95% CI	NPV 95% CI	LR+ 95% CI	LR- 95% CI	Global accuracy 95% CI	AUC 95% CI
Overall	67% (55-79%)	97% (95-99%)	86% (75-97%)	92% (88-95%)	23 (11-49)	0.34 (0.24-0.48)	91% (88-94%)	0.85 (0.78-0.92)
Naïve	74% (59-88%)	96% (92-100%)	89% (77-100%)	90% (84-96%)	19 (7-51)	0.27 (0.16-0.45)	90% (84-95%)	0.88 (0.80-0.96)
NDIRS Naïve	73% (54-92%)	93% (86-100%)	83% (65-100%)	89% (80-97%)	11 (4-29)	0.29 (0.15-0.55)	87% (80-95%)	0.86 (0.75-0.96)
IRMS Naïve	75% (51-99%)	100% (99-100%)	100% (96-100%)	92% (82-100%)	-	0.25 (0.11-0.58)	93% (86-100%)	0.91 (0.79-1.0)
Post-treatment	55% (31-78%)	98% (95-100%)	80% (56-100%)	93% (89-98%)	25 (8-82)	0.46 (0.29-0.73)	92% (87-96%)	0.79 (0.65-0.93)
NDIRS Post-Treatment	53% (26-80%)	99% (96-100%)	90% (66-100%)	91% (85-98%)	46 (6-336)	0.48 (0.29-0.79)	91% (85-97%)	0.81 (0.67-0.95)
IRMS Post-Treatment	60% (7.1-100%)	96% (90-100%)	60% (7-100%)	96% (90-100%)	16 (3-75)	0.42 (0.14-1.22)	93% (86-100%)	0.78 (0.44-1.0)
Overall after performing RT-PCR in stool	94% (85-100%)	97% (95-99%)	86% (75-97%)	99% (97-100%)	35 (17-73)	0.07 (0.02-0.20)	97% (95-99%)	0.96 (0.91-1.0)
Naïve after performing RT-PCR in stool	91% (80-100%)	96% (93-100%)	89% (77-100%)	97% (94-100%)	25 (10-67)	0.09 (0.03-0.27)	95% (91-99%)	0.996 (0.99-1.0)
Post-treatment after performing RT-PCR in stool	100% (96-100%)	98% (95-100%)	80% (56-100%)	100% (99-100%)	50 (16-153)	0.00	98% (96-100%)	0.94 (0.88-1.0)

SAT: Stool Antigen Test; UBT: Urea Breath Test; CI: Confidence Interval; PPV: Positive-Predictive-Value; NPV: Negative-Predictive-Value; LR+: Positive Likelihood Ratios; LR-: Negative Likelihood Ratios; AUC: Area under the ROC Curve; IRMS: Isotope ratio mass spectrometer; NDIRS: Nondispersive isotope-selective infrared spectrometer RT-PCR: Real-Time Polymerase Chain Reaction.

Table 1.

Conclusion: The new LIAISON® Meridian *H. pylori* SA SAT shows a good accuracy for diagnosis of *H. pylori* infection.

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P0127

HOW ARE JAPANESE PATIENTS WITH AUTOIMMUNE GASTRITIS AFFECTED BY *H. PYLORI* INFECTION?: AN EVALUATION OF SEROLOGICAL, ENDOSCOPIC, AND HISTOLOGICAL FINDINGS

N. Sumi¹, K. Haruma^{2,3}, K. Inoue³, K. Mabe⁴, N. Kimura⁵, T. Watanabe⁶, R. Aoki⁷, T. Kotera⁸, M. Ayaki⁹, N. Manabe⁹, A. Shiotani¹⁰, T. Kamada¹, T. Takao¹

¹Kawasaki Medical School, Health Care Medicine, Kurashiki, Japan, ²Kawasaki Medical School, General Internal Medicine 2, Kurashiki, Japan, ³Junpukai Health Maintenance Center, Okayama, Japan, ⁴Junpukai Health Maintenance Center Kurashiki, Kurashiki, Japan, ⁵Oami Municipal Hospital, Chiba, Japan, ⁶Watanabe Gastroenterology Surgery Hospital, Kurashiki, Japan, ⁷Tokushima Health Screening Center, Tokushima, Japan, ⁸Uji-Tokushukai Medical Center, Uji, Japan, ⁹Kawasaki Medical School, Endoscopy and Ultrasonography, Kurashiki, Japan, ¹⁰Kawasaki Medical School, Gastroenterology, Kurashiki, Japan

Contact E-Mail Address: naoksmith@gmail.com

Introduction: *Helicobacter pylori* (Hp) infection is an etiologic agent of autoimmune gastritis (AIG). However, AIG incidence in Japan is low despite high rates of Hp infection and atrophic gastritis. Therefore, AIG pathogenesis in Japan may differ from that in the West.

Aims & Methods: This study aimed to investigate the effects of Hp infection on endoscopic, serological, and histological findings and to clarify its involvement AIG pathogenesis in Japan. A total of 99 Japanese patients (mean age ± standard error [SE], 64.7 ± 1.2 years; 57 women) were diagnosed with AIG at ten institutes in Japan between January 2010 and November 2020.

We evaluated the serum gastrin, anti-parietal cell antibody (APCA), anti-intrinsic factor antibody (AIFA), pepsinogen (PG), clinical findings (pernicious anemia), and endoscopic findings by Hp infection status.

AIG was defined as follows:

1. Predominantly atrophic corpus on endoscopy;
2. APCA elevation by 20 times or more, AIFA, endocrine cell micronest (ECM), and enterochromaffin-like (ECL) cell hyperplasia; and,
3. Hypergastrinemia (serum gastrin > 500 pg/mL).

Hp infection status was defined by the presence of serum Hp-IgG antibody. In addition, the group with a history of Hp eradication confirmed on the questionnaire was defined as the Hp eradication group. Data among the three groups classified by Hp status were analyzed using the Kruskal-Wallis and χ -square tests. Statistical significance was set at $P < 0.05$.

Results: There were 69, 19, and 11 cases in the Hp-negative, Hp eradication, and Hp-positive groups, respectively. Serum gastrin (mean ± SE) was significantly lower in the Hp-positive (1477.6 ± 266.8 pg/mL) and Hp eradication groups (1734.4 ± 264.6 pg/mL) than that in the Hp-negative group (3035.9 ± 243.6 pg/mL). PGII was significantly higher in the Hp-positive group (16.0 ± 2.5 ng/mL) than that in the negative (10.4 ± 0.6 ng/mL) and eradication groups (9.9 ± 0.9 ng/mL). Serum PGI, PGI/II, APCA positive rate, ECM positive rate, and pernicious anemia rate were not significant among the three groups.

Endoscopic findings showed that atrophy in the antrum was significantly higher in the Hp-positive (90.9%) and eradication groups (73.7%) than that in the negative group (31.9%). Diffuse redness in the corpus was significantly higher in the Hp-positive group than that in the negative group (63.6% vs. 13.0%).

Conclusion: Hp infection affected serum gastrin, PGII, and endoscopic findings in AIG.

Furthermore, there were AIG cases not associated with Hp infection. In cases of extensive atrophy of the antrum and corpus, it is necessary to consider AIG cases caused by Hp infection.

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P0128

PCR IMPROVES DETECTION OF *HELICOBACTER PYLORI* IN UNSELECTED ADULT PATIENTS UNDERGOING ROUTINE GASTROSCOPY

T. Butler¹, F. Fitzgibbon², D. McNamara³, S. Smith¹

¹Trinity College Dublin/Tallaght University Hospital, Clinical Medicine (Trinity College Dublin) & Gastroenterology (Tallaght University Hospital), Dublin, Ireland, ²Technological University Dublin, Biological & Health Sciences, Dublin, Ireland, ³Tallaght University Hospital, Gastroenterology, Dublin, Ireland

Contact E-Mail Address: thbutler@tcd.ie

Introduction: Accurate detection of *H. pylori* is essential for effective patient management. Reduced prevalence and wide usage of PPI's can negatively impact commonly employed tests, including rapid urease tests (CLO), culture and standard histological examinations. Additional tests in at risk patients could improve detection.

Aims & Methods: Aims: To compare the performance of a PCR-based assay for the detection of *H. pylori* versus routine histological testing in an Irish context.

Methods: Following ethical approval and informed consent, adults were prospectively recruited. During routine gastroscopy subjects had 2 additional antrum and corpus biopsies taken for DNA extraction and PCR using custom-designed primers for the urease gene. CLO tests and antral and corpus histology (H&E and IHC, where indicated in the hospital laboratory) were performed as standard.

Results: In all, 118 patients with available histology and PCR results were included in the analysis. 27 had chronic active gastritis (CAG), of which 21 (78%), 20 (74%) and 13 (48%) had positive histology, PCR and CLO tests respectively. Of interest, in 44 subjects with chronic inactive gastritis (CIG), 11 (25%) had a positive PCR and only 1 (2%) positive histology. PCR detected the urease gene in 31 (26%) patients indicative of infection; 20 and 11 with CAG and CIG respectively. Based on PCR the sensitivity, specificity, PPV and NPV for histology were 67%, 98%, 89% and 89% respectively.

Conclusion: PCR-based testing should be included in cases where no *Helicobacter*-like organisms are detected on routine histology, particularly if the patient has a presentation of chronic gastritis irrespective of activity.

Disclosure: Nothing to disclose.

P0129

ALCOHOL INCREASES TREATMENT FAILURE FOR *HELICOBACTER PYLORI* ERADICATION IN ASIAN POPULATIONS

X. Wang¹, J. Yu¹

¹Changzhou No.2 People's Hospital, Gastroenterology, Changzhou, China

Contact E-Mail Address: wxy20009@126.com

Introduction: Although the underlying link between alcohol consumption and the risk of *Helicobacter pylori* (*H. pylori*) eradication failure has been revealed in previous studies, there are some conflicting reports in this regard. Based on the published research, this study aims to address these conflicts.

Aims & Methods: Eligible studies were screened and retrieved through January 2022 using PubMed, Web of Science, and a manual review of references. Results were expressed as odds ratios (ORs) and 95% confidence intervals (CIs). Subgroup, publication bias, and sensitivity analyses were also conducted.

Results: A total of 40 studies were included in the meta-analysis. No significant association was found between alcohol consumption and the risk of *H. pylori* eradication failure (OR = 1.09, 95% CI, 0.94–1.26). However, in subgroup analyses stratified by region, alcohol consumption was associated with increased treatment failure for *H. pylori* eradication in Asian patients (OR = 1.23, 95% CI, 1.03–1.47).

Moreover, in Asian patients, when the duration of therapy was >7 days (OR = 1.17, 95% CI, 1.10–1.25) or when the treatment regimen included nitroimidazoles (OR = 1.16, 95% CI, 1.09–1.24), alcohol consumption was associated with an increased risk of *H. pylori* eradication failure. Increased alcohol intake (>40 g/day) was also associated with a higher risk of *H. pylori* eradication failure (OR = 3.17, 95% CI, 1.56–6.41).

Alcohol consumption reduced the *H. pylori* eradication rate in Asian patients in whom bismuth-containing quadruple therapy (OR = 1.17, 95% CI, 1.10–1.25) was used to treat *H. pylori* infection; however, alcohol consumption had no effect on *H. pylori* eradication rate in Asian patients who were administered a vonoprazan (VPZ)-based therapy regimen (OR = 1.73, 95% CI, 0.98–3.05).

Conclusion: Alcohol consumption dose-dependently increases the risk of *H. pylori* eradication failure in Asian populations. However, a VPZ-based treatment regimen can prevent this effect.

Disclosure: Nothing to disclose.

P0130

THE EFFECT OF LACTOBACILLUS REUTERI-CONTAINING QUADRUPLE THERAPY IN FIRST-LINE ERADICATION THERAPY FOR *HELICOBACTER PYLORI* INFECTION: A SINGLE-CENTER OPEN-LABEL RANDOMIZED CONTROLLED STUDY

C. Li¹, B. Suo¹, X. Tian¹, Y. Zhang¹, X. Ren¹, Z. Song¹

¹Peking University Third Hospital, Department of Gastroenterology, Beijing, China

Contact E-Mail Address: 17865190329@163.com

Introduction: With the increasing resistance rate of *Helicobacter pylori* to levofloxacin, clarithromycin, metronidazole and other antibiotics, the efficacy of commonly used eradication regimens recommended by guidelines gradually declines, and may lead to increased antibiotic resistance rates, gut microbiota disruption and various adverse reactions.

Studies have shown that probiotics can reduce *Helicobacter pylori* infection and improve the adverse reactions of eradication therapy by producing antibacterial substances, inhibiting bacterial colonization, and enhancing mucosal barrier, etc.

Aims & Methods: This study aims to determine whether Lactobacillus Reuteri-containing quadruple therapy is inferior to bismuth-containing quadruple therapy with respect to the efficacy, safety and compliance in Helicobacter pylori eradication. A total of 240 treatment-naïve Helicobacter pylori-positive patients were randomly divided into a Lactobacillus Reuteri-containing quadruple therapy group (Group A) and a bismuth-containing quadruple therapy group (Group B), with 120 cases in each group, receiving the two eradication regimens for 14 days respectively. Group A consisted of Lactobacillus Reuteri (2g, twice a day), esomeprazole (20mg, twice a day), amoxicillin (1g, twice a day), and levofloxacin (0.5g, once a day).

Group B consisted of bismuth potassium citrate (220mg, twice a day), esomeprazole (20mg, twice a day), amoxicillin (1g, twice a day), and levofloxacin (0.5g, once a day). The safety and compliance of patients were evaluated 1-3 days after the end of eradication therapy, and whether the Helicobacter pylori was successfully eradicated was determined by urea breath test about 8 weeks after the end of eradication therapy. Data were collected to analyze whether there were significant differences in eradication efficacy, incidence of adverse reactions and compliance between the two groups.

Results: Lactobacillus Reuteri-containing quadruple therapy and bismuth-containing quadruple therapy have comparable eradication rates in first-line Helicobacter pylori therapy (ITT analysis: 80.0% vs 81.7%, $p=0.743$, PP analysis: 88.7% vs 89.6%, $p=0.825$), and there was no significant difference in the incidence of overall adverse reactions (13.9% vs 20.5%, $p=0.183$) and compliance (93.9% vs 93.2%, $p=0.816$). Diarrhea occurred less frequently in the Lactobacillus Reuteri-containing quadruple therapy (3.5% vs 10.3%, $p=0.042$), while the incidence of other adverse reactions was similar between the two groups.

Conclusion: The efficacy, safety and patient compliance of Lactobacillus Reuteri-containing quadruple therapy in the first-line eradication treatment of Helicobacter pylori are similar to bismuth-containing quadruple therapy, and Lactobacillus Reuteri can reduce diarrhea in patients.

Disclosure: The authors declare no potential conflicts of interest.

P0131

EFFECTIVENESS AND SAFETY OF BISMUTH QUADRUPLE REGIMEN CONTAINING AMOXICILLIN AND FURAZOLIDONE FOR *HELICOBACTER PYLORI* INFECTION: A STUDY BASED ON REAL-WORLD DATA

J. Peng¹, S. Wu¹, J. Xie¹, K. Yang¹, D. Liu¹, N. Lu¹, Z. Yin¹, X. Shu¹, D. Huang¹, Y. Xie¹

¹The First Affiliated Hospital of Nanchang University, Nanchang, China

Contact E-Mail Address: pengjianxiang456@163.com

Introduction: *Helicobacter pylori* (*Hp*) infection is associated with numerous intragastric and extra gastric diseases, and *Hp* eradication is extremely important for the treatment and prevention of *Hp*-related diseases.

Under the background of increasing resistance rate of *Hp* to clarithromycin, metronidazole and levofloxacin, the eradication rate of *Hp* decreased largely. At present, *Hp* strains resistant to amoxicillin and furazolidone are rare.

Aims & Methods: We aimed to evaluate the effectiveness and safety of bismuth quadruple regimen containing amoxicillin and furazolidone for *Hp* infection, based on real-world data, so as to provide a theoretical basis for formulating an efficient and safe treatment scheme for *Hp* eradication.

This was a prospective observational study of bismuth quadruple regimen containing amoxicillin and furazolidone for *Hp* infection in real-world practice. From December 2019 to February 2022, patients who were con-

firmed to infected *Hp* by ¹³C-UBT DOB value > 6‰ or of ¹⁴C-UBT DPM value > critical value + 50% critical value or rapid urease test ≥ (++) (to rule out near the critical value of false positives) or histopathology or bacterial culture or stool antigen test received eradication treatment (acid suppressant, bismuth, amoxicillin and furazolidone) in *Hp* specialist clinics or partial general clinics at the First Affiliated Hospital of Nanchang University. Within ±2 days after *Hp* eradication, adverse events and compliance during treatment were obtained via clinic or telephone return visit. At least 4 weeks after completion of therapy, *Hp* eradication was assessed by ¹³C-UBT or ¹⁴C-UBT or histopathology.

Results: A total of 625 patients completed this study, the overall eradication rate was 87.4% (546/625) by intention-to-treat (ITT) analysis and 89.5% (537/600) by per-protocol (PP) analysis. The ITT eradication rates for 10-day and 14-day regimen were 86.3% vs 89.0%, respectively ($P=0.328$). The ITT eradication rates for initial treatment and rescue treatment were 88.7% vs 79.8%, respectively ($P=0.017$). 89 patients (14.2%) experienced at least one adverse event, the majority of adverse events were mild and overall compliance rate was 96.0%. The incidence of adverse reactions for 10-day regimen were higher than 14-day regimen (16.8% vs 10.2%, $P=0.020$). The incidence of adverse reactions for initial treatment and rescue treatment were 14.7% vs 11.7%, respectively ($P=0.445$). Nausea/vomiting (3.7%), headache/dizziness (3.1%), abdominal pain/bloating (2.4%), skin rash (2.1%), anorexia (1.4%) and asthenia (1.1%) were common adverse events.

Conclusion: Bismuth quadruple regimen containing amoxicillin and furazolidone proved safe and provided fair initial eradication in real-world practice.

Disclosure: Nothing to disclose.

P0132

EFFECTIVENESS AND SAFETY OF BISMUTH QUADRUPLE REGIMEN CONTAINING FURAZOLIDONE AND TETRACYCLINE FOR *HELICOBACTER PYLORI* INFECTION: A STUDY BASED ON REAL-WORLD DATA

J. Peng¹, J. Xie¹, S. Wu¹, D. Liu¹, K. Yang¹, D. Huang¹, Y. Xie¹

¹The First Affiliated Hospital of Nanchang University, Nanchang, China

Contact E-Mail Address: pengjianxiang456@163.com

Introduction: *Helicobacter pylori* (*Hp*) infection is associated with numerous intragastric and extra gastric diseases, and *Hp* eradication is extremely important for the treatment and prevention of *Hp*-related diseases. Under the background of increasing resistance rate of *Hp* to clarithromycin, metronidazole and levofloxacin, the eradication rate of *Hp* decreased largely. At present, *Hp* strains resistant to furazolidone and tetracycline are rare.

Aims & Methods: We aimed to evaluate the effectiveness and safety of bismuth quadruple regimen containing furazolidone and tetracycline for *Hp* infection, based on real-world data, so as to provide a theoretical basis for formulating an efficient and safe treatment scheme for *Hp* eradication.

This was a prospective observational study of bismuth quadruple regimen containing furazolidone and tetracycline for *Hp* infection in real-world practice. From December 2019 to February 2022, patients who were confirmed to infected *Hp* by ¹³C-UBT DOB value > 6‰ or of ¹⁴C-UBT DPM value > critical value + 50% critical value or rapid urease test ≥ (++) (to rule out near the critical value of false positives) or histopathology or bacterial culture or stool antigen test received eradication treatment (acid suppressant, bismuth potassium citrate, furazolidone and tetracycline) in *Hp* specialist clinics or partial general clinics at the First Affiliated Hospital of Nanchang University. Within ±2 days after *Hp* eradication, adverse events

and compliance during treatment were obtained via clinic or telephone return visit. At least 4 weeks after completion of therapy, *Hp* eradication was assessed by ¹³C-UBT or ¹⁴C-UBT or histopathology.

Results: A total of 495 patients completed this study, the overall eradication rate was 96.2% (476/495) by intention-to-treat (ITT) analysis and 98.3% (465/473) by per-protocol (PP) analysis. The ITT eradication rates for 10-day and 14-day regimen were 96.1% vs 96.5%, respectively ($P=0.819$). The ITT eradication rates for initial treatment and rescue treatment were 96.2% vs 96.1%, respectively ($P=1.000$). 100 patients (20.2%) experienced at least one adverse event, the majority of adverse events were mild and overall compliance rate was 95.6%. The incidence of adverse reactions for 10-day regimen were lower than 14-day regimen (18.2% vs 27.0%, $P=0.039$). The incidence of adverse reactions for initial treatment and rescue treatment were 18.6% vs 24.8%, respectively ($P=0.130$). Nausea/vomiting (6.3%), abdominal pain/bloating (3.2%), headache/dizziness (3.0%), diarrhea (2.8%), dry/bitter taste (1.6%), asthenia (1.6%) and anorexia (1.2%) were common adverse events.

Conclusion: Bismuth quadruple regimen containing furazolidone and tetracycline proved both highly effective and safe in real-world practice, both for initial treatment and rescue treatment.

Disclosure: Nothing to disclose.

P0133

OPTIMIZATION OF VONOPRAZAN-AMOXICILLIN DUAL THERAPY FOR ERADICATING *HELICOBACTER PYLORI* INFECTION IN CHINA: A PROSPECTIVE, RANDOMIZED CLINICAL PILOT STUDY

Y. Hu¹, X. Xu¹, Y. Ouyang¹, C. He¹, N. Li¹, C. Xie¹, C. Peng¹, Z. Zhu¹, Y. Xie¹, X. Shu¹, N. Lu¹, Y. Zhu¹

¹The First Affiliated Hospital of Nanchang University, Nan Chang, China

Contact E-Mail Address: 360041934@qq.com

Introduction: Vonoprazan-amoxicillin (VA) dual therapy has been shown to achieve acceptable cure rates for treatment of *Helicobacter pylori* (*H. pylori*) in Japan. Its effectiveness in other regions is unknown. We aimed to explore the efficacy of VA dual therapy as first-line treatment for *H. pylori* infection in China.

Aims & Methods: This was a single center, prospective, randomized clinical pilot study conducted in China. Treatment naïve *H. pylori* infected patients were randomized to receive either low or high dose amoxicillin-vonoprazan consisting of amoxicillin 1 g either b.i.d. or t.i.d. plus VPZ 20 mg b.i.d. for 7 or 10 days. ¹³C-urea breath tests were used to assess the cure rate at least 4 weeks after treatment.

Results: 323 patients were assessed and 119 subjects were randomized. The eradication rates of b.i.d. amoxicillin for 7 days and 10 days, t.i.d. amoxicillin for 7 days and 10 days were 66.7% (16/24), 89.2% (33/37), 81.0% (17/21) and 81.1% (30/37) ($P=0.191$) by intention-to-treat analysis, respectively, and 72.7% (16/22), 89.2% (33/37), 81.0% (17/21) and 81.1% (30/37) ($P=0.454$) by per-protocol analysis, respectively.

Conclusion: Neither 7- or 10-day VA dual therapy with b.i.d. or t.i.d. amoxicillin provides satisfied efficacy as the first-line treatment for *H. pylori* infection in China. Further optimization is needed.

Disclosure: The authors declare that there are no conflicts of interest.

P0134

ALTERED GUT MICROBIOTA AND SHORT-CHAIN FATTY ACIDS AFTER VONOPRAZAN-AMOXICILLIN DUAL THERAPY FOR *HELICOBACTER PYLORI* ERADICATION

Y. Hu¹, X. Xu¹, Y. Ouyang¹, C. He¹, N. Li¹, C. Xie¹, C. Peng¹, Z. Zhu¹, X. Shu¹, Y. Xie¹, N. Lu¹, Y. Zhu¹

¹The First Affiliated Hospital of Nanchang University, Nan Chang, China

Contact E-Mail Address: 360041934@qq.com

Introduction: The combination of Vonoprazan (VPZ) with amoxicillin (VA therapy) has been shown to achieve acceptable eradication rates for *Helicobacter pylori* (*H. pylori*). Our aim was to explore the short-term effect of VA therapy on the gut microbiota and short-chain fatty acids (SCFAs).

Aims & Methods: 119 *H. pylori*-positive patients were randomized into low or high dose VA therapy (i.e., amoxicillin 1 g b.i.d. or t.i.d.) and VPZ 20 mg b.i.d. for 7 or 10 days. 13 *H. pylori*-negative patients served as normal controls. Fecal samples were collected from *H. pylori*-positive and negative patients. The gut microbiota and SAFCs were analyzed by 16S rRNA gene sequencing and Gas Chromatography-Mass Spectrometry, respectively.

Results: The gut microbiota of *H. pylori*-positive patients had higher richness, diversity and better evenness of gut microbiota and a slightly increased abundance of SCFAs compared to matched patients.

The integrated analysis of gut microbiota and SCFAs identified that *Prevotellaw* was associated with SCFAs alterations. 53 patients were studied before and after *H. pylori* eradication divided into low (L-VA) and high amoxicillin dosage (H-VA). The diversity and composition of gut microbiota among L-VA patient showed no differences at the three time points.

However, among H-VA patients, the diversity was decreased and the microbial composition was altered immediately after H-VA eradication but restored by the confirmation time point. The decreased abundance of *Ruminococcus* and *Eubacterium* were associated with the alteration of SCFAs level.

Conclusion: Vonoprazan-amoxicillin dual therapy for *H. pylori* eradication has minimal negative effects on gut microbiota and SCFAs.

Disclosure: The authors declare that there are no conflicts of interest.

P0135

COMPARISON OF THE EFFECTIVENESS OF *HELICOBACTER PYLORI* ERADICATION REGIMENS BETWEEN THE ELDERLY AND NON-ELDERLY POPULATIONS: DATA FROM THE EUROPEAN REGISTRY ON *H. PYLORI* MANAGEMENT (HP-EUREG)

P. Jonaitis¹, J. Kupcinskas¹, Á. Pérez-Aísa², D. Vaira³, B. Tepeš⁴, D.S. Bordin⁵, M. Castro-Fernandez⁶, A.J. Lucendo⁷, L. Vologzhanina⁸, L. Bujanda Fernández de Piérola⁹, M. Denkovski¹⁰, A. Lanas¹¹, M. Leja¹², G. Babayeva¹³, U. Mahmudov¹⁴, L. Rodrigo¹⁵, F. Lerang¹⁶, G. Fadieienco¹⁷, R.A. Abdulkhakov¹⁸, J. Huguet Malavés¹⁹, O. Zaytsev²⁰, L. Fernández-Salazar²¹, A. Sarsenbaeva²², I. Bakulin²³, A.G. Gravina²⁴, M.C. Perona Vincenti²⁵, S. Alekseenko²⁶, J. Barrio Andrés²⁷, M. Areia²⁸, O. Núñez Martínez²⁹, P. Bogomolov³⁰, B.J.G. Rodriguez³¹, M. Domínguez Cajal³², J. Gomez Camarero³³, S. Georgopoulos³⁴, P. Almela Notari³⁵, A. Tonkic³⁶, R. Pellicano³⁷, H. Şimşek³⁸, L. Kunovský³⁹, A. Gasbarrini⁴⁰, J.M. Botargues Bote⁴¹, G.M. Buzás⁴², O. Perez Nyssen⁴³, L. Moreira Ruiz⁴⁴, I. Puig⁴⁵, F. Mégraud⁴⁶, C. O'Morain⁴⁷, J. Gisbert⁴³, L.V. Jonaitis¹,
On behalf of the Hp-EuReg Investigators

¹Lithuanian University of Health Sciences, Department of Gastroenterology, Kaunas, Lithuania, ²Unidad de Digestivo, Hospital Costa del Sol Marbella, Málaga, Redes de Investigación Cooperativa Ori Entada a Resultados en Salud (RICORS), Marbella, Spain, ³University of Bologna, Department of Surgical and Medical Sciences, Bologna, Italy, ⁴AM DC Rogaska, Rogaska Slatina, Gastroenterology, Rogaska Slatina, Slovenia, ⁵A. S. Loginov Moscow Clinical Scientific Center, Tver State Medical University, Moscow, Russian Federation, ⁶Hospital de Valme, Sevilla, Spain, ⁷Hospital General de Tomelloso, Dept. de Gastroenterology, Tomelloso, Spain, ⁸Gastrocentr, Perm, Russian Federation, ⁹Hospital Donostia/Instituto Biodonostia, Centro de Investigación Biomédica en Red de Enfermedades Hepáticas y Digestivas (CIBERehd), Universidad del País Vasco (UPV/EHU), San Sebastián, Spain, ¹⁰Interni Oddelek, Diagnostic Centre, Bled, Slovenia, ¹¹Hospital Clínico Universitario Lozano Blesa, Department Medicine & Gastroenterology, Zaragoza, Spain, ¹²Digestive Diseases Centre GASTRO, Institute of Clinical and Preventive Medicine & Faculty of Medicine, University of Latvia, Riga, Latvia, ¹³Azerbaijan State Advanced Training Institute for Doctors named after A. ALIYEV, Terapiya, Baku, Azerbaijan, ¹⁴Modern Hospital, Baku, Azerbaijan, ¹⁵Hospital de Asturias, Oviedo, Spain, ¹⁶Central Hosspital of Ostfold, Medicine, Grålum, Norway, ¹⁷Digestive Ukrainian Academy of Medical Sciences, Kyiv, Ukraine, ¹⁸Kazan State Medical University, Kazan, Russian Federation, ¹⁹Hospital General Universitario de Valencia, Valencia, Spain, ²⁰First Clinical Medical Centre, Kovrov, Russian Federation, ²¹Hospital Clínico de Valladolid, Valladolid, Spain, ²²Chelyabinsk Regional Clinical Hospital, Chelyabinsk, Russian Federation, ²³North-Western State Medical University, Saint Petersburg, Russian Federation, ²⁴Università degli Studi della Campania Luigi Vanvitelli, Naples, Italy, ²⁵Hospital Quiron Marbella, Dept. of Gastroenterology, Marbella, Spain, ²⁶Far Eastern State Medical University, Khabarovsk, Russian Federation, ²⁷Hospital Río Hortega, Valladolid, Spain, ²⁸Portuguese Oncology Institute of Coimbra, Gastroenterology, Coimbra, Portugal, ²⁹Hospital Universitario La Moraleja, Madrid, Spain, ³⁰Universal Clinic - Private Medical Center, Moscow, Russian Federation, ³¹Hospital Virgen de la Macarena, Sevilla, Spain, ³²Hospital San Jorge Huesca, Huesca, Spain, ³³Hospital Universitario de Burgos, Burgos, Spain, ³⁴Athens Medical, P. Faliron General Hospital, Athens, Greece, ³⁵Hospital General Universitario de Castellón,

Castello, Spain, ³⁶University Hospital of Split, School of Medicine, Split, Croatia, ³⁷Outpatient Clinic, Molinette-SGAS Hospital, University of Turin, Turin, Italy, ³⁸Internal Medicine, Hacettepe, University School of Medicine, Ankara, Turkey, ³⁹Masaryk Memorial Cancer Institute, Department of Gastroenterology and Digestive Endoscopy, Brno, Czech Republic, ⁴⁰Medicina Interna, Fondazione Policlinico Universitario A. Gemelli IRCCS, Università Cattolica del Sacro Cuore, Rome, Italy, ⁴¹Hospital Universitari de Bellvitge, L'Hospitalet de Llobregat, Barcelona, Spain, ⁴²Ferencvaros Health Centre, Budapest, Hungary, ⁴³Hospital Universitario de La Princesa, Instituto de Investigación Sanitaria Princesa (IIS-Princesa), Universidad Autónoma de Madrid (UAM), and Centro de Investigación Biomédica en Red de Enfermedades Hepáticas y Digestivas (CIBERehd), Madrid, Spain, ⁴⁴Hospital Clínic de Barcelona, Centro de Investigación Biomédica en Red en Enfermedades Hepáticas y Digestivas (CIBERehd), IDIBAPS (Institut d'Investigacions Biomèdiques August Pi i Sunyer), University of Barcelona, Barcelona, Spain, ⁴⁵Althaia Xarxa Assistencial Universitària de Manresa and Universitat de Vic-Universitat Central de Catalunya (UVicUCC), Manresa, Spain, ⁴⁶INSERM U 1312, Université de Bordeaux, Bordeaux, France, ⁴⁷Trinity College Dublin - Faculty of Health Sciences, Dublin, Ireland

Contact E-Mail Address: Laimas.Jonaitis@lsmuni.lt

Introduction: The overall prevalence of *H. pylori* infection in Europe is declining; however, it still remains high in the elderly population. Therefore, it is important to assess the treatment efficacy and possible differences in the elderly and non-elderly populations.

Aims & Methods: To evaluate and compare the efficacy of first- and second-line *H. pylori* eradication regimens between the non-elderly and elderly European populations.

The "European Registry on *H. pylori* Management" (Hp-EuReg) is a European multicenter prospective non-interventional registry recording information of *H. pylori* infection management. Data from the year 2013 to 2022 were recorded at AEG-REDCap e-CRF. Data were subject to quality review. The subjects were divided into non-elderly (18-59 years) and elderly (≥60 years) groups. Per-Protocol (PP) and modified Intention-To-Treat (mITT) analyses were performed to evaluate effectiveness of the six most frequently used regimens in each group. In the multivariate analysis, the effect was evaluated by calculating OR and 95% CI. Statistical significance was considered at $p < 0.05$.

Results: Overall 49,461 patients were included in the Hp-EuReg. There were 34,994 (71%) non-elderly and 14,467 (29%) elderly patients. In first-line treatment, quadruple therapies were prescribed in 45% of the cases, and triple therapies in 44%. In second-line treatment, quadruple therapies were prescribed in 51% of the cases, and triple therapies in 44%. The treatment schemes prescribed are detailed in Table 1. The overall first-line treatment effectiveness was 89% by PP and 88% by mITT in the non-elderly, and 90% by PP and 89% by mITT in the elderly ($p < 0.05$). The overall second-line treatment effectiveness was 84% both by PP and mITT analyses in the non-elderly and elderly groups ($p > 0.05$). In the multivariate analysis, the elderly group was associated with significantly higher overall mITT eradication rate in the first-line treatment as compared to the non-elderly (OR=1.13; 95% CI 1.05-1.12; $p < 0.005$); however, there were no significant differences in the overall second-line treatment mITT effectiveness. The effectiveness by treatment scheme and line is reported in Table 1, with statistically significant differences in the first-line treatment mITT cure rates reported between age groups when either quadruple PPI-clarithromycin-amoxicillin-metronidazole therapy was prescribed or when sequential PPI-clarithromycin-amoxicillin-tinidazole was used. In second-line, no statistically significant differences were reported in the mITT effectiveness in any of the treatment schemes evaluated.

Comparison of First-line Treatment Regimens Between the Non-elderly and Elderly Populations						
Treatment	Non-Elderly (18-59 years)			Elderly (≥60 years)		
	Use, N	PP % (95% CI)	mITT % (95% CI)	Use, N	PP % (95% CI)	mITT % (95% CI)
Triple PPI+C+A	10,540	87 (86-87)	86 (85-87)*	4,065	88 (87-89)	87 (86-89)*
Triple PPI+C+M	1,150	86 (84-88)	86 (83-88)	491	83 (79-86)	83 (79-86)
Quadruple PPI+C+A+M	4,199	90 (89-91)*	89 (88-90)*	1,940	91 (90-93)*	91 (90-92)*
Quadruple PPI+C+A+B	3,489	92 (91-93)	92 (91-93)	1,086	91 (89-93)	90 (88-92)
Pylera® (single capsule) ¹	3,233	94 (93-95)	93 (92-94)	1,519	94 (93-95)	93 (92-95)
Sequential C+A+T	1,291	90 (88-92)*	90 (88-91)*	623	94 (92-96)*	94 (91-96)*

Comparison of Second-line Treatment Regimens Between the Non-elderly and Elderly Populations						
Treatment	Non-Elderly (18-59 years)			Elderly (≥60 years)		
	Use, N	PP % (95% CI)	mITT % (95% CI)	Use, N	PP % (95% CI)	mITT % (95% CI)
Triple PPI+A+L	1,422	83 (80-85)	82 (80-84)	524	80 (76-84)	80 (76-83)
Triple PPI+C+A	323	78 (72-83)	78 (72-83)	102	84 (74-91)	84 (74-91)
Quadruple PPI+A+L+B	584	89 (86-92)	89 (86-91)	225	86 (80-91)	86 (80-91)
Quadruple PPI+C+A+M	234	84 (79-89)	84 (78-88)	91	86 (77-92)	86 (77-93)
Quadruple PPI+M+T+C+B	224	86 (80-91)	84 (78-88)	101	87 (78-93)	88 (79-94)
Pylera® (single capsule) ¹	843	89 (87-91)	89 (86-91)	384	92 (89-95)	91 (88-94)

PP – per protocol; mITT – modified Intention-To-Treat; 95% CI – 95% confidence interval; PPI – proton pump inhibitor; C – clarithromycin; A – amoxicillin; M – metronidazole; B – bismuth; T – tinidazole; L – levofloxacin; Tc – tetracycline; ¹Pylera®: three-in-one single-capsule containing metronidazole, tetracycline and bismuth. * statistically significant differences between the age groups, p<0.05.

Table 1. Most frequent first- and second-line *H. pylori* eradication prescriptions and their efficacies in the non-elderly and elderly populations

Conclusion: The overall effectiveness of both first- and second-line *H. pylori* eradication regimens in Europe is suboptimal (<90%). The effectiveness of the most frequent first- and second-line triple therapies in the non-elderly and elderly populations is also suboptimal (<90%). Optimal effectiveness (>90%) was mostly achieved by using quadruple therapies. Although statistically significant, no clinically relevant differences in the effectiveness between elderly and non-elderly patients was observed in the most frequently prescribed first-line treatments. No differences were observed either in second-line prescriptions.

Disclosure: Nothing to disclose.

P0136

A PHASE 1, DOUBLE-BLIND, PARALLEL-GROUP STUDY TO EVALUATE THE PHARMACOKINETICS, SAFETY AND TOLERABILITY OF VONOPRAZAN- OR ESOMEPRAZOLE-BASED BISMUTH-CONTAINING QUADRUPLE THERAPY FOR *HELICOBACTER PYLORI* ERADICATION IN CHINA

J. Miao¹, C. Hu¹, J. Tang¹, W. Wang², Y. Wang¹, R. Men³, L. Yang³, L. Gu⁴, N. Yoshida⁵, R. Czerniak⁶

¹West China Hospital, Sichuan University, Phase I Unit, Chengdu, China, ²ICU, West China Hospital, Sichuan University, Chengdu, China, ³West China Hospital, Sichuan University, Gastroenterology and Hepatology, Chengdu, China, ⁴Takeda Development Center Asia, Shanghai, China, ⁵Takeda Development Center Japan, Osaka, Japan, ⁶Takeda Pharmaceuticals International Co, Massachusetts, United States

Contact E-Mail Address: miaosiyi1971@163.com

Introduction: *Helicobacter pylori* (Hp) eradication can reduce the recurrence of gastric and duodenal ulcers and the risk of gastric cancer¹. Chinese guidelines for Hp eradication recommend bismuth-containing quadruple therapy comprising two antibiotics and a proton pump inhibitor (PPI)². Vonoprazan, a potassium-competitive acid blocker, demonstrated potent and sustained acid-inhibitory effects, making it a candidate for PPI replacement in quadruple therapy³. This study evaluated bismuth exposure in vonoprazan- or esomeprazole-based quadruple therapy in a Hp-positive healthy Chinese population.

Aims & Methods: This phase 1, double-blind, parallel-group study was implemented at a single study site in China (April–November 2021). Eligible, Hp-positive healthy subjects aged 18–60 years were randomised 1:1 to receive quadruple therapy comprising vonoprazan (20 mg) or esomeprazole (20 mg), bismuth potassium citrate (600 mg [equivalent to 220 mg of bismuth]), clarithromycin (500 mg), and amoxicillin (1000 mg) twice daily for 2 weeks.

The primary endpoint was to evaluate plasma and urine pharmacokinetic (PK) parameters of bismuth with vonoprazan- or esomeprazole-based quadruple therapy on Day 14, summarised by descriptive statistics. Similarity of plasma PK parameters was inferred for the treatment groups if the 90% CIs of geometric mean ratio for bismuth AUC₀₋₁₂ and C_{max} were within 0.5–2.0 confidence limits. Secondary endpoints were the percentage of subjects who experienced ≥1 TEAEs and those who discontinued treatment due to an AE. Hp eradication was determined by carbon-13 urea breath test (¹³C-UBT) at a follow-up visit 4 weeks after treatment.

Results: Of 44 enrolled subjects (vonoprazan, n=22; esomeprazole, n=22), mean age was 34.5 and 31.6 years with 63.6% and 59.1% being male, respectively. The mean duration of exposure to treatment was 13.5 and 13.0 days for vonoprazan and esomeprazole, respectively. The key plasma and urine PK parameters of bismuth were similar between the two groups (Table 1).

On Day 42, ¹³C-UBT for Hp infection was negative in 100% and 94.4% of subjects receiving vonoprazan and esomeprazole, respectively. The incidence of TEAEs was similar between the treatment groups; most were mild, and no serious AEs occurred. Dysgeusia was most frequently reported in 68.2% and 81.8% of subjects receiving vonoprazan and esomeprazole, respectively. Two and five subjects receiving vonoprazan and esomeprazole, respectively, discontinued the study due to TEAEs. All study subjects had normal results of neurological examinations throughout the study. No new safety concerns related to potential drug-drug interactions were identified.

PK parameter	Geometric LS mean (95% CI)	Ratio (vonoprazan vs esomeprazole)	90% CI of geometric mean ratio	95% CI of geometric mean ratio
AUC ₀₋₁₂ (h*ng/mL)				
Vonoprazan (n=20)	146 (117, 183)	1.07	(0.82, 1.40)	(0.78, 1.48)
Esomeprazole (n=18)	137 (108, 173)			
C _{max} (ng/mL)				
Vonoprazan (n=20)	42.8 (32.6, 56.2)	1.30	(0.94, 1.81)	(0.88, 1.93)
Esomeprazole (n=18)	32.9 (24.7, 43.8)			
Ae ₀₋₁₂ (μg)	Mean (SD)			
Vonoprazan (n=20)	1026 (546.0)	--	--	--
Esomeprazole (n=18)	1037 (562.5)			

Ae₀₋₁₂, amount of drug excreted in urine during a dose interval; AUC₀₋₁₂, area under the plasma drug concentration-time curve; C_{max}, maximum plasma drug concentration; CI, confidence interval; LS, least squares; PK, pharmacokinetic; SD, standard deviation; τ, length of dosing interval ¹PK analysis set comprised subjects who received study treatment, completed minimum protocol-specified procedures with no significant protocol deviations and were evaluable for PK

Table 1: Comparison of key bismuth PK parameters (PK analysis set¹)

Conclusion: Vonoprazan did not differentially affect PK parameters of bismuth in comparison with esomeprazole. The results suggest that vonoprazan may be an option of bismuth-containing quadruple therapy for Hp eradication in China.

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is an employee of Takeda Development Center Japan. RC is an employee of Takeda Pharmaceuticals International Co., Cambridge Massachusetts, United States of America.

P0137

REINFORCED MEDICATION ADHERENCE IMPROVES *H. PYLORI* ERADICATION RATE IN DEVELOPING COUNTRIES: A SYSTEMATIC REVIEW AND META-ANALYSIS OF RANDOMIZED CONTROLLED TRIALS

R. Zeng¹, Y. Xie¹

¹The First Affiliated Hospital of Nanchang University, Department of Gastroenterology, Nanchang, China

Contact E-Mail Address: 3402871273@qq.com

Introduction: The eradication rate of *H. pylori* (*Helicobacter pylori*) remains variable for the same eradication regime even in the identical region, eradication regimen even in the identical region, especially in developing countries. There are many well-known factors involved, such as strains, drugs, and genetic polymorphisms.

However, the factor of compliance during medication is often ignored. In recent years, a number of randomized controlled trials (RCTs) have investigated the effect of enhanced medication adherence on eradication rates. The patients with poor compliance may be more prominent in developing countries owing to the complicated regimens, adverse reactions and low levels of education.

To address this dilemma, reinforced medication adherence maybe a promising strategy to improve *H. pylori* eradication rate. Herein, we conducted a systematic review and meta-analysis of RCTs to assess the effect of medication adherence on *H. pylori* eradication rates in developing countries.

Aims & Methods: A systematic review was conducted in international databases (Web of Science, Cochrane Library, PubMed, and EMBASE) and national databases (CBM, WanFang Data, CNKI, and VIP Database) to identify relevant RCTs from inception to April 2022. The Cochrane Collaboration's tool for assessing the risk of bias in RCTs was used to assess the quality and risk of bias of the included studies. The core indicator was the changes in eradication rates after enhanced adherence. Meta-analysis was performed to estimate the pooled relative risk (RR) with 95% confidence intervals (CI) using R4.1.2.

Results: A total of 3286 patients with confirmed *HP* infection were included in 19 RCTs, including 1632 patients in the intervention group and 1652 patients in the control group. Interventions include telephone, message, WeChat, and combined regime.

The results of meta-analysis showed that the eradication rate of the intervention group was significantly different from that of the control group in the intentional analysis (ITT) [RR=1.25, 95%CI(1.12, 1.31), $P<0.0001$] and compliance protocol analysis (PP) [RR=1.16, 95%CI(1.08, 1.24), $P<0.0001$].

The compliance of the intervention group was high [RR=1.27, 95%CI(1.16, 1.40), $P<0.0001$], the incidence of adverse reactions was lower than the control group [RR=0.72, 95%CI(0.52, 0.99), $P=0.04$], gastrointestinal symptom relief was better than control group [RR=1.23, 95%CI(1.06, 1.43), $P=0.005$], the patient satisfaction [RR=1.26, 95%CI(1.19, 1.35), $P<0.0001$] and disease knowledge rate [SMD=1.82, 95%CI(0.77, 2.86), $P=0.0007$] were better than the control group. Egger funnel plot suggested that there was no potential publication bias among included studies ($P=0.718$).

Conclusion: Guided therapy improved patients' treatment compliance and *HP* eradication rate, reduced adverse reactions, improved disease-related symptoms, improved patients' satisfaction with medical services, and effectively improved residents' *HP* related knowledge literacy, which has the value of promotion and application.

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Disclosure: Nothing to disclose.

P0138

ROLE OF COMPLIANCE IN *HELICOBACTER PYLORI* TREATMENTS: RESULTS FROM THE EUROPEAN REGISTRY ON *H. PYLORI* MANAGEMENT (HP-EUREG)

P. Suárez¹, L. Ferrer-Barceló¹, J.M. Huguet¹, Á. Pérez-Aísa², B. Vaira³, L.V. Jonaitis⁴, B. Tepeš⁵, D.S. Bordin^{6,7,8}, A. Keco-Huerga⁹, A.J. Lucendo¹⁰, L. Vologzhanina¹¹, L. Bujanda Fernández de Piérola^{12,13,14}, N. Brglez Jurecic¹⁵, A. Lanás¹⁶, M. Leja¹⁷, G. Babayeva¹⁸, U. Mahmudov¹⁹, M. Caldas Álvarez²⁰, L. Rodrigo²¹, F. Lerang²², G. Fadieienco²³, R.A. Abdulkhakov²⁴, O. Zaytsev²⁵, T. Ilchishina²⁶, L. Fernández-Salazar²⁷, A. Silkanovna Sarsenbaeva²⁸, I. Bakulin²⁹, A.G. Gravina³⁰, M.C. Perona Vincenti³¹, S. Alekseenko³², J. Barrio Andrés³³, M. Areia³⁴, O. Núñez Martínez³⁵, P. Bogomolov³⁶, B.J. Gomez Rodriguez³⁷, M. Dominguez-Cajal³⁸, J. Gomez-Camarero³⁹, S. Georgopoulos⁴⁰, P. Almela Notari⁴¹, A. Tonkic⁴², R. Pellicano⁴³, H. Simsek⁴⁴, S. Smith⁴⁵, T. Rokkas⁴⁶, A. Canno-Catalá⁴⁷, I. Puig⁴⁷, O. Perez Nyssen⁴⁸, F. Mégraud⁴⁹, C. O'Morain⁵⁰, J. Gisbert²⁰,

On behalf of the Hp-EuReg Investigators

¹Consorcio Hospital General Universitario de Valencia, Gastroenterology, Valencia, Spain, ²Agencia Sanitaria Costa del Sol, Red de Investigación en Servicios de Salud en Enfermedades Crónicas (REDISSEC), Marbella, Spain, ³University of Bologna, Surgical and Medical Sciences, Bologna, Italy, ⁴Lithuanian University of Health Sciences Dept. of Gastroenterology, Gastroenterology, Kaunas, Lithuania, ⁵AM DC Rogaska, Gastroenterology, Rogaska Slatina, Slovenia, ⁶A.S. Loginov Moscow Clinical Scientific Center, Moscow, Russian Federation, ⁷Tver State Medical University, Tver, Russian Federation, ⁸A.I. Yevdokimov Moscow State University of Medicine and Dentistry, Moscow, Russian Federation, ⁹Hospital de Valme, Sevilla, Spain, ¹⁰Hospital General de Tomelloso, Dept. de Gastroenterology, Tomelloso, Spain, ¹¹Gastrocentr, Perm, Moscow, Russian Federation, ¹²Hospital Donostia, Instituto Biodonostia, San Sebastián, Spain, ¹³Centro de Investigación Biomédica en Red de Enfermedades Hepáticas y Digestivas (CIBERehd), San Sebastián, Spain, ¹⁴Universidad del País Vasco (UPV/EHU), San Sebastián, Spain, ¹⁵Interni Oddelek, Diagnostic Centre, Bled, Slovenia, ¹⁶University of Zaragoza University Hospital Dept. of Medicine-Gastroenterology, Dept. Medicine & Gastroenterology, Zaragoza, Spain, ¹⁷Institute of Clinical and Preventive Medicine & Faculty of Medicine, University of Latvia, Digestive Diseases Centre GASTRO, Riga, Latvia, ¹⁸Azerbaijan State Advanced Training Institute for Doctors named after A. Aliyev, Gastroenterology,

Department of Therapy, Baku, Azerbaijan, ¹⁹Modern Hospital, Baku, Azerbaijan, ²⁰Hospital Universitario de La Princesa, Instituto de Investigación Sanitaria Princesa (IIS-Princesa), Universidad Autónoma de Madrid (UAM), and Centro de Investigación Biomédica en Red de Enfermedades Hepáticas y Digestivas (CIBERehd), Gastroenterology and Hepatology, Madrid, Spain, ²¹Hospital de Asturias, Oviedo, Spain, ²²Central Hosspital of Ostfold, Medicine, Grålum, Norway, ²³Digestive Ukrainian Academy of Medical Sciences, Kyiv, Ukraine, ²⁴Kazan State Medical University, Kazan, Russian Federation, ²⁵First Clinical Medical Centre, Kovrov, Russian Federation, ²⁶SM Clinic, Saint Petersburg, Russian Federation, ²⁷Hospital Clínico Universitario de Valladolid, Valladolid, Spain, ²⁸Chelyabinsk Regional Clinical Hospital, Chelyabinsk, Russian Federation, ²⁹North-Western State Medical University, Propedeutics of Internal Diseases, Gastroenterology and Dietology, Moscow, Russian Federation, ³⁰Università degli Studi della Campania “Luigi Vanvitelli”, Division of Hepatogastroenterology, Napoli, Italy, ³¹Hospital Quiron Marbella, Dept. of Gastroenterology, Marbella, Spain, ³²Far Eastern State Medical University, Khabarovsk, Russian Federation, ³³Hospital Universitario Rio Ortega, Valladolid, Spain, ³⁴Portuguese Oncology Institute of Coimbra, Gastroenterology, Coimbra, Portugal, ³⁵Hospital Universitario La Moraleja, Gastroenterology, Madrid, Spain, ³⁶Universal Clinic - Private Medical Center, Moscow, Russian Federation, ³⁷Hospital Virgen de la Macarena, Sevilla, Spain, ³⁸Hospital San Jorge, Huesca, Spain, ³⁹Hospital Universitario de Burgos, Burgos, Spain, ⁴⁰Athens Medical, P. Faliron General Hospital, Gastroenterology/Hepatology, Athens, Greece, ⁴¹Hospital General Universitario de Castellón, Castellón, Spain, ⁴²University Hospital of Split, School of Medicine, University of Split, Split, Croatia, ⁴³Outpatient Clinic, Molinette-SGAS Hospital, University of Turin, Turin, Italy, ⁴⁴Internal Medicine, Hacettepe, University School of Medicine, Ankara, Turkey, ⁴⁵Trinity College Dublin, Clinical Medicine (Trinity College Dublin) & Gastroenterology (Tallaght University Hospital), Dublin, Ireland, ⁴⁶Henry Dunant Hospital, Athens, Greece, ⁴⁷Althaia Xarxa Assistencial Universitària de Manresa and Universitat de Vic-Universitat Central de Catalunya, Manresa, Spain, ⁴⁸Hospital Universitario de La Princesa, Instituto de Investigación Sanitaria Princesa (IIS-Princesa), Universidad Autónoma de Madrid (UAM), and Centro de Investigación Biomédica en Red de Enfermedades Hepáticas y Digestivas (CIBERehd), Gastroenterology Unit, Madrid, Spain, ⁴⁹Université de Bordeaux, INSERM U 1312, Bordeaux, France, ⁵⁰Trinity College Dublin, Faculty of Health Sciences, Dublin, Ireland

Contact E-Mail Address: opnyssen@gmail.com

Introduction: The adherence to *Helicobacter pylori* eradication treatment is a cornerstone for achieving an adequate treatment efficacy.

Aims & Methods: Objective: To determine which factors could influence on the compliance of eradication treatments employed in Europe. Methods: Systematic prospective non-interventional registry (Hp-EuReg) of the clinical practice of European gastroenterologists. Treatment compliance was defined as adequate with >90% drug intake. The data was collected from 2013 until September 2021 at AEG-REDCap e-CRFand was subject to quality control. Modified intention-to-treat (mITT) analyses were performed. The multivariate analysis evaluated the factors associated with the effectiveness of the treatments and the compliance.

Results: Of the 38,698 available records, 646 (1.7%) did not have adequate compliance. There was a higher rate of non-compliance in patients with dyspepsia than in those treated for peptic ulcer (1.7% vs. 1.4%; $p < 0.05$). 7-day treatments showed greater compliance than 10- or 14-day pre-

scriptions (0.8% vs. 1.8 and 1.6%, respectively; $p < 0.001$). Non-adherence was lower in first-line as compared to rescue treatment (1.5% vs 2.2%; $p < 0.001$). Non-adherence in the three most frequent first-line treatments was: 1.1% with PPI-Clarithromycin-Amoxicillin; 2.3% with PPI-Clarithromycin-Amoxicillin-Metronidazole; and 1.8% with bismuth quadruple therapy (single capsule Pylera®); $p < 0.001$. Compliant patients achieved greater eradication rates in those treatment schemes as compared to those with poor compliance: 86% vs. 44%; 90% vs. 71% and 93% vs. 64% respectively; $p < 0.001$.

In the multivariate analysis, the variable which was most significantly associated with eradication success was the correct compliance with the treatment (OR: 6.3; 95%CI: 5.2-7.7; $p < 0.001$). Non-compliance was greater in the presence of adverse events as compared to the cases without (5% vs 0.6%; $p < 0.001$).

Conclusion: Compliance with *H. pylori* eradication treatment is very high. Factors associated with poor compliance include treatment for uninvestigated/functional dyspepsia, rescue-treatment, prolonged treatment regimens and the presence of adverse effects, as well as the use of sequential and concomitant treatments. Adequate treatment compliance was the variable most closely associated with eradication success.

Disclosure:

Dra. P. Suarez has no conflicts of interest to declare.

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P0139

EMPIRIC “THREE-IN-ONE” BISMUTH QUADRUPLE THERAPY FOR HELICOBACTER PYLORI ERADICATION IN THE SECOND LINE: A PROSPECTIVE STUDY IN SOUTHERN ITALY

G. Losurdo¹, I. Lacavalla², F. Russo³, G. Riezzo³, M. Rendina², E.G. Ierardi², A. Di Leo²

¹University of Bari, Section of Gastroenterology, Dept. Emergency and Organ Transplantation, Bari, Italy, ²Section of Gastroenterology, DETO, University of Bari, Dr., Bari, Italy, ³National Institute of Gastroenterology “S. de Bellis” Research Hospital, Laboratory of Nutritional Pathophysiology, Castellana Grotte, Italy

Contact E-Mail Address: giuseppelos@alice.it

Introduction: The eradication of *Helicobacter pylori* (*H. pylori*) may be difficult due to antibiotic resistance. Indeed, after one failure, a second-line therapy is needed, a Bismuth containing quadruple therapy (BQT) with the three in one capsule formulation is becoming very popular. Therefore, we aimed to evaluate effectiveness and safety of BQT in second line.

Aims & Methods: We recruited consecutive patients with one therapy failure. Patients received for ten days the three-in-one BQT Pylera® therapy, in combination with a proton-pump inhibitor (PPI), decided at the choice of the investigator, at full dose bid. Eradication rate was calculated as intention-to-treat (ITT) and per-protocol (PP) and 95% confidence intervals (CI) were calculated.

Results: Seventy-three patients were recruited, 41 females and 32 males (mean age 53.0±13.1 years) Fifty-five patients had previously failed triple therapy with amoxicillin and clarithromycin and the remaining 18 sequential therapy.

Seventy-two patients assumed at least 90% capsules, while only one did not complete therapy due to adverse events (nausea and diarrhea). BQT was successful at ITT in 62 subjects (eradication rate 84.9%, 95%CI 76.7-93.1%). At PP analysis, the eradication rate was 86.1% (95%CI 78.1%-94.1%).

Failure was not influenced by the type of PPI ($p=0.08$) or previously failed regimen ($p=0.27$); in detail, BQT was effective in 81.8% of those who failed triple and in 94.4% of patients failing sequential therapy. Adverse events were observed in 14 subjects (20.5%), the most common ones were diarrhea (6 patients) and weakness (6 patients).

Conclusion: In conclusion, our report confirmed that BQT is effective as an empiric second-line regimen.

Disclosure: Nothing to disclose.

P0140

EFFECT OF METRONIDAZOLE RESISTANCE ON *HELICOBACTER PYLORI* ERADICATION REGIMENS

G. Losurdo¹, M. Pricci², M. De Bellis¹, F. Russo³, G. Riezzo³, B. D'Attoma³, A. Iannone¹, M. Rendina¹, E.G. Ierardi¹, A. Di Leo¹
¹Section of Gastroenterology, DETO, University of Bari, Dr., Bari, Italy, ²THD SpA, Correggio, Italy, ³National Institute of Gastroenterology "S. de Bellis" Research Hospital, Laboratory of Nutritional Pathophysiology, Castellana Grotte, Italy

Contact E-Mail Address: giuseppelos@alice.it

Introduction: According to guidelines, in our geographic area, characterized by a clarithromycin resistance rate >15%, bismuth containing quadruple therapy (BQT) or concomitant therapy (CT) should be used in first line. Both regimens contain metronidazole, however the effect of metronidazole resistance on CT and BQT has not been fully elucidated yet. We aimed to investigate whether metronidazole resistance may impact on eradication rates of CT/BQT in *H. pylori* naïve patients.

Aims & Methods: We prospectively recruited patients with *H. pylori* infection in the period January 2020–December 2021. Recruited patients received either CT or BQT, both lasting 10 days. Before therapy, patients collected a fecal sample using the THD fecal test device. *H. pylori* DNA was extracted and, by means of real time polymerase chain reaction (RT-PCR), mutations in *rdxA/frxA* gene were investigated for metronidazole resistance.

Moreover, we investigated the A2143G point mutation in the bacterium gene encoding for 23S rRNA subunit for clarithromycin resistance. Treatment was blindly prescribed regardless of molecular investigation result (post-hoc analysis).

Results: Ninety-six patients were recruited; 29 patients received BQT and 67 CT. No drop outs were observed. The overall eradication rate was 91 out of 96 (94.8%, 95% CI 90.4–99.2%) and, in detail, it was 29/29 (100%) for BQT and 62/67 (92.5%, 95% CI 86.2–98.8) for CT. Metronidazole resistance was detected in 18 patients (18.8%, 95% CI 11–26.6%), while clarithromycin resistance in 19 (19.8%, 95% CI 11.9–27.7%). All 18 patients with metronidazole resistance underwent eradication. Five had assumed BQT and 13 CT. Conversely, eradication rate in metronidazole sensitive strains was 73/78 (93.6%, 95% CI 88.2–99%). Of these, 24 received BQT, with a 100% success, and 54 assumed CT with 5 failures. In detail, 2 failing patients were resistant to clarithromycin and the remaining 3 were surprisingly susceptible to both clarithromycin and metronidazole. We did not find any statistical significance in eradication rate between metronidazole resistant and sensitive strains ($p = 0.58$).

Conclusion: In our series, metronidazole resistance does not seem to affect eradication rate of BQT and CT regimens.

Disclosure: Nothing to disclose.

P0141

ANTIBIOTIC RESISTANCE OF *HELICOBACTER PYLORI* IN PRIMARY CARE: AN OBSERVATIONAL COHORT STUDY

G. van den Brink¹, L.M. Koggel², J.J.H. Hendriks², P.D. Siersema², M.G.J. de Boer³, M.E. Numans¹

¹Leiden University Medical Center, Public Health and Primary Care, Leiden, Netherlands, ²Radboudumc, Gastroenterology & Hepatology, Nijmegen, Netherlands, ³Leiden University Medical Center, Internal Medicine and Infectious Diseases, Leiden, Netherlands

Contact E-Mail Address: lieke.koggel@radboudumc.nl

Introduction: *Helicobacter pylori* (*H. pylori*) is causally associated with chronic gastritis, peptic ulcer and gastric cancer, with a reported prevalence of 19–35%. Due to increasing antibiotic resistance, the worldwide efficacy of *H. pylori* eradication treatment has decreased.

Aims & Methods: This study aimed to determine eradication success of *H. pylori* in primary care in the Netherlands, as a proxy measure for antibiotic resistance development. Real-world routine health care data from Electronic Medical Records from general practices in the region Leiden/The Hague was used. Data was provided by ELAN (Extramural LUMC Academic Network). Patients with an ICDPC-code for gastric symptoms or an ATC code for acid inhibition in the period 2010–2020 were selected. Patients with *H. Pylori* infection were detected based on having received eradication treatment.

We investigated antibiotic resistance, defined as the prescription of a second eradication treatment within 12 months. The types of antibiotics prescribed as first eradication treatment were evaluated for resistance rates. If no second treatment was prescribed within 12 months, patients were suspected to have been successfully eradicated.

Results: We identified 138,455 patients with gastric symptoms or acid inhibition from 80 general practices. Mean age was 57 years (SD 18.2) of whom 43% were male. A total of 5,224 (4%) patients received a first eradication treatment and were considered *H. pylori* positive. The antibiotic treatment combinations amoxicillin-clarithromycin, amoxicillin-metronidazole and clarithromycin-metronidazole were used in 4,847 (93%), 154 (3%) and 111 (2%) of first eradication treatments, respectively.

A second eradication treatment was prescribed within one year to 416 (8%) patients. Thereof, 380 (8%) patients received amoxicillin-clarithromycin, 16 (10%) amoxicillin-metronidazole and 11 (10%) clarithromycin-metronidazole as first eradication treatment and were considered antibiotic resistant.

Conclusion: Almost one-tenth of *H. pylori* infections in primary care are not successfully treated after a first treatment with clarithromycin and/or metronidazole and require a second eradication treatment. Therefore, antibiotic resistance should be kept in mind when treating patients with *H. pylori*.

Disclosure: Supported by a grant from the Antibiotic Resistance Care Network Holland West

P0142

EFFECTIVENESS AND SAFETY OF HIGH-DOSE DUAL THERAPY: RESULTS OF THE EUROPEAN REGISTRY ON *HELICOBACTER PYLORI* MANAGEMENT (HP-EUREG)

L. Fernández-Salazar¹, Á. Pérez-Aísa², B. Vaira³, L.V. Jonaitis⁴, B. Tepeš⁵, D.S. Bordin⁶, A. Keco-Huerga⁷, A. Lucendo Villarin⁸, L. Vologzhanina⁹, L. Bujanda Fernández de Piérola¹⁰, N. Brglez Jurecic¹¹, A. Lanas¹², M. Leja¹³, E. Mammadov¹⁴, G. Babayeva¹⁵, M. Caldas Álvarez¹⁶, L.R. Rodrigo Sáez¹⁷, F. Lerang¹⁸, G. Fadieienko¹⁹, R. Abdulkhakov²⁰, J.M. Huguet²¹, O. Zaytsev²², T. Ilchishina²³, A. Silkanovna Sarsenbaeva²⁴, I. Bakulin²⁵, A. G. Gravina²⁶, M. Perona²⁷, S. Alekseenko²⁸, J. Barrio²⁹, M. Areia³⁰, O. Núñez³¹, P. Bogomolov³², B.J. Gómez Rodríguez³³, M. Domínguez-Cajal³⁴, J. Gómez Camarero³⁵, S. Georgopoulos³⁶, P. Almela Notari³⁷, A. Tonkic³⁸, R. Pellicano³⁹, H. Simsek⁴⁰, S. Hrubá⁴¹, A. Gasbarrini⁴², J.M. Botargues Bote⁴³, G.M. Buzas⁴⁴, T. Rokkas⁴⁵, I. Puig⁴⁶, O. Perez Nyssen⁴⁷, F. Mégraud⁴⁸, C. O' Morain⁴⁹, J.P. Gisbert⁵⁰, On behalf of the Hp-EuReg

¹Hospital Clínico Universitario de Valladolid. Universidad de Valladolid, Medicine Dep Gastroenterology, Valladolid, Spain,

²Digestive Unit. Hospital Costa del Sol Marbella. Redes de Investigación Cooperativa orientada a resultados en salud (RICORS), Marbella (Málaga), Spain, ³University of Bologna, Department of Surgical and Medical Sciences, Bologna, Italy,

⁴Lithuanian University of Health Sciences Dept. of Gastroenterology, Gastroenterology, Kaunas, Lithuania, ⁵Abakus Medico d.o.o., Gastroenterology, Rogaska Slatina, Slovenia, ⁶Department of pancreata. S. Loginov Moscow clinical scientific center. Tver State Medical University. A.I. Yevdokimov Moscow State University of Medicine and Dentistry, Moscow, Russian Federation, ⁷Hospital de Valme, Sevilla, Spain, ⁸Hospital General de Tomelloso, Aparato Digestivo, Tomelloso, Spain, ⁹Gastrocentr, Perm, Moscow, Russian Federation, ¹⁰Instituto Biodonostia, San Sebastián, Spain, ¹¹Interni Oddelek, Diagnostic Centre, Bled, Slovenia, ¹²University of Zaragoza University Hospital Dept. of Medicine-Gastroenterology, Dept.

Medicine & Gastroenterology, Zaragoza, Spain, ¹³Institute of Clinical and Preventive Medicine & Faculty of Medicine, University of Latvia, Digestive Diseases centre GASTRO, Riga, Latvia, ¹⁴Department of Therapy, Azerbaijan State Advanced Training Institute for Doctors named after A.ALIYEV, Baku, Azerbaijan, ¹⁵Azerbaijan State Advanced Training Institute for doctors named after A.ALIYEV, Terapiya, Baku, Azerbaijan, ¹⁶Hospital Universitario de La Princesa, Instituto de Investigación Sanitaria Princesa (IIS-Princesa), Universidad Autónoma de Madrid (UAM), and Centro de Investigación Biomédica en Red de Enfermedades Hepáticas y Digestivas (CIBERehd), Gastroenterology and Hepatology, Madrid, Spain, ¹⁷Hospital Central de Asturias, Oviedo, Spain, ¹⁸Central Hospital of Ostfold, Medicine, Grålum, Norway, ¹⁹Digestive Ukrainian Academy of Medical Sciences, Kyiv, Ukraine, ²⁰Kazan State Medical University, Karzan, Russian Federation, ²¹Hospital General Universitario, Valencia, Spain, ²²First Clinical Medical Center, Kovrov, Russian Federation, ²³SM-clinic, Saint-Petersburg, Russian Federation, ²⁴Chelyabinsk Regional Clinical Hospital, Chelyabinsk, Russian Federation, ²⁵North-western State Medical University, St Petersburg, Russian Federation, ²⁶Università degli Studi della Campania "Luigi Vanvitelli", Napoli, Italy, ²⁷Hospital Quirón, Marbella, Spain, ²⁸Far Eastern State Medical University, Khabarovsk, Russian Federation, ²⁹Hospital Universitario Río Hortega, Valladolid, Spain, ³⁰Portuguese Oncology Institute, Coimbra, Portugal, ³¹Hospital Universitario La Moraleja, Madrid, Spain, ³²Universal Clinic - Private Medical Center, Moscow, Russian Federation, ³³Hospital Virgen de la Macarena,

Sevilla, Spain, ³⁴Hospital San Jorge, Huesca, Spain, ³⁵Hospital Universitario, Burgos, Spain, ³⁶Athens Medical, P. Faliron General Hospital, Athens, Greece, ³⁷Hospital General Universitario, Castellón, Spain, ³⁸University Hospital of Split, School of Medicine, Split, Croatia, ³⁹Outpatient clinic, Molinette-SGAS Hospital, University of Turin, Turin, Italy, ⁴⁰Internal Medicine, Hacettepe, University School of Medicine, Ankara, Turkey, ⁴¹Department of Gastroenterology and Hepatology, 1st Internal Clinic, University Hospital in Pilsen, Faculty of Medicine in Pilsen, Charles University, Pilsen, Czech Republic, ⁴²Medicina Interna, Fondazione Policlinico Universitario A. Gemelli IRCCS, Università Cattolica del Sacro Cuore, Roma, Italy, ⁴³Hospital Universitari de Bellvitge, L'Hospitalet de Llobregat, Spain, ⁴⁴Ferencváros Health Centre, Budapest, Hungary, ⁴⁵Henry Dunant Hospital, Athens, Greece, ⁴⁶Althaia Xarxa Assistencial Universitària de Manresa and Universitat de Vic-Universitat Central de Catalunya (UVicUCC), Manresa, Spain, ⁴⁷INSERM U1312, Université de Bordeaux, Bordeaux, France, ⁴⁸Trinity College, Dublin, Ireland

Contact E-Mail Address: opnyssen@gmail.com

Introduction: Introduction: Randomized clinical trials and meta-analyses, primarily from Asian countries, have reported good effectiveness with high-dose dual therapy (HDDT, i.e., PPIs plus high amoxicillin doses) when prescribed for *H. pylori* first-line or rescue treatment. However, combining amoxicillin with PPIs in the 1990s in several European countries yielded suboptimal results. The objective was to analyse the effectiveness, compliance and safety of HDDT in the European real clinical practice.

Aims & Methods: Methods: International, multicenter, prospective non-interventional Registry aimed at evaluating the decisions and outcomes of *H. pylori* management by European gastroenterologists. All infected adult cases treated with HDDT were registered at AEG-REDCap e-CRF up to June 2021. Patients receiving HDDT (amoxicillin 1,000 mg three times a day plus a PPI), with or without bismuth, in any treatment line and for at least 10 days, were selected for inclusion.

Results: Sixty patients received HDDT (98% compliance), 19 of them as first-line and 41 as rescue treatment (2nd–6th line). Overall HDDT effectiveness was 52% (per-protocol) and 51% (modified intention-to-treat, mITT). First-line and rescue treatment lines were similarly effective. Cure rates were lower when patients had previously received metronidazole (mITT 32% vs. 70%, p<0.05), tetracycline (mITT 26% vs. 69%, p<0.05) or rifabutin (mITT 25% vs. 65%, p<0.005). Adding bismuth to HDDT in rescue treatment did not yield better results. Adverse event incidence was 30%, diarrhoea being the most common (20% of patients); no serious adverse events were reported.

HDDT	ITT n/N (%)	p	PP n/N (%)	p	mITT n/N (%)	p
Overall	28/32 (46.7%)		28/54 (51.9%)		28/55 (50.9%)	
1st line	11/19 (57.9%)	0.235	11/17 (64.7%)	0.200	11/17 (64.7%)	0.171
2 nd -6 th line	17/41 (41.5%)		17/37 (45.9%)		17/38 (44.7%)	
2nd line	2/4 (50%)	0.187	2/3 (66.7%)	0.102	2/3 (66.7%)	0.110
3rd line	2/5 (40%)		2/4 (50%)		2/4 (50%)	
4th line	1/2 (50%)		1/2 (50%)		1/2 (50%)	
5th line	12/23 (52.2%)		12/21 (57.1%)		12/22 (54.5%)	
6th line	0/7 (0%)		0/7 (0%)		0/7 (0%)	

Conclusion: Although safe and with proven good compliance, HDDT does not represent an effective option in European first-line or rescue *H. pylori* treatment, even when bismuth is added.

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ing from Mayoly and Allergan. Dr. Pérez-Aísa has received compensation from Allergan and Mylan for formative actions. Dr. Jonaitis has served as speaker for KRKA. The remaining authors have declared no conflict of interest.

P0143

DIFFERENCES OF *HELICOBACTER PYLORI* DIAGNOSTICS AND TREATMENTS IN THE ELDERLY AND NON-ELDERLY POPULATIONS: DATA FROM THE EUROPEAN REGISTRY ON *H. PYLORI* MANAGEMENT (HP-EUREG)

P. Jonaitis¹, J. Kupcinskas¹, Á. Pérez-Aísa², D. Vaira³, B. Tepeš⁴, D.S. Bordin⁵, M. Castro-Fernandez⁶, A.J. Lucendo⁷, L. Vologzhanina⁸, L. Bujanda Fernández de Piérola⁹, M. Denkovski¹⁰, A. Lanas¹¹, M. Leja¹², G. Babayeva¹³, U. Mahmudov¹⁴, L. Rodrigo¹⁵, F. Lerang¹⁶, G. Fadieienco¹⁷, R.A. Abdulkhakov¹⁸, J. Huguet Malavés¹⁹, O. Zaytsev²⁰, L. Fernández-Salazar²¹, A. Sarsenbaeva²², I. Bakulin²³, A.G. Gravina²⁴, M.C. Perona Vincenti²⁵, S. Alekseenko²⁶, J. Barrio Andrés²⁷, M. Areia²⁸, O. Núñez Martínez²⁹, P. Bogomolov³⁰, B.J. Gomez Rodríguez³¹, M. Domínguez Cajal³², J. Gomez Camarero³³, S. Georgopoulos³⁴, P. Almela Notari³⁵, A. Tonkic³⁶, R. Pellicano³⁷, H. Şimşek³⁸, L. Kunovsky³⁹, A. Gasbarrini⁴⁰, J.M. Botargues Bote⁴¹, G.M. Buzás⁴², O. Perez Nyssen⁴³, L. Moreira Ruiz⁴⁴, I. Puig⁴⁵, F. Mégraud⁴⁶, C. O'Morain⁴⁷, J. Gisbert⁴³, L.V. Jonaitis¹,
On behalf of the Hp-EuReg Investigators

¹Lithuanian University of Health Sciences, Department of Gastroenterology, Kaunas, Lithuania, ²Unidad de Digestivo, Hospital Costa del Sol Marbella, Málaga, Redes de Investigación Cooperativa orientada a resultados en salud (RICORS), Marbella, Spain, ³Department of Surgical and Medical Sciences, University of Bologna, Bologna, Italy, ⁴AM DC Rogaska, Rogaska Slatina, Rogaska Slatina, Slovenia, ⁵A. S. Loginov Moscow clinical scientific center, Moscow, Russia; Tver State Medical University, Moscow, Russian Federation, ⁶Hospital de Valme, Sevilla, Spain, ⁷Hospital General de Tomelloso, Dept. de Gastroenterology, Tomelloso, Spain, ⁸Gastrocentr, Perm, Russian Federation, ⁹Hospital Donostia/Instituto Biodonostia, Centro de Investigación Biomédica en Red de Enfermedades Hepáticas y Digestivas (CIBERehd), Universidad del País Vasco (UPV/EHU), San Sebastián, Spain, ¹⁰Interni Oddelek, Diagnostic Centre, Bled, Slovenia, ¹¹Hospital Clínico Universitario Lozano Blesa, Dept. Medicine & Gastroenterology, Zaragoza, Spain, ¹²Digestive Diseases Centre GASTRO, Institute of Clinical and Preventive Medicine & Faculty of Medicine, University of Latvia, Riga, Latvia, ¹³Azerbaijan State Advanced Training Institute for doctors named after A.ALIYEV, Terapiya, Baku, Azerbaijan, ¹⁴Modern Hospital, Baku, Azerbaijan, ¹⁵Hospital de Asturias, Oviedo, Spain, ¹⁶Central Hospital of Ostfold, Medicine, Grålum, Norway, ¹⁷Digestive Ukrainian Academy of Medical Sciences, Kyiv, Ukraine, ¹⁸Kazan State Medical University, Kazan, Russian Federation, ¹⁹Hospital General Universitario de Valencia, Valencia, Spain, ²⁰First Clinical Medical Centre, Kovrov, Russian Federation, ²¹Hospital Clínico de Valladolid, Valladolid, Spain, ²²Chelyabinsk Regional Clinical Hospital, Chelyabinsk, Russian Federation, ²³North-Western State Medical University, Saint-Petersburg, Russian Federation, ²⁴Università degli Studi della Campania "Luigi Vanvitelli", Naples, Italy, ²⁵Hospital Quiron Marbella, Dept. of Gastroenterology, Marbella, Spain, ²⁶Far Eastern State Medical University, Khabarovsk, Russian Federation, ²⁷Hospital

Río Hortega, Valladolid, Spain, ²⁸Portuguese Oncology Institute of Coimbra, Gastroenterology, Coimbra, Portugal, ²⁹Hospital Universitario La Moraleja, Madrid, Spain, ³⁰Universal Clinic - Private Medical Center, Moscow, Russian Federation, ³¹Hospital Virgen de la Macarena, Sevilla, Spain, ³²Hospital San Jorge Huesca, Huesca, Spain, ³³Hospital Universitario de Burgos, Burgos, Spain, ³⁴Athens Medical, P. Faliron General Hospital, Athens, Greece, ³⁵Hospital General Universitario de Castellón, Castello, Spain, ³⁶University Hospital of Split, School of Medicine, Split, Croatia, ³⁷Outpatient clinic, Molinette-SGAS Hospital, University of Turin, Turin, Italy, ³⁸Internal Medicine, Hacettepe, University School of Medicine, Ankara, Turkey, ³⁹Department of Gastroenterology and Digestive Endoscopy, Masaryk Memorial Cancer Institute, Brno, Czech Republic, ⁴⁰Medicina Interna, Fondazione Policlinico Universitario A. Gemelli IRCCS, Università Cattolica del Sacro Cuore, Rome, Italy, ⁴¹Hospital Universitari de Bellvitge, L'Hospitalet de Llobregat, Barcelona, Spain, ⁴²Ferencváros Health Centre, Budapest, Hungary, ⁴³Hospital Universitario de La Princesa, Instituto de Investigación Sanitaria Princesa (IIS-Princesa), Universidad Autónoma de Madrid (UAM), and Centro de Investigación Biomédica en Red de Enfermedades Hepáticas y Digestivas (CIBERehd), Madrid, Spain, ⁴⁴Hospital Clínic de Barcelona, Centro de Investigación Biomédica en Red en Enfermedades Hepáticas y Digestivas (CIBERehd), IDIBAPS (Institut d'Investigacions Biomèdiques August Pi i Sunyer), University of Barcelona, Barcelona, Spain, ⁴⁵Althaia Xarxa Assistencial Universitària de Manresa and Universitat de Vic-Universitat Central de Catalunya (UVicUCC), Manresa, Spain, ⁴⁶INSERM U1312, Université de Bordeaux, Bordeaux, France, ⁴⁷Trinity College Dublin - Faculty of Health Sciences, Trinity College Dublin; Dublin/IE, Faculty of Health Sciences, Dublin, Ireland

Contact E-Mail Address: Laimas.Jonaitis@lsmuni.lt

Introduction: The prevalence of *H. pylori* infection in the elderly population still remains quite high and this group is usually characterized by multimorbidity, polypharmacy and age-related physiological changes. Therefore, there might be some peculiarities in the diagnostics and treatment of *H. pylori* in such population.

Aims & Methods: **Aims:** To compare the diagnostics and treatments of *H. pylori* infection in the elderly and non-elderly populations.

Methods: The "European Registry on *H. pylori* Management" (Hp-EuReg) is an international European multicenter prospective non-interventional registry recording information of *H. pylori* infection management. Data from the year 2013 to 2022 were analysed.

The subjects were divided into non-elderly (18-59 years) and elderly (≥60 years) groups. Basic demographic information, previous eradication attempts, diagnostic methods, prescribed treatment and its outcome, and adverse events were analysed.

Results: The detailed statistical results are presented in Table 1. 14,467 elderly (29%) and 34,994 non-elderly (71%) patients were included in the Hp-EuReg. Differences of the main indications for *H. pylori* testing (functional dyspepsia and peptic ulcer disease) and the main symptoms before the treatment (dyspepsia and heartburn) were reported between both age groups.

Compared to non-elderly group, more patients in the elderly group were taking concurrent medications (27% vs. 55%, $p<0.05$) and more patients had drug allergies (4% vs. 6%, $p<0.05$). There were significant differences in most of the main *H. pylori* diagnostic tests prescribed before treatment between both age groups, the main being histological examination (47% vs. 38%, $p<0.05$), rapid urease test (RUT) (both groups 38%) and urea breath test (UBT) (25% vs. 31%, $p<0.05$). The main diagnostic tests post-treatment in both groups were UBT (66% and 62%, $p<0.05$), stool antigen

test (14% and 15%, $p<0.05$) and histological examination (5% and 4%, $p<0.05$). In both groups, 81% of the cases were treatment-naïve. For the first-line treatment, quadruple therapies were prescribed in 45% of the elderly and 46% of the non-elderly cases; and triple therapies in 42% and 45%, respectively ($p<0.05$).

For the second-line treatment, quadruple therapies were prescribed in 52% of the elderly and 51% of the non-elderly cases; and triple therapies in 43% and 45%, respectively ($p<0.05$). The duration of first-line treatment in the elderly and non-elderly was: 7 days in 14% and 12%, 10 days in 50% and 49%, and 14 days in 36% and 40% ($p<0.05$ in all groups).

	Elderly (≥60 years)	Non-elderly (18-59 years)	p-value
Gender, N (%)			
- Total	14,467 (29%)	34,994 (71%)	<0.05
- Male	5,365 (37%)	14,244 (41%)	<0.05
- Female	9,093 (63%)	20,730 (59%)	<0.05
Average age ± standard deviation	68.1±6.3	42.8±10.7	>0.05
Main treatment indications, N (%)			
- Functional dyspepsia	5,111 (36%)	13,248 (38%)	<0.05
- Peptic ulcer disease	2,893 (20%)	5,094 (15%)	<0.05
Main symptoms, N (%)			
- Dyspepsia	10,571 (73%)	27,070 (77%)	<0.05
- Heartburn	3,831 (26.3%)	9,183 (26.5%)	>0.05
Concurrent medications, N (%)	7,364 (55%)	8,834 (27%)	<0.05
Drug allergies, N (%)	796 (6%)	1,306 (4%)	<0.05
Main diagnostic methodspre-treatment, N (%)			
- Histology	6,840 (47%)	13,191 (38%)	<0.05
- Rapid urease test	5,463 (38%)	13,138 (38%)	>0.05
- Urea breath test	3,550 (25%)	10,702 (31%)	<0.05
Main diagnostic testspost-treatment, N (%)			
- Urea breath test	9,544 (66%)	21,755 (62%)	<0.05
- Stool antigen test	1,968 (13.6%)	5,401 (15.4%)	<0.05
- Histology	715 (5%)	1,529 (4%)	<0.05
Treatment compliance, N (%)	12,938 (97%)	31,270 (97%)	>0.05
PPI potency in first-line treatment, N (%)			
Low	5,275 (46%)	12,312 (45%)	>0.05
Standard	2,726 (24%)	6,831 (25%)	>0.05
High	3,516 (31%)	8,539 (31%)	>0.05
PPI potency in second-line treatment, N (%)			
Low	750 (40%)	1,691 (36%)	<0.05
Standard	423 (23%)	1,059 (23%)	>0.05
High	705 (38%)	1,983 (42%)	<0.05
First-line treatment duration, N (%)			
- 7 days	1,583 (14%)	3,170 (12%)	<0.05
- 10 days	5,700 (50%)	13,351 (49%)	<0.05
- 14 days	4,185 (37%)	11,019 (40%)	<0.05
Second-line treatment duration, N (%)			
- 7 days	75 (4%)	197 (4%)	>0.05
- 10 days	1,023 (56%)	2,618 (56%)	>0.05
- 14 days	744 (40%)	1,881 (40%)	>0.05
Adverse events (AEs)			
- Overall, N (%)	3,062 (23%)	8,144 (25%)	<0.05
- Treatment cessation due to AEs, %	1.5%	1.2%	>0.05

Table 1. The main differences in the demographics, diagnostics and treatment of *H. pylori* between the elderly and non-elderly populations

The overall duration of second-line treatment was 7 days in 4%, 10 days in 56% and 14 days in 40% of the cases in both groups. No significant differences in the prescribed PPI doses between the elderly and non-elderly were found in the first-line treatment, the most frequent being low-dose (46% vs. 45%, $p>0.05$), high-dose (both groups 31%, $p>0.05$) and standard-dose (24% vs. 25%, $p>0.05$). In the second-line, low PPI doses were more frequently prescribed in the elderly (40% vs. 36%, $p<0.05$), while high PPI

doses were more frequently prescribed in the non-elderly (38% vs. 42%, $p<0.05$). There were no differences in the frequency of standard doses of PPI (both groups 23%).

No differences were found in terms of the treatment compliance in both groups. Statistically significantly less adverse events (AEs) were reported in the elderly group compared to non-elderly (22.8% vs. 25.1%, $p<0.05$); however, there were no differences in the rate of treatment withdrawal due to AEs (1.5% vs. 1.2%, $p>0.05$). The AEs were usually mild to moderate in intensity and lasted up to 14 days.

Conclusion: The diagnostics and treatment of *H. pylori* infection does not generally differ between the elderly and non-elderly groups. The main differences were reported in the concurrent medications, drug allergies, adverse events and the type of prescribed regimen (triple vs. quadruple) both in first- and second-line treatment. However, treatment compliance was similar between groups and the treatment was generally well-tolerated.

Disclosure: Nothing to disclose.

P0144

ERRORS IN EMPIRICAL ANTIBIOTIC THERAPIES FOR *HELICOBACTER PYLORI* ERADICATION IN 45,778 PATIENTS: DATA FROM THE EUROPEAN REGISTRY ON *H. PYLORI* MANAGEMENT (HP-EUREG)

S.J. Martínez-Domínguez¹, E. Alfaro¹, P. Carrera-Lasfuentes¹, A. Lanás¹, Á. Pérez-Aísa², D. Vaira³, G. Fiorini³, I.M. Saracino³, L.V. Jonaitis⁴, B. Tepeš⁵, D.S. Bordin⁶, A. Keco-Huerga⁷, M. Castro Fernandez⁷, A.J. Lucendo⁸, L. Vologzhanina⁹, L. Bujanda Fernández de Piérola¹⁰, N. Brglez Jurecic¹¹, M. Denkovski¹¹, M. Leja¹², R. Bumane¹², E. Mammadov¹³, G. Babayeva¹⁴, U. Mahmudov¹⁵, M. Caldas Álvarez¹⁶, L.R. Rodrigo Sáez¹⁷, F. Lerang¹⁸, G. Fadieienco¹⁹, R.A. Abdulkhakov²⁰, J.M. Huguet²¹, O. Zaytsev²², T. Ilchishina²³, L. Fernández-Salazar²⁴, N. Alcaide Suárez²⁵, B. Velayos Jiménez²⁶, A. Sarsenbaeva²⁷, I. Bakulin²⁸, A.G. Gravina²⁹, M. Romano²⁹, M.C. Perona Vincenti³⁰, S. Alekseenko³¹, J. Barrio Andrés³², M. Areia³³, O. Núñez Martínez³⁴, P. Bogomolov³⁵, B.J. Gómez Rodríguez³⁶, M. Domínguez Cajal³⁷, A. Cano³⁸, I. Puig³⁸, O. Perez Nyssen¹⁶, J. Gisbert¹⁶,
On behalf of the Hp-EuReg investigators

¹Hospital Clínico Universitario Lozano Blesa, Zaragoza, Spain, ²Agencia Sanitaria Costa del Sol, Marbella, Spain, ³University of Bologna, Surgical and Medical Sciences, Bologna, Italy, ⁴Lithuanian University of Health Sciences, Gastroenterology, Kaunas, Lithuania, ⁵Abakus Medico d.o.o., Gastroenterology, Rogaska Slatina, Slovenia, ⁶A.S. Loginov Moscow Clinical Scientific Center, Pancreatic, Biliary and Upper GI Diseases, Moscow, Russian Federation, ⁷Hospital de Valme, Sevilla, Spain, ⁸Hospital General de Tomelloso, Gastroenterology, Tomelloso, Spain, ⁹Gastrocentr, Perm, Russian Federation, ¹⁰Instituto Biodonostia, San Sebastián, Spain, ¹¹Interni Oddelek, Diagnostic Centre, Bled, Slovenia, ¹²University of Latvia, Digestive Diseases Centre GASTRO, Riga, Latvia, ¹³Azerbaijan State Advanced Training Institute for Doctors named after A. Aliyev, Baku, Azerbaijan, ¹⁴Azerbaijan State Advanced Training Institute for Doctors named after A. Aliyev, Terapiya, Baku, Azerbaijan, ¹⁵Modern Hospital, Baku, Azerbaijan, ¹⁶Hospital de La Princesa, Gastroenterology and Hepatology, Madrid, Spain, ¹⁷Hospital de Asturias, Oviedo, Spain, ¹⁸Central Hosspital of Ostfold, Medicine, Grålum, Norway, ¹⁹National Therapy Institute named after L.T. Malaya under the Ukraine Academy of Medical Sciences, Kharkiv, Ukraine, ²⁰Kazan State Medical University, Kazan, Russian Federation, ²¹Hospital General Universitario de Valencia, Valencia, Spain, ²²First Clinical Medical Centre, Kovrov, Russian Federation, ²³SM-Clinic, Saint Petersburg, Russian Federation, ²⁴Hospital Clínico de Valladolid, Valladolid, Spain, ²⁵Hospital Universitario Rio Hortega, Valladolid, Spain, ²⁶Hospital Clinico Universitario, Valladolid, Spain, ²⁷Chelyabinsk Regional Clinical Hospital, Moscow, Russian Federation, ²⁸North-Western State Medical University n.a. I.I. Mechnikov, Propedeutics of Internal Diseases, Gastroenterology and Dietology n.a. S.M. Riss, Moscow, Russian Federation, ²⁹University of Campania Luigi Vanvitelli, Precision Medicine, Division of Hepatogastroenterology, Naples, Italy, ³⁰Hospital Quiron Marbella, Gastroenterology, Marbella, Spain, ³¹Far Eastern State Medical University, Russia, Russian Federation, ³²Rio Hortega University Hospital, Valladolid, Spain, ³³Portuguese Oncology Institute of Coimbra, Gastroenterology, Coimbra, Portugal, ³⁴Hospital Sanitas La Moraleja, Gastroenterology, San Sebastian de los Reyes, Spain, ³⁵Universal Clinic - Private Medical Center, Moscow, Russian Federation, ³⁶Hospital Virgen de la Macarena, Sevilla, Spain, ³⁷Hospital San Jorge, Huesca,

Spain, ³⁸Althaia Xarxa Assistencial Universitaria de Manresa and Universidad de Vic-Universidad Central de Cataluña (UVicUCC), Manresa, Spain

Contact E-Mail Address: samuelmartinez94@hotmail.com

Introduction: Failure of eradication therapy based on macrolides, quinolones or metronidazole is associated with increased *H. pylori* antibiotic resistance; and so, prescribing the same antibiotic as in previous eradication treatment should be avoided. In addition, quinolones are not recommended in first-line therapy given the higher incidence of adverse events reported.

Aims & Methods: Objectives: To describe the frequency of use of quinolones in first-line therapy and the frequency of use of clarithromycin, levofloxacin or metronidazole in second-line, after failure of a first-line therapy based on these same antibiotics.

International, multicenter, prospective, non-interventional registry of the clinical practice of European gastroenterologists. All infected adult patients were systematically registered at AEG-REDCap e-CRF from 2013 to December 2021. *Variables included:* Patient's demographics, previous eradication attempts, prescribed treatment, adverse events, and outcomes. A modified intention-to-treat (mITT) analysis was performed. Data were quality reviewed.

Results: In total, 45,778 patients from 29 countries were included in analysis, being the most frequent: Spain (40%), Russia (16%), Italy (10%), Slovenia (8.1%), and Lithuania (4.8%). First-line therapy was prescribed in 36,699 (80%) cases, second-line in 6,435 (14%), and third- to sixth-line in 2,644 (5.7%). Among those first-line therapies, 952 (2.6%) included levofloxacin, with a decrease in the consumption over the years (from 15% in 2013 to 5.9% in 2021) and differing between countries (Italy 3.4%, Lithuania 2.3%, Russia 2.0%, Slovenia 0.5%, Spain 1.9%; $p < 0.001$). In second line, 2,878 cases used levofloxacin, 1,295 clarithromycin and 1,086 metronidazole. After a first-line eradication failure, clarithromycin was repeated in second-line therapy in 788 patients (16%), metronidazole in 312 (18%) and levofloxacin in 43 (28%) cases. A detailed analysis by country is presented in Table 1.

Antibiotic	Total n (%)	Italy n (%)	Lithuania n (%)	Russia n (%)	Slovenia n (%)	Spain n (%)	Other n (%)	p value
Clarithromycin	788 (16.0)	83 (13.8)	27 (10.7)	272 (46.8)	19 (5.6)	263 (10.3)	124 (21.1)	<0.001
Amoxicillin	3,403 (70.7)	410 (64.4)	243 (97.2)	435 (69.2)	191 (92.3)	1,695 (68.2)	429 (71.1)	<0.001
Metronidazole	312 (17.6)	3 (2.8)	1 (4.5)	21 (28.0)	11 (7.6)	198 (17.2)	78 (28.8)	<0.001
Levofloxacin	43 (28.1)	3 (11.1)	0 (0.0)	15 (71.4)	-	19 (22.9)	43 (28.1)	<0.001

Table 1. Antibiotic prescriptions in second-line therapy, after first-line failure with the same antibiotic, by country.

Conclusion: The erroneous administration of quinolones in first-line therapy has decreased in recent years in Europe. After a first line-therapy failure with either clarithromycin, levofloxacin or metronidazole, the same antibiotic is frequently (and incorrectly) prescribed in second-line therapy.

Disclosure: Nothing to disclose.

P0145

PROSPECTIVE RANDOMIZED STUDY: HIGH-DOSE AMOXICILLIN DUAL THERAPY VERSUS BISMUTH QUADRUPLE THERAPY FOR *HELICOBACTER PYLORI* ERADICATION

V. Macedo Silva^{1,2,3}, T. Lima Capela^{1,2,3}, M. Freitas^{1,2,3}, P. Boal Carvalho^{1,2,3}, J. Magalhães^{1,2,3}, J. Berkeley Cotter^{1,2,3}

¹Hospital da Senhora da Oliveira, Gastroenterology Department, Guimarães, Portugal, ²Life and Health Sciences Research Institute (ICVS), School of Medicine, University of Minho, Braga, Portugal, ³ICVS/3B's, PT Government Associate Laboratory, Braga / Guimarães, Portugal

Contact E-Mail Address: tiagolimacapela@gmail.com

Introduction: *Helicobacter pylori* (HP) eradication is recommended for prevention of gastric complications such as peptic ulcer disease or adenocarcinoma.

Currently, bismuth quadruple therapy (BQT) is indicated as first-line treatment in areas with a high incidence of dual metronidazole and clarithromycin resistance, with its use being limited by its tolerability and financial costs. A novel regimen with high-dose amoxicillin (HDA) dual therapy has emerged as an alternative. The aim of this study was to compare the results of these two treatments on HP eradication.

Aims & Methods: Prospective randomized study including 100 consecutive patients undergoing HP eradication. Each patient was randomized to one branch of treatment: BQT (bismuth 140mg + metronidazole 125mg + tetracycline 125mg, 4 times a day, for 10 days) or HDA (amoxicillin 1000mg alternating with amoxicillin 500mg, 4 times a day, for 14 days), both associated with esomeprazole 40mg twice a day. Four weeks after treatment, efficacy (stool HP antigen test and symptom persistence) and tolerability (side effects and treatment interruption) were assessed in each branch.

Results: A total of 100 patients were included, 54% women, with a mean age of 55±14 years. From these, 14 lost follow-up. Effective eradication proven by negative stool antigen test was significantly higher in patients randomized to HDA when compared to BQT (96% vs 83%; $p=0.047$). This difference was even higher considering only those patients refractory to previous therapies for HP eradication (100% vs 72%; $p=0.030$).

Furthermore, the percentage of patients with dyspeptic symptoms after treatment was also lower with HDA treatment (4% vs 19%; $p=0.021$).

The incidence of side effects (2% vs 9%; $p=0.133$) and treatment interruption (2% vs 4%; $p=0.460$) did not significantly differ between both treatments.

Conclusion: When compared to BQT, treatment with HDA presented higher efficacy in eradicating HP infection, without differences in reported side effects or therapeutic adherence. This treatment represents an interesting alternative for populations with increasing incidences of resistance to the currently recommended antibiotic regimens.

Disclosure: Nothing to disclose.

P0146 WITHDRAWN

P0147

ROLE OF THE PROTON PUMP INHIBITORS IN *HELICOBACTER PYLORI* ERADICATION: RESULTS FROM THE EUROPEAN REGISTRY ON *H. PYLORI* MANAGEMENT (HP-EUREG)

M. Castro Fernandez¹, M. Pabón-Carrasco², A. Keco-Huerga¹, Á. Pérez-Aísa³, D. Vaira⁴, L. Jonaitis⁵, B. Tepes⁶, D. Bordin⁷, A. Lucendo⁸, L. Vologzhanina⁹, L. Bujanda¹⁰, N. Brglez Jurecic¹¹, A. Lanás¹², M. Leja¹³, E. Mammadov¹⁴, U. Mahmudov¹⁵, M. Caldas¹⁶, L. Rodrigo¹⁷, F. Lerang¹⁸, G. Fadieienco¹⁹, R. Abdulkhakov²⁰, J.M. Huguet Malavés²¹, O. Zaytsev²², T. Ilchishina²³, L. Fernández-Salazar²⁴, A. Silkanovna Sarsenbaeva²⁵, I. Bakulin²⁶, A.G. Gravina²⁷, M. Perona²⁸, S. Alekseenko²⁹, J. Barrio³⁰, M. Areia³¹, Ó. Nuñez³², P. Bogomolov³³, B.J. Gomez Rodriguez³⁴, M. Dominguez-Cajal³⁵, J. Gomez Camarero³⁶, S. Georgopoulos³⁷, P. Almela Notari³⁸, A. Tonkic³⁹, R. Pellicano⁴⁰, H. Simsek⁴¹, L. Kunovsky⁴², A. Gasbarrini⁴³, J.M. Botargues Bote⁴⁴, I. Puig⁴⁵, O. Perez Nyssen¹⁶, F. Mégraud⁴⁶, C. O'Morain⁴⁷, J. P. Gisbert¹⁶, On behalf of the Hp-EuReg investigators.

¹Hospital Universitario de Valme, Digestivo, Sevilla, Spain, ²Universidad de Sevilla, Centro Universitario de Enfermería Cruz Roja, Sevilla, Spain, ³Agencia Sanitaria Costa del Sol, Red de Investigación en Servicios de Salud en Enfermedades Crónicas (REDISSEC), Marbella, Spain, ⁴Department of Surgical and Medical Sciences, University of Bologna, Bologna, Italy, ⁵Lithuanian University of Health Sciences, Kaunas, Lithuania, ⁶AM DC Rogaska, Rogaska Slatina, Slovenia, ⁷A. S. Loginov Moscow clinical scientific center, Moscow, Russia; Tver State Medical University, Tver, Russia; A.I. Yevdokimov Moscow State University of Medicine and Dentistry, Moscow, Russian Federation, ⁸Hospital General de Tomelloso, Tomelloso, Spain, ⁹Gastrocentr, Perm, Russian Federation, ¹⁰Hospital Donostia/Instituto Biodonostia, Centro de Investigación Biomédica en Red de Enfermedades Hepáticas y Digestivas (CIBERehd), Universidad del País Vasco (UPV/EHU), San Sebastián, Spain, ¹¹Interni Oddelek, Diagnostic Centre, Bled, Slovenia, ¹²Hospital Clínico Universitario Lozano Blesa, Zaragoza, Spain, ¹³Digestive Diseases Centre GASTRO, Institute of Clinical and Preventive Medicine & Faculty of Medicine, University of Latvia, Riga, Latvia, ¹⁴Department of Therapy, Azerbaijan State Advanced Training Institute for Doctors named after A.Aliyev, Baku, Azerbaijan, ¹⁵Modern Hospital, Baku, Azerbaijan, ¹⁶Hospital Universitario de La Princesa, Instituto de Investigación Sanitaria Princesa (IIS-Princesa), Universidad Autónoma de Madrid (UAM), and Centro de Investigación Biomédica en Red de Enfermedades Hepáticas y Digestivas (CIBERehd), Madrid, Spain, ¹⁷Hospital de Asturias, Oviedo, Spain, ¹⁸Østfold Hospital Trust, Grålum, Norway, ¹⁹Digestive Ukrainian Academy of Medical Sciences, Kyiv, Ukraine, ²⁰Kazan State Medical University, Kazan, Russian Federation, ²¹Hospital General Universitario, Valencia, Spain, ²²First Clinical Medical Centre, Kovrov, Russian Federation, ²³SM-clinic, Saint-Petersburg, Russian Federation, ²⁴Hospital Clínico Universitario, Valladolid, Spain, ²⁵Chelyabinsk Regional Clinical Hospital, Chelyabinsk, Russian Federation, ²⁶North-western State Medical University, St Petersburg, Russian Federation, ²⁷Università degli Studi della Campania "Luigi Vanvitelli", Napoli, Italy, ²⁸Hospital Quirón, Marbella, Spain, ²⁹Far Eastern State Medical University, Vladivostok, Russian Federation, ³⁰Hospital Río Hortega, Valladolid, Spain, ³¹Portuguese Oncology Institute, Coimbra, Portugal, ³²Hospital Universitario La Moraleja, Madrid, Spain, ³³Universal Clinic - Private Medical Center, Moscow, Russian Federation, ³⁴Hospital Virgen de la Macarena, Seville, Spain, ³⁵Hospital San Jorge, Huesca, Spain, ³⁶Hospital Universitario

de Burgos, Burgos, Spain,³⁷Athens Medical, P. Faliron General Hospital, Athens, Greece,³⁸Hospital General Universitario, Castellón, Spain,³⁹University Hospital of Split, School of Medicine, University of Split, Split, Croatia,⁴⁰Outpatient clinic, Molinette-SGAS Hospital, University of Turin, Turin, Italy,⁴¹Internal Medicine, Hacettepe, University School of Medicine, Ankara, Turkey,⁴²2nd Department of Internal Medicine - Gastroenterology and Geriatrics, University Hospital Olomouc, Department of Surgery, University Hospital Brno, Brno, Czech Republic,⁴³Medicina Interna, Fondazione Policlinico Universitario A. Gemelli IRCCS, Università Cattolica del Sacro Cuore, Roma, Italy,⁴⁴Hospital Universitari de Bellvitge, L'Hospitalet de Llobregat,, L'Hospitalet de Llobregat, Spain,⁴⁵Althaia Xarxa Assistencial Universitària de Manresa and Universitat de Vic-Universitat Central de Catalunya (UVicUCC), Manresa, Spain,⁴⁶INSERM U1312, Université de Bordeaux, Bordeaux, France,⁴⁷Trinity College Dublin, Dublin, Ireland

Contact E-Mail Address: opnyssen@gmail.com

Introduction: Management of *Helicobacter pylori* infection (*H. pylori*) requires co-treatment with proton pump inhibitors (PPIs) and the use of antibiotics to achieve successful eradication

Aims & Methods: To evaluate the role of PPIs in the eradication of *H. pylori*, based on the "European Registry on *Helicobacter pylori* Management" (Hp-EuReg).

The Hp-EuReg is a multicentre, prospective, non-interventional, registry assessing decisions and outcomes of *H. pylori* management by European gastroenterologists in routine clinical practice. Countries recruiting more than 1,000 patients were included. Effectiveness was assessed by modified intention-to-treat (mITT). Data were quality reviewed.

Results:

	Eradication rate n/N (%) mITT	Low Dose	Standard Dose	High Dose	p-value
10 days N: 12214 (55.3%)	Triple PPI+CM/ A	1277/1634 (78.2)	1088/1261 (86.3)	417/466 (89.5)	0.0001
	Quadruple sequential PPI+C+AT/M	981/1112 (88.2)	48/51 (94.1)	603/647 (93.2)	0.002
	Quadruple Concomitant PPI+C+A+T/M	1262/1437 (87.8)	507/580 (87.4)	440/476 (92.4)	0.013
	Quadruple with bismuth PPI+C+A+B	200/233 (85.8)	213/235 (90.6)	93/101 (93.0)	0.137
	Pylera®/ Quadruple with bismuth PPI+B+M+Tc	1533/1683 (91.1)	865/917 (94.3)	1300/1371 (94.8)	0.0001
14 days N: 7782 (35.2%)	Triple PPI+C+M/ A	426/528 (80.7)	758/850 (89.2)	1273/1391 (91.5)	0.0001
	Quadruple Concomitant PPI+C+AT/M	597/702 (85.0)	385/429 (89.7)	1573/1685 (93.4)	0.0001
	Quadruple with bismuth PPI+C+A+B	165/180 (91.6)	797/859 (92.8)	969/1067 (90.8)	0.299
	Pylera®/ Quadruple with bismuth PPI+B+M+Tc	18/20 (90.0)	55/59 (93.2)	11/12 (91.6)	0.893

A: amoxicillin; B: bismuth; C: clarithromycin; M: metronidazole; Tc: tetracycline; T: tinidazole; mITT: modified intention to treat; PPI: proton pump inhibitor; N= Total treated; n=Success; *Low dose PPI - 4.5 to 27 mg omeprazole equivalent; standard dose PPI - 32 to 40 mg omeprazole equivalent; high dose PPI - 54 to 128 mg omeprazole equivalent, b.i.d

Table 1.

Overall, 22,078 patients from 5 countries were analysed. Optimal (>90%) first-line mITT effectiveness was achieved with the following treatments: 14-day clarithromycin-amoxicillin-bismuth quadruple therapy, and 14-

day metronidazole-tetracycline-bismuth quadruple therapy, both independently of the PPI dose prescribed; in all 10- or 14-day therapies with high-dose PPIs (except with standard 10-day triple therapy); in 10-day sequential and 10-day quadruple clarithromycin-amoxicillin-bismuth, and 10-day quadruple metronidazole-tetracycline-bismuth with standard-dose PPIs. None of the 7-day therapies achieved optimal cure rates regardless of the PPI dose used. The PPI dose was significantly associated with the effectiveness of: 10- or 14-day standard triple and quadruple concomitant therapies, and 10-day quadruple sequential and metronidazole-tetracycline-bismuth therapies. Table 1 details the mITT effectiveness by duration and PPI dose used.

Conclusion: In first-line *H. pylori* treatment, ≥90% effectiveness is obtained with standard-dose PPIs in 10-day sequential and 10- or 14-day bismuth quadruple therapies and with high-dose PPIs in all 10- or 14-day therapies except with standard 10-day triple therapy.

Disclosure: Nothing to disclose.

P0148 WITHDRAWN

P0149

EFFECTIVENESS AND SAFETY OF NOVEL VONOPRAZAN-BASED REGIMEN FOR *H. PYLORI* ERADICATION: A SINGLE CENTER, PROSPECTIVE, RANDOMIZED TRIAL

X. Wang¹, J. Yu¹, L. Tang¹

¹The Affiliated Changzhou No. 2 People's Hospital of Nanjing Medical University, Gastroenterology, Changzhou, China

Contact E-Mail Address: wxy20009@126.com

Introduction: To date, vonoprazan-based regimens for *H. pylori* infection in Japan have been shown to achieve acceptable eradication rates. However, its effectiveness and safety is unclear in Chinese.

Aims & Methods: This study aimed to evaluate the efficacy and safety of the novel Vonoprazan-based regimen as first-line treatment for *H. pylori* and to compare with bismuth-based quadruple regimen. This prospective, randomized clinical trial was performed in China. Patients with *H. pylori* and naive to treatment were randomly assigned to either VAS group (vonoprazan 20 mg twice/day, amoxicillin 750 mg three times/day and *S. boulardii* 250 mg twice/day) for 10 days or PCAB group (Esomeprazole 20 mg, amoxicillin 1000 mg, clarithromycin 500 mg and bismuth 220 mg twice/day) for 14 days. Eradication success was evaluated by ¹³C-urea breath test at least 4 weeks after treatment and adverse events were recorded. Factors associated with eradication success and cost-effectiveness analyses were also performed.

Results: 135 subjects were screened and 126 were randomized. The eradication rates of VAS and PCAB groups were 87.3% and 88.9% ($p=1.000$) by intention-to-treat analysis, and 87.3% and 91.8% ($p=0.560$) by per-protocol analysis, respectively. The incidence of adverse events in PCAB group was significantly higher than that in VAS group (17.5% VS 4.8% $P=0.044$). In the VAS group, successful *H. pylori* eradication was associated with small body surface area (BSA) (eradication rate: 92.2% in patients with BSA <1.831 vs. 66.7% in those with BSA ≥1.831, $p=0.037$) and non-smokers (eradication rate: 92.9% in non-smokers vs. 42.9% in smokers, $p=0.003$). Cost-effectiveness ratio of VAS group was less than that of PCAB group (4.64 vs. 4.79, Chinese Yuan, per percent).

Conclusion: This novel Vonoprazan-based regimen is as effective as bismuth-based quadruple regimen, with less adverse events and more cost-effective. This regimen is more suitable for small BSA and non-smoking patients.

Disclosure: Nothing to disclose.

P0150

AN EVOLVING RESISTANT PANDEMIC. RISING COMMUNITY *H. PYLORI* TREATMENT FAILURE TO CLARITHROMYCIN-BASED TRIPLE THERAPY: AN OBSERVATIONAL STUDY

T. Butler^{1,2}, P. Armstrong², M.T. Gregg², S. Smith¹, D. McNamara^{1,2}
¹Trinity College Dublin, Clinical Medicine, Dublin, Ireland, ²Tallaght University Hospital, Gastroenterology, Dublin, Ireland

Contact E-Mail Address: thbutler@tcd.ie

Introduction: Clarithromycin-based triple therapy is commonly prescribed as a first-line treatment for *H. pylori* in Ireland. Worldwide, increased clarithromycin resistance has been reported. It is unclear whether this is due to personalised antibiotic exposure inducing resistance over time, or endemic community prevalence of a resistant strain of *H. pylori*, acquired from youth.

We hypothesise that older age cohorts would have had more exposure to antibiotics and that increased resistance rates, leading to treatment failure with age, would support a developed resistance model.

Aims & Methods: To identify treatment failure rates to first-line clarithromycin-based triple therapy and to compare rates according to age and gender.

All patients referred for their post-eradication 13C-urea breath test (UBT), having received clarithromycin-based triple therapy (40 mg esomeprazole b.i.d., 500 mg clarithromycin b.i.d., amoxicillin 1 g b.i.d. for 14 days) between 2019 and 2022 were identified and included in the analysis. Following clarithromycin triple therapy a positive UBT, delta-over-baseline >4, was considered a surrogate marker of clinical resistance.

Results: In all 482 patients were identified (mean age = 50.6 ± 16.8 ; 45.6% (n=220) male, 54.4 (n=262) . The overall clarithromycin resistance rate was found to be 25.5 % (n=123). We found no statistical difference in resistance rates across ages or between age groups, divided into decades analysed via two-way ANOVA.

Dividing the cohort into those aged less than 45 and greater than 45, the resistance rates were also statistically similar (26.6% (n=49) versus 24.8% (n=74), respectively; Fisher's exact test, p=0.69).

It was also found that failure rates were comparable for both male and female patients (21.8% (n=48) versus 28.6% (n=75), respectively, Fisher's exact test, p = 0.094).

Conclusion: Across adult age groups, clarithromycin resistance has reached alarmingly high levels with 1 in 4 patients failing first-line therapy. In addition, it suggests a high community prevalence of clarithromycin-resistant *H. pylori*. The authors propose that clarithromycin-based triple therapy should no longer be used without sensitivity testing as a treatment for *H. pylori* in Ireland.

Disclosure: Nothing to disclose.

P1031

HELICOBACTER PYLORI INFECTION MEDIATES P53 REGULATION OF MITF-INDUCED MITOPHAGY

J. Rong¹, H. Wang¹, Y. Xie¹
¹The First Affiliated Hospital of Nanchang University, Department of Gastroenterology, Nanchang, China

Contact E-Mail Address: 915939113@qq.com

Introduction: Mitophagy is a type of selective autophagy that is essential for maintaining cellular homeostasis. Helicobacter pylori (*H. pylori*) infection is closely related to the development of gastric cancer (GC), however, the mechanism by which *H. pylori* infection regulates mitophagy in GC remains unclear.

Aims & Methods: In vivo and in vitro models of *H. pylori* infection were constructed to study the relationship between *H. pylori* infection and mitophagy. The interaction between p53 and MITF was verified by immunoprecipitation (CO-IP). Overexpression of p53 and ROS inhibitor NAC treatment were used to study the relationship between p53, mitoSOX and MITF in GC, and the role of MITF in mitophagy induced by *H. pylori* infection.

Results: *H. pylori* infection can upregulate mitoSOX production and induce mitochondrial membrane depolarization, mitochondrial fission and mitophagy in GC. NAC treatment can reduce mitoSOX production and reduce mitophagy induced by *H. pylori* infection. *H. pylori* infection can up-regulate the expression of MITF, and knocking down MITF can inhibit the mitophagy induced by *H. pylori* infection. NAC treatment could attenuate the up-regulation of MITF expression induced by *H. pylori* infection. *H. pylori* infection can down-regulate the expression of p53. MITF protein interacts with p53 protein in GC cell. Overexpression of p53 weakens the expression of MITF by inhibiting the production of mitoSOX, thus weakening the mitophagy induced by *H. pylori* infection.

Conclusion: *H. pylori* infection regulates mitochondrial oxidative stress through p53, thus mediating MITF to regulate mitophagy in GC.

References:

Disclosure: Nothing to disclose.

P1032

HELICOBACTER PYLORI INFECTION INHIBITS P53 REGULATION OF PGK1-MEDIATED GLYCOLYSIS

J. Rong¹, H. Wang¹, Y. Xie¹
¹The First Affiliated Hospital of Nanchang University, Department of Gastroenterology, Nanchang, China

Contact E-Mail Address: 915939113@qq.com

Introduction: Phosphoglycerate kinase 1(PGK1) is a key enzyme in the glycolysis pathway and is closely related to the development of various cancers. However, the mechanism of PGK1 in gastric cancer (GC) and its relationship with helicobacter pylori (*H. pylori*) infection remain unclear.

Aims & Methods: *H. pylori* positive and negative gastric tissue samples were collected to detect the expression of PGK1. In vitro and in vivo *H. pylori* infection model, the relationship between PGK1 and *H. pylori* was studied. The effects of PGK1 on cell proliferation, invasion, migration and glycolysis were verified by CCK-8 and EdU cell proliferation, colony formation, Transwell and lactic acid detection. The interaction between PGK1 and p53 was determined by immunoprecipitation.

Results: We found that PGK1 was highly expressed in GC tissues compared to adjacent noncancerous tissues. During the progression from mild chronic non-atrophic gastritis to GC, the expression of PGK1 gradually increased in human gastric tissue and was associated with *H. pylori* infection. PGK1 overexpression promotes GC cell proliferation, invasion and migration, whereas PGK1 knockdown inhibits GC cell proliferation, invasion and migration. *H. pylori* infection promotes the entry of PGK1 into mitochondria, up-regulates lactate, ECAR, and down-regulates OCR in GC. PGK1 protein interacts with p53 protein in GC cell. Overexpression of p53 suppressed *H. pylori* infection-induced lactate elevation by reducing PGK1 expression.

Conclusion: This study showed that *H. pylori* infection plays a key role in the development of GC by regulating the expression of PGK1 through p53.

References:

Disclosure: Nothing to disclose.

Poster presentations

Small intestinal

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P0151

APRAGLUTIDE DOES NOT IMPACT ANTI-TUMOR AND IMMUNOSUPPRESSIVE EFFICACY OF CONDITIONING CHEMOTHERAPY IN MICE

V. Dimitriadou¹, B. Biemans¹, N.N. Youssef², M. Minden³

¹VectivBio, Preclinical Development, Basel, Switzerland, ²VectivBio, Basel, Switzerland, ³University of Toronto, Department of Medical Biophysics, Toronto, Canada

Contact E-Mail Address: nader.youssef@vectivbio.com

Introduction: Conditioning chemotherapy reduces tumor burden and provides immunoablation to prevent graft rejection with hematopoietic cell transplantation, but often induces mucosal barrier breakdown and mucositis.

Apraglutide is a novel, long-acting synthetic glucagon-like peptide-2 (GLP-2) analog that has been shown to protect the gastrointestinal (GI) epithelium from chemotherapy-induced injury, improves survival, and allows better weight maintenance in mice undergoing chemotherapy.

Aims & Methods: Preclinical studies aim to evaluate the impact of apraglutide on the efficacy of chemotherapy in reducing tumor load and inducing immunosuppression.

Study 1 assessed cytarabine's antitumor effects in leukemic NOD/SCID mice. Apraglutide or vehicle was administered on Days -4 to 4. Cytarabine or vehicle was administered on Days 0 to 4. Bone marrow and spleen samples were collected on Day 7 for determination of the percentage of hCD45+ cells.

Study 2 assessed the effect of apraglutide on cytarabine-induced immunosuppression and included three groups of BALB/c mice: (A) vehicle-only; (B) cytarabine-only on Days 0 to 4; (C) cytarabine on Days 0 to 4 plus apraglutide pre-treatment on Days -4, -2, and continued as concomitant treatment on Days 0, 3, 6, 9, and 12. Red blood cells, platelets, white blood cells (WBC), neutrophils (NEU), and lymphocytes (LYMPH), were assessed. A cohort was allowed to survive for four weeks to evaluate the effect of apraglutide on immunosuppression recovery.

Study 3 assessed the effect of apraglutide on melphalan-induced immunosuppression. Three groups of BALB/c mice were included: (A) vehicle-only; (B) melphalan-only on Day 0; (C) melphalan on Day 0 plus apraglutide pre-treatment on Days -8, -6, -4, -2, and continued as concomitant treatment on Days 0, 2, 4, and 6. WBC, NEU, and LYMPH were assessed.

Results: Study 1 showed that human leukemia cells reduction did not differ significantly between cytarabine-only and apraglutide-treated groups but were significantly greater when compared to the vehicle-only group. The percentage of hCD45 in bone marrow after chemotherapy was 35.5±4% with cytarabine-only and 33.9±4.2% with apraglutide-treated mice.

A dramatic decrease in leukocytes at the end of the treatment period in Study 2 indicated that cytarabine-induced immunosuppression was not impaired by apraglutide treatment (91% reduction in lymphocytes with both cytarabine-only and apraglutide-treated mice). Apraglutide did not impact the recovery of hematological parameters four weeks after the end of treatment.

Study 3 showed that melphalan elicited immunosuppression as evidenced by leukocyte decrease. Mice treated with melphalan, with or without apraglutide, had severe reductions in WBC and LYMPH vs. vehicle-only.

Conclusion: The addition of apraglutide treatment did not impair the anti-tumor efficacy of cytarabine *in vivo*. Moreover, combination with apraglutide had no negative impact on cytarabine- or melphalan-induced immunosuppression. Apraglutide did not negatively impact the anti-tumor or immunosuppressive effects of chemotherapy.

Disclosure: The study was sponsored by VectivBio and conducted in collaboration with the University of Toronto. V. Dimitriadou and B. Biemans received fee for service as a consultant. N.N. Youssef is an employee of VectivBio.

P0152

QUANTITATIVE MAGNETIC RESONANCE ENTEROGRAPHY SHOWS EVIDENCE OF TREATMENT RESPONSE IN PEDIATRIC SMALL BOWEL CROHN'S DISEASE: A PROSPECTIVE STUDY

J. Dillman¹, A. Menys^{2,3}, J. Tkach¹, L. Denson⁴

¹Cincinnati Children's Hospital Medical Center, Department of Radiology, Cincinnati, United States, ²Motilent, London, United Kingdom, ³University College London, Centre for Medical Imaging, London, United Kingdom, ⁴Cincinnati Children's Hospital Medical Center, Department of Pediatrics, Cincinnati, United States

Contact E-Mail Address: alex.menys@motilent.co.uk

Introduction: There is a diverse and effective range of approaches to the management of Crohn's Disease but matching the patient with the best treatment is dependent on using the appropriate test. This is particularly important in a pediatric population.

Cross sectional imaging is important not just in establishing the location and behavior of the disease but also in grading inflammatory activity. GI-Quant is a recently FDA/CE cleared tool that quantifies bowel wall motion as a biomarker of disease activity based on MR enterography (MRE). It is hypothesized that a positive change in bowel wall motion is an early indicator of mucosal healing (1).

The MRE exam can be routinely performed in the clinic without the need for gadolinium contrast material administration or a spasmolytic (2).

Aims & Methods: The aim of this study was to investigate whether the now commercially available software GIQuant (Motilent, London, UK) could detect therapeutic response in a pediatric population after the initiation of anti-TNFalpha therapy at:

- i. 6-week and,
- ii. 6 month time points.

Secondly, we aimed to explore the inter-reader agreement of the GIQuant score.

20 children and young adults (mean age 14.6) with newly diagnosed ileal Crohn disease underwent research MRI examinations of the small bowel, including dynamic cine imaging (2-images/s 60s scan duration). Patients with Crohn's disease underwent imaging before as well as six weeks and six months after anti-TNF alpha therapy initiation.

Terminal ileal intestinal motility scores (from GIQuant) were generated from cine imaging (2D steady-state free precession) by two blinded operators, with higher GIQuant scores indicating greater intestinal motility.

Linear mixed models were used to assess if intestinal motility scores changed (increased) over time in response to treatment.

Inter-operator absolute agreement was assessed using intra-class correlation (ICC).

Results:

1. Intestinal motility scores changed over time in response to biologic therapy for both operators (operator 1, $p=0.036$; operator 2, $p=0.034$). Intestinal motility scores increased significantly between the baseline and six month visits for both operators (operator 1, $p=0.0065$; operator 2, $p=0.0078$);
2. There was no difference in peristalsis between the six week and six month visits ($p>0.95$ for both operators).
3. There was excellent absolute agreement in intestinal motility scores between operators ($ICC=0.89$).

Conclusion: GIQuant could detect treatment response as early as six weeks post initiation in this pediatric cohort. Interestingly, the six week and six month observation was non-significantly different (although both were from baseline), however there was a large amount of variation in the group.

The next question is, what do we do with this information?

Recent observations from the STARDUST (3) study suggested that endoscopy performed earlier (16 weeks) with corresponding therapeutic adjustment did not improve outcomes over standard practice and it may prove to be the same with transmural measures of small bowel disease.

Regardless, the change at 6 months suggests the importance of earlier follow-up than one year given the breadth of therapeutic options. Strong inter-reader agreement is reassuring and GIQuant needs neither nor gadolinium or spasmolytic potentially improving patient compliance.

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Disclosure: Alex Menys is CEO and shareholder in Motilent.

P0153

ANALYSIS OF BLOOD AND FECAL INTESTINAL MICROBIOTA FOCUSING ON ENDOTOXIN IN PATIENTS WITH CHRONIC IDIOPATHIC INTESTINAL-PSEUDO OBSTRUCTION

T. Ogata¹, T. Jono¹, K. Tanaka^{1,2}, K. Takahashi¹, T. Kobayashi¹, T. Kessoku^{1,2}, A. Fuyuki¹, H. Ohkubo¹, A. Nakajima¹

¹Yokohama City University Graduate School of Medicine, Gastroenterology and Hepatology, Yokohama, Japan, ²Yokohama City University Graduate School of Medicine, Palliative Medicine, Yokohama, Japan

Contact E-Mail Address: tomo1993baske@gmail.com

Introduction: Chronic Idiopathic Intestinal-pseudo Obstruction (CIIP) is a severe, rare gastrointestinal intractable disease. Hyperendotoxemia has been reported to be associated with infections, fatigue, and depression, but the association between CIIP patients and endotoxin remains unclear. The purpose of this study was to investigate and fecal intestinal microbiota with a focus on endotoxin in CIIP patients.

Aims & Methods: Fecal and blood samples were collected from 10 CIIP patients who were not taking antibiotics, had not undergone surgery, and whose diagnosis was confirmed by cine MRI, as well as from 15 healthy

subjects (HC). Intestinal flora analysis was performed at the phylum and genus level using next generation sequencing. Diversity analysis was performed using the Shannon index. Endotoxin-producing bacteria were defined as the genera *Gemmiger*, *Bacteroides*, *Escherichia/Shigella*, *Akkermansia*, and *Klebsiella*. Peripheral blood endotoxin was measured using endotoxin activity assay.

Results: At the phylum level, Firmicutes (83% vs. 62%, $p<0.05$ CIIP vs HC), Proteobacteria (7.3 vs. 2.9%, $p<0.05$), Verrucomicrobia (10.1% vs. 0.4%, $p<0.05$) and Fusobacteria (3.1% vs. 0%, $p<0.05$) were significantly increased in CIIP patients compared to HC.

At the genus level, *Lactobacillus* (28.8% vs 0.1%, $p<0.01$) and *Akkermansia* (9.2% vs 0.4%, $p<0.05$) were significantly increased; *Blautia* (8% vs 26%, $p<0.001$), *Lachnospiraceae_incertae_sedis* (4% vs 13%, $p<0.001$), *Faecalibacterium* (2% vs 11%, $p<0.001$), *Rosebria* (1% vs 7%, $p<0.01$) and *Collinsella* (0.1% vs 1.7%, $p<0.001$) were significantly decreased in CIIP patients compared to HC.

In addition, endotoxin-producing bacteria in stool were significantly increased in CIIP patients, and blood endotoxin levels were significantly elevated in CIIP patients (0.26 vs 0.08, $p<0.001$).

Conclusion: The present study suggests that increased of endotoxin-producing bacteria may be the cause of the abnormal endotoxemia, and that treatment of CIIP patients with a focus on endotoxin may provide a new approach to reduce infectious deaths and alleviate symptoms.

Disclosure: Nothing to disclose.

P0154

THE DIAGNOSTIC CAPABILITIES OF NON-INVASIVE FECAL BIOMARKERS OF NSAID-INDUCED INTESTINAL LESIONS IN PATIENTS WITH OSTEOARTHRITIS

O. Gubska¹, A. Kuzminets¹

¹Bogomolets National Medical University, Therapy, Infectious Diseases and Dermatology Postgraduate Education, Kyiv, Ukraine

Contact E-Mail Address: andrewkuzminets@gmail.com

Introduction: Osteoarthritis (OA) is a common disease among the population, especially the elderly, requiring frequent nonsteroidal anti-inflammatory drugs (NSAIDs), which are harmful to the upper and lower parts of the gastrointestinal tract.

Aims & Methods: To analyze the diagnostic possibilities of non-invasive fecal biomarkers of NSAID-induced intestinal lesions in patients with OA and to check the possibility of predicting the presence of such lesions based on fecal biomarkers.

We investigated 91 patients with OA of different localizations and degrees (then divided into three subgroups depending on NSAIDs use and their selectivity) and 30 people without OA as a control group (CG). We studied the following fecal biomarkers: calprotectin (FC), secretory immunoglobulin A (sIgA), and hemoglobin/haptoglobin (Hb/Hp) complex (ELISA method).

Results: The FC content in OA patients was significantly higher than in CG (147.19 (IQR 132.76-161.8) mg/kg vs 20.91 (IQR 19.5-32.53) mg/kg ($p<0.001$). It was 68.78 (IQR 61.48-90.3) mg/kg in those not taking NSAIDs, 259.65 (IQR 234.67-294.99) mg/kg in those taking non-selective and 111.93 (IQR 105.31- 149.63) mg/kg in those taking selective NSAIDs.

We found a significant difference between all 3 subgroups from the CG ($p<0.01$). NSAIDs subgroups differed from the "non-NSAIDs" ($p<0.01$). In "non-NSAIDs" subgroup patients, the moderately elevated (50-200 mg/kg) level of FC was significantly more common than in CG (OR = 4.92; 95% CI 1.273-23.965; $p=0.0012$); non-selective NSAIDs subgroup had a significantly higher prevalence of elevated (>200 mg/kg) FC than in "non-NSAIDs" subgroup.

Hb/Hp complex content in CG was 0.73 (IQR 0.65-0.79) mg/kg vs 4.77 (IQR 3.41-6.81) mg/kg in the OA group. In OA-“non-NSAIDs” - 1.88 (IQR 1.23-2.6) mg/kg, non-selective-NSAIDs - 9.38 (IQR 7.47-13.29) mg/kg and in selective NSAIDs - 2.98 (1.34-4.62) mg/kg. OA-non-selective-NSAIDs differed significantly from CG and “non-NSAIDs”. The OA-selective-NSAIDs differed from the non-selective and CG ($p < 0.05$). OA patients had elevated Hb/Hp complex while in the CG it was not elevated in all cases. OA-non-selective-NSAIDs had elevated levels of Hb/Hp complex significantly more frequent than CG ($p < 0.001$) and “non-NSAIDs” (OR=4.229; 95% CI 1.288-15.289; $p < 0.001$).

SIgA content differed in OA patients from the CG (1088.83 (IQR 986.0-1.291.25) mg/kg vs 593.57 (IQR 549.0-761.91) mg/kg, $p < 0.01$), but not in subgroups ($p > 0.05$).

The developed logistic model allows to predict the risk of NSAID-induced intestinal lesions. It looks like $\ln(P/(1-P)) = -2.168 + 0.2986 \cdot (\text{Hb/Hp}) + 0.0083 \cdot \text{FC}$. AUC of the model is 0.872 (95% CI 0.773 - 0.97), $p < 0.05$; the optimal threshold = 0.987.

At the chosen threshold, the sensitivity of the model is 65% (95% CI 40.8% - 84.6%), specificity 90% (95% CI 73.5% - 97.9%), Positive Predictive Value - 81.2% (95% CI 54.4 - 96), Negative Predictive Value - 79.4% (95% CI 62.1 - 91.3).

Conclusion: The NSAID enteropathy manifests in increased FC and Hb/Hp complex content. Our model can predict such lesions. These markers are slightly increased in OA patients even if they do not take NSAIDs. SIgA content is not affected by NSAIDs intake.

Disclosure: This study was partly funded by R-Biopharm AG, Darmstadt, Germany, by supplying the reagent kits for FC and SIgA determination.

P0155

A PHASE 1, OPEN-LABEL EVALUATION OF THE PHARMACOKINETICS AND SAFETY OF A SINGLE DOSE OF APRAGLUTIDE IN SUBJECTS WITH NORMAL AND IMPAIRED RENAL FUNCTION

G. Greig¹, D. Cong², N. Hurley¹, E. Michel¹, N.N. Youssef¹

¹VectivBio, Basel, Switzerland, ²ICON PRA Health Sciences, Biostatistics, Dublin, Ireland

Contact E-Mail Address: nader.youssef@vectivbio.com

Introduction: Patients with intestinal failure associated with short bowel syndrome (SBS-IF) have an increased risk of complications, including renal dysfunction. With currently available glucagon-like peptide 2 (GLP-2) therapy, dosage adjustments are recommended for patients with moderate and severe renal impairment and end-stage renal disease. Apraglutide has unique pharmacokinetic (PK) and pharmacodynamic (PD) properties, with preclinical studies indicating low clearance, slow absorption, and high protein binding resulting in a longer half-life than subcutaneously injected native GLP-2 and other GLP-2 analogs. Apraglutide is degraded into small peptides and amino acids via catabolic pathways, similar to endogenous GLP-2.

Previous preclinical PK and metabolism trials showed no intact parent compound (apraglutide) was found in urine, suggesting renal elimination does not play a significant role in apraglutide removal.

Aims & Methods: This Phase 1, non-randomized, open-label, parallel-group trial evaluated the PK and tolerability of a single dose of subcutaneous apraglutide 5 mg in subjects with renal impairment and healthy volunteers matched for age and body weight.

Part 1 assessed subjects with severe renal impairment (eGFR < 30 mL/min/1.73 m² not on hemodialysis) and subjects with normal renal function (eGFR ≥ 90). According to plan, the study was stopped after completion of Part 1 because exposure of subjects with severe renal impairment was not greater than that of healthy subjects.

Results: Eight subjects with severe renal impairment and eight healthy matched subjects were enrolled and completed the study. There was no apraglutide overexposure in subjects with severe renal impairment compared to the healthy subjects. The geometric mean renal/healthy ratio was AUC_{inf} (0.693) and C_{max} (0.620). Three out of eight (37.5%) subjects with severe renal impairment reported 7 AEs, and 2/8 (25%) subjects with normal renal function reported 3 AEs. All AEs had resolved at the end of the study. The investigators considered 5 AEs related to apraglutide; all were reported by the subjects with severe renal impairment (1 increased alanine transaminase; 2 nausea and emesis; 1 erythematous papule; 1 ecchymosis at the injection site). The treatment-related AEs do not differ from those reported to date in other apraglutide clinical studies. No serious AE or death was reported. No clinically relevant changes within groups or differences between groups were observed over time in clinical chemistry, hematology, urine, or other safety parameters. No relevant changes in vital signs (blood pressure, heart rate, and body temperature) or ECGs occurred from screening to follow-up.

Conclusion: Exposure to apraglutide in subjects with severe renal impairment is not increased compared to healthy subjects. A single dose of 5-mg apraglutide in subjects with severe renal disease and healthy matched subjects was well-tolerated, and no unexpected safety issues were raised. The study results are clinically significant as 28% of patients with SBS-IF have renal impairment (Wang P et al. 2021) and may not be candidates for treatment with currently available GLP-2, which requires dose adjustment. By contrast, apraglutide dose adjustments are not necessary for subjects with renal impairment.

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Disclosure: The study was sponsored by VectivBio. N. Hurley and N. Youssef are employees of the study sponsor. G. Greig and E. Michel received fee for service as consultants who designed and oversaw the conduct of the study.

P0156

NATURAL HISTORY OF CHRONIC INTESTINAL PSEUDO-OBSTRUCTION AND NEED FOR PALLIATIVE CARE

K. Tanaka^{1,2}, H. Ohkubo^{2,3}, A. Yamamoto², Y. Takeda¹, K. Takahashi², Y. Kasai², A. Ozaki², M. Iwaki², T. Kobayashi², T. Yoshihara², N. Misawa², A. Fuyuki², S. Kato⁴, T. Higurashi², K. Hosono², M. Yoneda², K. Takeo⁵, M. Taguri⁶, N. Kobayashi⁷, Y. Ichikawa⁷, A. Nakajima², T. Kessoku²

¹Yokohama City University Hospital, Palliative Medicine, Yokohama, Japan, ²Yokohama City University Hospital, Gastroenterology Division, Yokohama, Japan, ³Toshiba Rinkan Hospital, Gastroenterology, Sagami, Japan, ⁴Yokohama City University Hospital, Clinical Cancer Genomics, Yokohama, Japan, ⁵Kanagawa Dental University Yokohama Clinic, Internal Medicine, Yokohama, Japan, ⁶Yokohama City University Graduate School of Medicine, Data Science, Yokohama, Japan, ⁷Yokohama City University Hospital, Oncology, Yokohama, Japan

Contact E-Mail Address: kosuke.tssik@gmail.com

Introduction: The natural history of chronic intestinal pseudo-obstruction (CIPO), a rare disease characterized by episodes of non-mechanical obstruction, is unclear in adults.

Aims & Methods: This study evaluated the clinical course of CIPO and palliative care needs. From April 2011 to March 2021, 74 patients who underwent cine magnetic resonance imaging, and had a definitive diag-

nosis were prospectively included. We investigated the disease etiology and outcomes, age of onset, nutritional status at consultation (body mass index [BMI], serum albumin), hydrogen breath test (HBT) results, and total parenteral nutrition (TPN) during the disease course.

Results: Forty-seven patients (64%) were women, with mean ages of 44 and 49 years at onset and diagnosis, respectively. Primary CIPO was observed in 48 patients (65%). Secondary CIPO was observed in 26 cases (35%); among them, 18 (69%) had scleroderma. The mean BMI, serum albumin, and HBT positivity rate were 17 kg/m², 3.8 mg/dL, and 60%, respectively. TPN management and invasive decompression therapy were performed in 23 (31%) and 18 (24%) patients, respectively. Intestinal sterilization was performed in 51 (69%) patients and was effective in 33 (65%); of these, 28 (85%) were taking metronidazole. Seven (9%) patients used opioids. There were nine deaths (12%), including five (56%) from infection and two (22%) from suicide. Of the deaths, six (67%) and four (44%) underwent TPN management and decompression therapy, respectively. Fifty-one patients (69%) needed palliative care.

Conclusion: CIPO is a rare, severe, and unrecognized disease. Standardization of treatment strategies, including palliative care and psychiatric interventions, is warranted.

Disclosure: Nothing to disclose.

P0157

EFFICACY AND SAFETY OF RIFAXIMIN FOR PATIENTS WITH CHRONIC INTESTINAL PSEUDO-OBSTRUCTION: A RANDOMIZED, DOUBLE-BLIND, PLACEBO-CONTROLLED, PHASE 2A TRIAL

T. Kessoku^{1,2}, H. Ohkubo^{1,3}, T. Ogata¹, T. Jono¹, K. Tanaka^{1,2}, K. Takahashi¹, A. Yamamoto¹, T. Takatsu¹, T. Yoshihara¹, N. Misawa¹, K. Ashikari¹, A. Fuyuki^{1,2}, T. Higurashi¹, T. Misumi⁴, S. Shinoda⁴, Y. Horikoshi⁵, E. Misugi⁵, H. Asuke⁶, K. Miyazawa⁶, I. Sato⁶, A. Nakajima¹

¹Yokohama City University Graduate School of Medicine, Gastroenterology and Hepatology, Yokohama, Japan, ²Yokohama City University Hospital, Palliative medicine, Yokohama, Japan, ³Toshiba Rinkan Hospital, Gastroenterology, Yokohama, Japan, ⁴Yokohama City University School of Medicine, Department of Biostatistics, Yokohama, Japan, ⁵Yokohama City University Hospital, Research and Development Support Section, YCU Center for Novel and Exploratory Clinical Trials (Y-NEXT), Yokohama, Japan, ⁶ASKA Pharmaceutical Co., Ltd., Medical Affairs, Tokyo, Japan

Contact E-Mail Address: takaomi0027@gmail.com

Introduction: Chronic intestinal pseudo-obstruction (CIPO) is a rare intractable gastrointestinal disease which decreases quality of life. CIPO is caused by the stagnation of intestinal contents and small intestinal bacterial overgrowth (SIBO); this occurs mainly in the small intestine, due to decreased gastrointestinal peristalsis. If this condition worsens, it becomes a serious intractable disease that leads to nutritional disorders caused by small intestinal insufficiency, and bloodstream infections (sometimes fatal) due to the breakdown of barrier function (1).

SIBO is recognized in CIPO regardless of the origin (idiopathic or secondary). SIBO has been reported as a complication in 43% of systemic sclerosis patients, (2) regardless of the presence of CIPO. Rifaximin-a (RFX) is a rifamycin antibacterial agent that exhibits antibacterial activity against gram-positive, gram-negative, aerobic, and anaerobic bacteria by inhibiting bacterial RNA synthesis.

In addition, it is absorbed minimally even when administered orally, and acts mainly in the gastrointestinal tract. Therefore, this drug is localized in the gastrointestinal tract, and is expected to be an effective drug for treating SIBO.

Aims & Methods: The aim of this study to evaluate the efficacy and safety of RFX in patients with CIPO. This randomized, double-blind, placebo-controlled, phase 2a study (ClinicalTrials.gov; NCT04118699) recruited adult patients with CIPO (idiopathic CIPO and CIPO secondary to systemic sclerosis), and those with ≥ 2 abdominal bloating as per the Global Symptom Score (GSS). GSS is defined on a scale of 0-3, with 0 being no symptoms and 3 being severe. Eligible patients were randomly assigned (2:1) to receive oral RFX (400 mg thrice daily) or placebo (PBO) for four weeks.

The primary endpoint was percent improvement in the GSS-abdominal distension score (score 0 or 1); an objective index, the volume in the small intestine was measured using CT. Small intestinal bacterial overgrowth (SIBO) was diagnosed with a glucose hydrogen breath test. Blood endotoxin was measured by endotoxin activity assay. Gut microbiota measurements were performed by illumina Miseq. Efficacy analysis was performed by full set analysis. This trial was registered with ClinicalTrials.gov; NCT04118699.

Results: Between November 26, 2019 and May 24, 2021, 15 patients were screened; 12 eligible patients were assigned to the RFX group (n=8) or the placebo group (n=4). The rate of improvement in abdominal distension score (GSS) was 75% (3/4 patients, 95% CI: 19-99) in the PBO group and 25% (2/8, 95% CI: 3-65) in the RFX group (p=0.2).

There was no significant difference in the absolute change in small intestinal volume and the SIBO disappearance rate, between groups. There were no significant changes in intestinal bacteria before and after medication between the two groups. In CIPO with SIBO alone, the SIBO disappearance rate decreased in the RFX group (RFX: 3/4 (75%), PBO: 1/4 (25%), p=0.15). The absolute change in the hydrogen concentration from the baseline to the maximum value in the HBT was significantly lower in the RFX group than that in the PBO group (PBO vs. RFX, 131 vs. -108, p=0.03). The CT gas volume and blood endotoxin level also tended to decrease in the RFX group (CT gas volume: PBO vs. RFX, 79 vs. -7, p=0.08; endotoxin activity: PBO vs. RFX, 0.02 vs. -0.12, p=0.08). No life-threatening events, severe adverse events, or treatment-related deaths occurred during the study.

Conclusion: RFX is safe for CIPO and may potentially reduce small intestinal gas volume and hydrogen gas concentration in CIPO patients.

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Disclosure: Nothing to disclose.

P0158

EVALUATION OF INTESTINAL PERMEABILITY TESTING AS BIOMARKER FOR ADAPTIVE RESPONSE IN SHORT BOWEL SYNDROME

J. Büttner¹, S. Pevny¹, E. Blüthner¹, B. Bochow-Fitzner¹, S. Naranjo¹, D. Thurmman¹, M. Saegbarth¹, S. Maasberg², C. Jochum¹, F. Tacke¹, U.-F. Pape^{2,1}

¹Charité-Universitätsmedizin Berlin Campus Mitte, Medical Department, Division of Hepatology and Gastroenterology, Berlin, Germany, ²Asklepios Medical School Hamburg, Department of Internal Medicine and Gastroenterology, Hamburg, Germany

Contact E-Mail Address: janine.buettner@charite.de

Introduction: The human intestinal tract reacts to extensive resection with spontaneous intestinal adaption. Therapy with GLP-2 analogues (GLP-2-A) enhances intestinal adaption by promoting mucosal growth and intestinal absorption. Clinical response to GLP-2-A treatment is characterized by a

significant reduction in parenteral volume or calorie demands but varies widely. Currently there are no biomarkers available to predict either spontaneous intestinal adaption or response to GLP-2-A therapy nor to assist with clinical management of GLP-2-A.

In addition, the mechanisms in intestinal barrier regulation of intestinal permeability (IP) during adaptive response or therapy are not well understood. We analyzed whether measurement of IP is a useful biomarker to describe the regulation mechanisms in the intestinal barrier in patients with Short Bowel Syndrome (SBS) with or without GLP-2-A.

Aims & Methods: IP was assessed using a sugar drink test containing lactulose (Lac), mannitol (Man) and sucrose (Sac). Urinary recovery rate of each sugar was analyzed by HPLC analysis. Clinical data were collected for remaining small bowel length, PN requirements, and therapy with GLP2-A.

Results: SBS patients showed increased Lac/Man ratio compared to controls, (n= 24/14, p=0.0004). Man recovery was decreased in SBS (mean SBS 4.3% vs. controls 10.7%, p= 0.00011), whereas LAC recovery was similar to controls (mean SBS 0.18% vs. controls 0.22%, p= 0.32). Gastroduodenal permeability (Sac recovery) was similar to controls (mean SBS 0.14 % vs controls 0.11 %, p=0.73).

For Man recovery, a positive correlation with the remaining small bowel length was found ($r^2 = 0.408$, p=0.004 (SBS wo GLP-2) while Lac recovery showed less correlation ($r^2=0.24$, p=0.041). No correlation was found for Sac recovery ($r^2=0.023$, p=0.55).

Man recovery was elevated in patients treated with GLP-2-A compared to therapy naïve patients (wo GLP-2 4.28% vs. with GLP-2 therapy 6.68%; Δ Man recovery 56%). Lac recovery showed only minor changes (wo GLP-2 0,175 % vs. with GLP-2 therapy 0,197%; Δ Lac recovery 12%). Sac recovery showed no changes (0.138% vs 0.135%)

An inverse correlation were found for Man recovery and parenteral nutrition requirements [kcal per week] ($r^2= 0.273$, p=0.01). No relation was found for Lac recovery ($r^2=0.09$, p=0.16) or Sac recovery ($r^2=0.003$, p=0.81).

Conclusion: Intestinal permeability testing based on sugar recovery in urine samples is applicable in SBS patients, but results have to be interpreted with caution as the mere use of the widely accepted marker "Lac/ Man ratio" leads to misleading results. In SBS patients, mannitol recovery correlates with remaining small bowel length and caloric i.v. needs and recovery rate in patients with GLP-2 treatment is higher compared to therapy naïve patients.

Therefore, we suggest that mannitol may serve as biomarker in order to gain additional information about absorptive processes or changes during GLP-2 therapy.

Disclosure: Nothing to disclose.

P0159

IMPACT OF FOOD INTAKE ON THE EFFICACY OF TEDUGLUTIDE TREATMENT IN ADULT PATIENTS WITH SHORT BOWEL SYNDROME

B. de Dreuille^{1,2}, C. Hutinet³, J. Bettolo³, C. Mailhat⁴, Y. Bouhnik², M. Le Gall¹, A. Bado¹, F. Joly^{1,2}

¹INSERM, UMR 1149, Paris, France, ²Hôpital Beaujon, Assistance Publique-Hôpitaux de Paris, Gastroenterology, IBD and Nutritional Support Department, Paris, France, ³Hôpital Beaujon, Assistance Publique-Hôpitaux de Paris, Dietetics Department, Paris, France, ⁴GETAID, Paris, France

Contact E-Mail Address: brune.de-dreuille@inserm.fr

Introduction: Teduglutide (TED), a GLP-2 agonist, is effective to reduce Parenteral Nutrition (PN) dependence in patients with Short Bowel Syndrome (SBS), with some heterogeneity of response between patients. PN reduction at 6 months of TED treatment is significantly associated with patients' oral intake at baseline (1).

Aims & Methods: We aimed to study the impact of food intake on TED efficacy in the longer term and the evolution of food intake during treatment. This work was a monocentric retrospective study conducted in an expert center of PN. We enrolled 49 SBS patients treated with TED for at least one year. Information regarding oral food intake and PN prescription at the time of initiation and during treatment were collected in medical charts. Food intake is expressed using a ratio: FIR = Daily caloric intake (kcal) / Resting Energy Expenditure (REE) (kcal). REE is calculated using Harris and Benedict formula.

Results: Baseline food intake at treatment initiation was collected for 49 patients, and at least two values of food intake during treatment were available for 44 of these patients. The mean follow-up duration of the patients is 27 months (± 2.8).

There is a positive correlation between food intake at treatment initiation and reduction of PN volume during treatment ($r=0.38$, p=0.007). Moreover, patients who reached PN weaning with TED (n=19) had a much higher food intake before TED than those who remained dependent to PN (n=30), p<0.001 (FIR=2.3 vs 1.6). These 19 weaned patients were all hyperphagic (FIR>1.5) before TED initiation.

In addition, patients who had the lowest food intake before TED initiation (non-hyperphagic, FIR<1.5, n=13) significantly increased their oral intake during treatment (p=0.001, FIR=1.0 vs 1.6).

Those who presented hyperphagia before TED maintained their oral intake.

Conclusion: This study confirms the positive impact of basal oral dietary intake on the efficacy of TED in the long term, which supports the idea of promoting food intake in SBS patients before TED initiation. Furthermore, treatment with TED seems to have a beneficial effect on patients' food intake when it was low before TED initiation, which could be linked with the better physical and/or psychological condition of the patients.

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P0160

HOW LONG-TERM PROTON PUMP INHIBITOR THERAPY AFFECTS THE GUT MICROBIOTA - A SINGLE-CENTER EXPERIENCE

D. Salvi^{1,2}, F. di Pierro¹, S. Piccirelli^{1,2}, V. Gerardi¹, C.L. Pugliano¹, C. Spada^{1,2}

¹Fondazione Poliambulanza Istituto Ospedaliero, Brescia, Italy,

²Fondazione Policlinico Universitario Agostino Gemelli IRCCS, Roma, Italy

Contact E-Mail Address: danielle.salvi@poliambulanza.it

Introduction: Proton Pump Inhibitors (PPI) are clinically used to treat gastroesophageal reflux disease and peptic ulcers. 4-8 weeks usage of PPI can be defined as PPI-long term use. Patients with PPI-long term use show hypochlorhydria and small intestine bacterial overgrowth (SIBO), reporting bloating as the main symptom.

Aims & Methods: The aim was to characterize the gut microbiota of patients under long-term PPI treatment and to assess if there was a signature of SIBO. The gut microbiota of 152 patients referred to Gastroenterology outpatient clinic was stratified based on PPI treatment [n=43 PPI-on, n=109 PPI-off]. A sub-analysis was performed considering only patients without probiotics-intake at the time or 3 months before stool sample [n=31 PPI-on, n=82 PPI-off]. Phyla and taxa were analyzed using 16S ribosomal RNA (rRNA) sequencing.

Comparisons between two groups were made using the normal approximation for the Wilcoxon two-sample test and statistical significance was defined as a p -value < 0.05 .

Results: Compared to PPI-off patients, PPI users demonstrated a lower richness ($p < 0.05$, 95% CI) and significant increased abundances for some taxa either frequently observed in oral microbiota or belonging to Proteobacteria like *Lactobacillus* ($p < 0.005$), *Lactococcus* ($p < 0.05$), *Streptococcus* ($p < 0.005$), *U. m. of Coriobacteriaceae* ($p < 0.005$) *Hafnia* ($p < 0.05$) and *Butyrivimonas* ($p < 0.005$). Other taxa demonstrated significant lower values (Table 1). Out of 43 patients treated with PPI, 29 reported bloating as the main symptom. Moving to the analysis on probiotic-free patients, a statistically significant increase of the same taxa was confirmed.

Taxa	Mean +/- SD PPI off	Mean +/- SD PPI on	p value
<i>Desulfovibrio</i>	0,0014146 +/- 0,0025685	0,0009511 +/- 0,0021916	0,0314
<i>Lachnospira</i>	0,0157966 +/- 0,0245135	0,0063728 +/- 0,0093963	0,0194
<i>Sutturella</i>	0,011324 +/- 0,0134658	0,0057433 +/- 0,0073252	0,0209
<i>Turicibacter</i>	0,0006922 +/- 0,0023865	0,0003446 +/- 0,0009684	0,0471

Table 1. Specific mean score for each taxa analyzed with Wilcoxon/Kruskal-Wallis two-sample test decreased in PPI on patients.

[SD: standard deviation.]

Conclusion: Long-term PPI treatment has an important impact on patients' gut microbiota and might worsen bloating symptoms. As already reported, PPI users show an increase in oral bacteria especially Lactobacillales. Due to the possible link existing between bloating, dysbiosis, and PPI use, intercepting subjects with this signature can lead to a PPI reduction, if possible, and/or the administration of antibiotics to reduce SIBO related symptoms.

Disclosure: Nothing to disclose.

P0161

SMALL INTESTINAL BACTERIAL OVERGROWTH (SIBO) IS ASSOCIATED WITH LIVER FIBROSIS AND INFLAMMATION

J. Keller¹, A. Bornhorst¹, S. Rose¹, V. Andresen¹, P. Layer¹

¹Israelitisches Krankenhaus Hamburg, Department of Medicine, Hamburg, Germany

Contact E-Mail Address: j.keller@ik-h.de

Introduction: In patients with non-alcoholic steatohepatitis (NASH), bacterial translocation from the gut lumen contributes to progression of liver steatosis, inflammation and fibrosis (Schnabl&Brenner 2014, Ghoshal et al. 2020). Studies indicate that bacterial translocation may occur predominantly in the small bowel, so that small intestinal bacterial overgrowth (SIBO) may be of particular pathophysiological relevance (Bruns et al. 2016).

Indeed, patients with NASH and patients with significant fibrosis were shown to have a significantly increased incidence of SIBO (Mikolasevic et al. 2021). It is unclear, however, whether patients with SIBO are generally at an increased risk of developing liver injury.

Aims & Methods: We aimed to investigate whether SIBO is associated with increased liver fibrosis or other signs of liver injury. Therefore, patients with unclear gastrointestinal symptoms compatible with SIBO (abdominal pain, bloating, diarrhea) underwent a standardized glucose-H₂-breath test (Keller et al. 2005, Hammer et al. 2021) as part of their diagnostic work-up. An increase in H₂-exhalation by ≥ 20 ppm was regarded as diagnostic of

SIBO (SIBO++), an increase between 10 and 19 ppm as suggestive (SIBO+). Patients with < 10 ppm increase in H₂-exhalation served as controls (SIBO-). Patients additionally underwent shear wave elastography for quantification of liver fibrosis (SWE), investigation of liver fat content (attenuation imaging, ATI) and of a parameter of liver inflammation (shearwave dispersion, DISP) using the Liver Analysis Tool (LAT, Canon). Demographic data and clinical data on preexisting liver injury and predisposing diseases (e.g. diabetes mellitus, hyperlipoproteinemia) were collected.

Results: 131 patients (95 females) were included. Their mean age was 43.5 $\pm$ 16.5 years, median BMI was 21.3[19.5-25.0]kg/m². 51 subjects were SIBO positive (SIBO++), 31 probably had SIBO (SIBO+, increase in H₂ ≥ 10 ppm), 49 were SIBO negative (SIBO-). Sex distribution, BMI and proportion of patients with preexisting liver injury or predisposing diseases were similar in all groups, however, SIBO++ were about 10 years older than SIBO+ and SIBO- patients ($p = 0.003$).

Data obtained by LAT showed significant differences between groups for SWE ($p = 0.043$). SIBO++ had significantly higher values than SIBO-; for SIBO+ we observed a trend towards higher values in comparison with SIBO- (tab.). For DISP and ATI, respectively, there was a trend towards higher values compared with SIBO-, if SIBO++ and SIBO+ were combined ($p < 0.067$).

According to multiple linear regression analysis, SIBO is a significant predictor of SWE ($R = 0.35$, $p < 0.001$) and DISP ($R = 0.31$, $p = 0.004$), independent of age, sex, BMI and preexisting liver injury or predisposing diseases.

	SWE, kPa	DISP, (m/s)/kHz	ATI, dB/cm/MHz
SIBO- (N=49)	4.2 [3.7-5.1]	11.8 [10.3-12.5]	0.54 [0.50-0.6]
SIBO+ (N=31)	4.9 [4.3-5.6] [§]	12.4 [11.0-13.4]	0.56 [0.53-0.59]
SIBO++ (N=51)	4.8 [4.1-5.8] [*]	11.9 [10.6-13.8]	0.57 [0.53-0.62]

^{*} $p = 0.015$ vs SIBO-, [§] $p = 0.092$ vs SIBO-

Table.

Conclusion: Patients with SIBO had increased liver fibrosis compared with controls, independent of known risk factors for liver fibrosis. This could be due to inflammatory processes induced by increased hepatic delivery of toxic bacterial metabolites and/or components, the more so as SIBO was also associated with increased shear wave dispersion, which is assumed to be a marker of liver inflammation. However, the exact clinical role of this parameter still remains to be elucidated.

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P0162

CLINICAL CHARACTERISTICS OF PATIENTS REFERRED FOR SUSPECTED SMALL INTESTINE BACTERIAL OVERGROWTH EVALUATED WITH BREATH TEST

E. Lastiri¹, A. Palacios¹, L. Alcala¹, J. Serra²

¹University Hospital Vall d'Hebron, Department of Gastroenterology, Department of Medicine, Universitat Autònoma de Barcelona, Barcelona, Spain, ²University Hospital Vall d'Hebron, Digestive System Research Unit, Barcelona, Spain

Contact E-Mail Address: lastiriernesto@hotmail.com

Introduction:

Small intestine bacterial overgrowth (SIBO) symptoms frequently overlap with the digestive symptoms seen in functional digestive disorders, especially irritable bowel syndrome. The most widely diagnostic method used to diagnose SIBO is breath test (BT) with hydrogen (H₂) and methane (CH₄) exhaled evaluation.

Aims & Methods:

Aims: To describe the clinical characteristics of patients referred for evaluation of suspected SIBO and to determine if there are clinical differences between SIBO positive vs SIBO negative and the different subtypes of SIBO (SIBO-H2 and SIBO-CH4).

Methods: Consecutive patients referred for glucose BT for suspected SIBO from september 2021 to february 2022 were invited to participate; all the participants completed validated questionnaires for digestive symptoms and the IBS severity score. Demographic and clinical data was obtained from the electronic records.

Results:

	SIBO-H2 n=9	SIBO-CH4 n= 12	p Value
Age in years (range)	60.92 ± 14.65 (50)	49.93 ± 15.85 (55)	
Sex - n (%)			
Male	4 (44.4)	3 (25.0)	0.31
Female	5 (55.6)	9 (75.0)	0.37
Current smoking - n (%)	8 (88.9)	10 (83.3)	0.61
Abdominal surgery history - n (%)	6 (66.7)	2 (11.8)	0.006
Systemic disease associated with SIBO - n (%)			
Systemic sclerosis	0 (0)	4 (23.5)	0.003
Diabetes mellitus	2 (22.2)	1 (8.3)	
Multiple sclerosis	0 (0)	0 (0)	
Postprandial symptoms - n (%)	3 (33.3)	10 (83.3)	0.03
Usual stool pattern (Bristol Stool Chart) - n (%)			
Type 1	2 (22.2)	6 (50.0)	0.20
Type 2	1 (11.1)	3 (25.0)	0.41
Type 3	0 (0)	6 (50.0)	0.02
Type 4	3 (33.3)	3 (25.0)	0.52
Type 5	2 (22.2)	5 (41.7)	0.32
Type 6	6 (66.7)	3 (25.0)	0.07
Type 7	5 (55.6)	1 (8.3)	0.03

Table. Demographic and Clinical Characteristics of patients with a breath test compatible with SIBO (n=21)

123 patients participated in the study (78.9% were female, 52.5± 16.1 years). A total of 26 (21.1%) patients had a BT compatible with SIBO (SIBO-H2 11.4%, SIBO-CH4 13.8% and SIBO-Mixed 4.1%). There were no clinical differences between patients with a positive test and patients with a negative test.

Comparing the clinical characteristics between the different subtypes of SIBO (table 1), patients with SIBO-CH4 had a higher prevalence of systemic sclerosis (23.5% vs 0% p=0.003) and presented more postprandial symptoms (83.3% vs 33.3% p =0.03). SIBO-H2 patients had a higher prevalence of past gastrointestinal surgery (66.7% vs 11.8% p= 0.006) and more frequent loose stools pattern (Bristol 6 - 7) (66.7% vs 25.0% p=0.07).

Conclusion: In our study, symptoms of patients with SIBO diagnosed by a positive BT and patients with a negative test are non specific. Comparing SIBO subtypes, The SIBO-CH4 subtype is associated with postprandial symptoms and SIBO-H2 is associated with loose stools.

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P0163

CLINICAL EFFECTIVENESS OF GLUTEN IMMUNOGENIC PEPTIDES DURING FOLLOW-UP OF CELIAC DISEASE

I. Latras Cortés¹, M. Cid Martínez², S. Diez Ruiz¹, V. Blázquez Ávila¹, I. González Puente¹, L. Alcoba Vega¹, R. González Núñez¹, A. Martín Izquierdo¹, S. Borrego Rivas¹, L. Vaquero Ayala¹, A.B. Domínguez Carballo¹, D. López Cuesta¹, S. Vivas Alegre¹, F. Jorquera Plaza¹

¹University Hospital of León, Department of Gastroenterology, León, Spain, ²University of Salamanca, Salamanca, Spain

Contact E-Mail Address: irenelatrascortes@gmail.com

Introduction: Gluten-free diet is the only therapy that provides clinical and histological remission of celiac disease. The detection of gluten immunogenic peptides (GIP) in fecal samples, only present if gluten ingestion, may constitute a useful tool to evaluate dietary adherence.

Aims & Methods: Observational, retrospective, longitudinal, between-groups design study. We collected clinical data from patients who had GIP measurement during follow-up from January 2017 to June 2021.

A descriptive and comparative analysis was performed using SPSS software.

The primary objective was to evaluate the clinical effectiveness of GIP measurement during follow-up of celiac patients. The secondary objective was to analyze the relation between GIP levels and demographic data (gender, age), laboratory results and histopathology.

Results: 103 patients were included, from whom 182 fecal samples were obtained. The characteristics are summarized in Table 1. 29 patients had positive levels of GIP; 12 of them normalized during follow-up (41.38%).

Age (years)	18.32 (SD=17.55)
Children / adults	58 (57%) / 43 (43%)
Gender (Female/male)	73 (71%) / 30 (29%)
Disease duration (months)	65.14 (SD=59.86)
GIP-positive	29 (28%)
Anti- tissue transglutaminase IgA (UI IgA/ml)	9.37 (SD=24.45)
Anti-gliadin IgA (mg/l)	11.87 (SD=33.44)
Anti-gliadin IgG (mg/l)	7.91 (SD=22.16)
Hemoglobin (g/dl)	14.08 (SD=1.23)
Mean corpuscular level (fL)	85.01 (SD=8.65)
Ferritin (ng/ml)	51.79 (SD=42.34)

Table 1. Characteristics of patients included (N=103). Quantitative variables are expressed as means and standard deviation (SD); qualitative variables are presented as total number of events and percentage.

No differences were found between hemoglobin, ferritin, mean corpuscular volume or antibodies levels and the result (positive/negative) of GIP in the total of samples nor analyzing samples of adults and children separately. Only anti-gliadin IgG antibodies were higher in GIP-positive patients (p=0.028). No differences were found between the result (positive/negative) of GIP and histology at diagnosis, gender or age (adults/children). It is important to mention that 77 patients had negative anti-tissue transglutaminase levels and 21 of them (27.27%) had GIP in feces. We didn't find differences in the result of GIP depending on age or disease duration. However, when pediatric patients were selected, positivity for GIPs increased with age (p=0.032).

Conclusion: - GIP are a useful tool in the follow-up of celiac patients to monitor dietary compliance, and may detect dietary transgression in subjects with negative antibodies.

- Antibody levels, age and disease duration are not associated with positivity rates of GIP.

- Only adolescents in the children group had more dietary transgressions according to detection of GIP.

Disclosure: Nothing to disclose.

P0164

IMPACT OF EPITHELIAL LYMPHOGRAM BY FLOW CYTOMETRY IN THE MANAGEMENT OF PREVIOUS INCONCLUSIVE DIAGNOSES OF CELIAC DISEASE

E.J. Laserna-Mendieta^{1,2,3,4}, M.P. Navarro Sánchez^{2,3,1}, L. Esparcia-Pinedo^{2,5}, A. Alfranca^{2,5}, R. Juárez-Tosina⁶, A.J. Lucendo^{7,2,3,8}

¹Hospital General de Tomelloso, Gastroenterology Research Unit, Tomelloso, Spain, ²Instituto de Investigación Sanitaria de La Princesa, Madrid, Spain, ³Instituto de Investigación Sanitaria de Castilla-La Mancha (IDISCAM), Toledo, Spain, ⁴Hospital Universitario de La Princesa, Laboratory Medicine, Madrid, Spain, ⁵Hospital Universitario de La Princesa, Immunology, Madrid, Spain, ⁶Hospital General Mancha Centro, Pathology, Alcázar de San Juan, Spain, ⁷Hospital General de Tomelloso, Gastroenterology, Tomelloso, Spain, ⁸Centro de Investigación Biomédica en Red Enfermedades Hepáticas y Digestivas, Madrid, Spain

Contact E-Mail Address: mpilar_ns@hotmail.com

Introduction: The use of flow cytometry to analyze the epithelial lymphogram has proven efficacy in assessing celiac disease (CeD) in patients with discordant results between serology, genetics and histology. In addition, it is the only method able to accurately diagnose CeD with non-atrophic enteropathy and when gluten has been excluded from the diet (1). Duodenal mucosa of CeD patients is characterized by increased densities of lymphocytes (CD45+) and TCRγδ+ sub-population, while CD3+CD103- are decreased. The institution of a gluten free diet (GFD) induces the reversion of these changes but the increase in TCRγδ+ lymphocytes, which remains elevated in 80-85% of CeD patients (2,3). In the last years, non-celiac gluten/wheat sensitivity (NCGS) has emerged as an entity with higher prevalence than CeD (6% vs 1%) (4).

It appears in patients in whom CeD and wheat allergy have been excluded, but their symptoms improve after GFD. The lack of additional methods to evaluate CeD in the past led many patients without villous atrophy and/or a positive serology to be diagnosed of CeD when they presented a genetic predisposition and a favorable response to GFD.

This study aims to evaluate the impact of using flow cytometry on duodenal mucosa samples of patients with an inconclusive previous diagnosis of CeD.

Aims & Methods: This study aims to evaluate the impact of using flow cytometry on duodenal mucosa samples of patients with an inconclusive previous diagnosis of CeD. Endoscopic biopsies obtained from two duodenal locations (second portion and bulb) were processed and marked with four antibodies (CD3, CD45, CD103 and TCRγδ), and analyzed using a Cytek Northern Lights (two lasers) flow cytometer.

The following cut-off values were used for TCRγδ+ lymphocytes (2): CeD confirmed with TCRγδ+≥8.5% in both locations; suggestive of NCGS with TCRγδ+<5% in both locations; and no conclusive, TCRγδ+>5% in one location. Demographic and clinical characteristic were compared between CeD-confirmed and NCGS-suspicious patient groups. Statistical significance was established for p-values<0.05.

Results: Biopsies from 25 patients (92% women) were analyzed. Mean age was 45±15 years and median GFD length was 8.3 years (range 2.1-11.9 years). Histology when CeD diagnosis was established was: Marsh 0 (n=1), Marsh 1 (n=19), Marsh 2 (n=4) and Marsh 3 (n=1). After flow cytometry evaluation and according to TCRγδ+ results, 6 patients had their

CeD confirmed (24%, all with Marsh 1 at diagnosis), 17 were classified as NCGS-suspicious (68%) and 2 showed no conclusive results (8%, including the patient with a Marsh 3 grade). Regarding increasing densities in CD45+ lymphocytes, 3 CeD-confirmed (50%) and 7 NCGS-suspicious (41%) patients showed lymphocytosis in at least one duodenal location.

For CeD serology, no patients had values above the upper normal limit currently. No statistical differences were observed between groups for time length under a GFD, anti-tissue transglutaminase IgA values in the latter serum analysis and CeD familiar background.

Finally, genetic HLA variants for high or moderate risk of CeD (DQ2.5, DQ2.2 and DQ8) were present in most CeD-confirmed and NCGS-suspicious patient groups. However, the low-risk DQ7.5 genotype was found in 2 CeD-confirmed patients (33%) but only in 1 patient of the NCGS group (6%).

Conclusion: The performance of epithelial lymphogram by flow cytometry in patients with GFD but diagnosed of CeD without villous atrophy and/or positive serology showed that 68% of them had no increase in TCRγδ+ lymphocytes. Therefore, they could present a NCGS instead of CeD and could eat small quantities of gluten according to their tolerance profile.

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P0165

COMPARISON OF OUTCOMES BETWEEN DIRECT OR STRUCTURED PEDIATRIC-TO-ADULT HEALTHCARE TRANSITION IN COELIAC DISEASE

C. Ciacchi¹, S. De Vivo¹, E. Di Feo¹, F. Zingone²

¹University of Salerno, Medicine Surgery Dentistry, Scuola Medica Salernitana, Salerno, Italy, ²University of Padua, Department of Surgery, Oncology and Gastroenterology, Padua, Italy

Contact E-Mail Address: fabiana.zingone@unipd.it

Introduction: In celiac disease (CeD), the transition from paediatric to adult care should be a collaborative process involving patients, relatives, and physicians, to have the adolescent gradually take full responsibility for the disease.

Aims & Methods: Our study aims to compare the structured transfer of care outcomes with a direct transfer from the pediatrician to adult care, in particular awareness and knowledge of CeD, adherence to the gluten-free diet, autonomy, and quality of life. In 2017, we guided the transition of a group of teenagers/young adults (YA) through a structured process with parents and the pediatrician.

In January 2021, we interviewed a subgroup of them again and compared them with a similar group of CeD patients diagnosed at pediatric age who did not receive any transition of care.

We evaluated the progress in knowledge of the disease, gluten-free diet (GFD) compliance, relationship with healthcare givers, autonomy in managing the disease's needs and quality of life, using standardized questionnaires in patients who underwent a transition and between this latter and those who did not perform a transition.

Results: Of 58 YA included in 2017, 38 were eligible for follow-up in 2021. Of them, we obtained complete answers in 20 (14 females, mean age 20.05±2.6 years). The remaining patients were not available or did not accept to participate. Twenty-five patients who did not receive any transition was also included (18 females, mean age 20.7±5.2 years).

Those who underwent a transition, at follow-up in 2021 showed improvement only in the knowledge of the disease compared to findings in 2017. Patients who underwent a structured transition were more informed than those without transition. At the same time, as per adherence to the GFD, autonomy, and quality of life measured by the CDDUX questionnaire, the groups did not show any significant score difference.

Conclusion: To our knowledge, the present study is the first to measure the outcomes of the structured vs. non-structured transition of care, showing that a structured transition improves the knowledge of the CeD but does not improve adherence, autonomy, or QoL of the young adults.

Disclosure: Nothing to disclose.

P0166

VACCINATION STATUS AND ATTITUDES TOWARDS VACCINES AMONG PATIENTS WITH COELIAC DISEASE

A. Costantino^{1,2}, M. Michelon³, L. Roncoroni⁴, C. Costantino⁵, V. Lombardo¹, A. Scricciolo¹, L. Doneda⁴, M. Vecchi^{1,2}, L. Elli¹
¹Foundation IRCCS Ca' Granda Ospedale Maggiore Policlinico, Gastroenterology and Endoscopy, Milano Italia, Italy, ²University of Milan, Department of Pathophysiology and Transplantation, Milan, Italy, ³University of Milan, Milan, Italy, ⁴University of Milan, Department of Biomedical, Surgical and Dental Sciences, Milan, Italy, ⁵University of Palermo, Department of Health Promotion Sciences, Maternal and Infant Care, Internal Medicine and Excellence Specialties "G. D'Alessandro", Palermo, Italy

Contact E-Mail Address: andreasconstantino@gmail.com

Introduction: In the last decades the public debate around vaccinations has achieved increasing attention.

Vaccines hesitancy (defined as a delay in acceptance or refusal of vaccination despite availability) and skepticism towards vaccinations in the general population have been investigated.^{1,2}

COVID-19 pandemic and the resulting new global vaccination campaign has contributed in exhuming again this issue.

Patients with chronic diseases, such as those affected by Coeliac Disease (CD), should be generally encouraged to receive common vaccines against preventable diseases (VPDs) particularly for that pathogens which could be specifically harmful for their condition.

In particular, previous studies have demonstrated an association between CD and hyposplenism or splenic hypofunction,³ with a possible increase in some infections (encapsulated bacteria);⁴ hence UEG guidelines suggest to vaccine hyposplenic CD patients against pneumococcus, and to consider additional vaccination against *Haemophilus*, meningococcus and influenza.⁵

However, patients with CD may be more fearful about vaccinations compared to general population, possibly because of their immune-mediated disorder.⁶

For this reason the identification of CD patients' vaccination status and attitudes toward vaccines is of great importance.

Aims & Methods: The aims of this study were to investigate coverage against VPDs, attitude towards vaccinations and its positive and negative determinants among CD patients.

An anonymous web-based adapted version of a validated questionnaire⁷ was sent to the mailing list of *Ioelglutine*, a nonprofit organization of CD adult patients followed at our tertiary referral Center in Milan, Italy.

Patients were asked to self-report their previous vaccinations; attitude towards vaccinations was defined as positive, negative, partially positive/negative. We investigated the influencing factors towards vaccinations calculating crude and adjusted odds ratios (AdjORs) with 95% confidence intervals (CIs).

Results: The questionnaire was sent to 412 patients with a response rate of 31.6% (130 patients, 25 men, median age 40, interquartile range 36–51). Patients self-reported to be vaccinated against the following diseases: 96 tetanus, 55 flu, 26 MMR, 25 meningitis, 21 pneumococcus. Thirty-two did not remember every previous vaccination.

One hundred and four (80%) had a positive attitude towards vaccines, 25 (19.2%) a partially positive/negative, one (0.8%) negative.

The determinants positively influencing attitude towards vaccinations were graduation (AdjOR 7.49, 95% CI 1.74–32.1) and the belief of possible return of VPDs with decline of vaccination coverage rates (AdjOR 7.42, 95% CI 1.32–41.6), while use of complementary and alternative medicines and past negative experience were negative associated (AdjOR 0.11, 95% CI 0.01–0.71, AdjOR 0.16, 95% CI 0.04–0.62, respectively).

Conclusion: Albeit 4 every 5 CD patients showed a strong positive attitude towards vaccinations, yet 1 every 5 had a partially negative position. Moreover, only a minority (~20%) reported to be vaccinated against some VPDs potentially harmful for their chronic illness.

Since CD patients should be encouraged to receive all common vaccines, the identification of the determinants influencing patients' attitude toward vaccinations may be helpful to optimize patient–doctor communication and to develop specific vaccination campaigns by patients' associations.

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P0167

LIVER ABNORMALITIES IN CELIAC DISEASE AND RESPONSE TO GLUTEN FREE DIET: A SYSTEMATIC REVIEW AND META-ANALYSIS

A. Jena¹, P. Kumar-M², A. Kumar¹, C.L. Birda¹, A. Choudhury¹, N. Kumar¹, D. Ramai³, A. Facciorusso⁴, J. Samanta¹

¹Post Graduate Institute of Medical Education and Research, Gastroenterology, Chandigarh, India, ²Post Graduate Institute of Medical Education and Research, Pharmacology, Chandigarh, India, ³University of Utah Health, Gastroenterology, Utah, United States, ⁴University of Foggia, Gastroenterology, Foggia, Italy

Contact E-Mail Address: anuraag2destiny@gmail.com

Introduction: Liver involvement in celiac disease (CeD) is known but its various etiologies and the effect of gluten free diet (GFD) on it is understudied.

Aims & Methods: We planned to study the spectrum of liver involvement in patients of CeD and the response of GFD on elevated transaminase levels. We searched PubMed & Embase databases from date of inception to 3rd September, 2020 to look for studies reporting on CeD and liver abnormalities. We searched for additional studies till March 7, 2022. Pooled proportion of patients of CeD with deranged transaminases, etiologies of various other liver diseases with CeD and the response to GFD in form of normalization of transaminases were estimated. Subgroup analysis based on the age group, geographic distribution and duration of GFD was also done.

Results: Total 42 studies (8976 patients) reported hypertransaminasemia in patients with celiac disease. The pooled proportion of patients elevated transaminases was 21.42% (95% CI: 17.02-26.59, I²=94%) overall with similar prevalence noted among adults (21.20%) and children (21.51%). The commonest etiology for the liver abnormalities was reported as celiac hepatitis at 49.23% (95% CI: 30.09-68.59, I²=87%) followed by other liver diseases. Compliance with GFD was noted in 87.83% of adults and 94.57% of children (overall 90.27%).

The proportion of CeD patients with liver abnormalities who showed response to GFD was 87.55% (95% CI: 82.80-91.13, I²=66%) overall with similar response among adults (86.03%) and pediatric population (90.48%). Western studies reported a similar response to GFD at 88.05% compared to the east (85.18%). (Table 1)

Patients of celiac disease with following parameter	Pooled proportion
Elevated transaminases	Overall: 21.42% (95%CI, 17.02-26.59%, I ² =94%), Adults: 21.2% (95%CI, 15.14-28.85%, I ² =93%), Children: 21.51% (95%CI, 15.49-29.06%, I ² =95%)
Compliance to gluten free diet (GFD) with elevated transaminases	Overall: 90.27% (95%CI, 85.91-93.38%, I ² =75%), Adults: 87.83% (95%CI, 82.01-91.94%, I ² =79%), Children: 94.57% (95%CI, 89.07-97.39%, I ² =12%)
Response to GFD with elevated transaminases	Overall: 87.55% (95%CI, 82.8-91.13%, I ² =66%), Adults: 86.03% (95%CI, 80.58-90.14%, I ² =68%), Children: 90.48%(95%CI, 80.44-95.65%, I ² =63%)
Response to GFD with elevated transaminases	West: 88.05% (95%CI, 83.05-91.72%, I ² =71%) East: 85.18% (95%CI, 66.41-94.35%, I ² =42%)
(based on hemisphere)	
Response to GFD with elevated transaminases (based on duration of GFD)	Less than 6 months: 87.57% (95%CI, 73.59-94.69%, I ² =69%), More than 12 months: 82.46% (95%CI, 72.12-89.52%, I ² =93%)

Table 1.

Conclusion: Liver involvement was noted in 21.42 % of CeD patients. Celiac hepatitis was reported in less than half of them. Good compliance and response were noted with GFD.

(PROSPERO No.: CRD42020207354)

Disclosure: None.

P0168

THE HEPATOBILIARY DISORDERS IN COELIAC DISEASE

R. Limam¹, S. Ben Azouz², N. Ben Douissa², H. Hassine², H. Kchir², N. Maamouri³

¹Rabta B, Tunis, Tunisia, ²Rabta B, Gastroenterology, Tunis, Tunisia, ³La Rabta Hospital, Tunis, Tunisia

Contact E-Mail Address: limamrihab33@gmail.com

Introduction: Different hepatic and biliary tract disorders may occur in coeliac disease. Some have been hypothesized to share genetic or immunopathogenetic factors, such as primary biliary cirrhosis, primary sclerosing cholangitis, and autoimmune hepatitis. Other hepatic changes in celiac disease may occur with malnutrition resulting from impaired nutrient absorption, including hepatic steatosis.

The aim of this study is to assess the prevalence, the different forms as well as the evolution of hepatobiliary manifestations in patients with coeliac disease (CD).

Aims & Methods: We conducted a retrospective descriptive study from 1999 till 2021, including all patients with CD followed in a gastroenterology department. Epidemiological and clinico-biological data were collected as well as the evolution on gluten-free diet (GFD).

Results: During the period of the study, 110 cases of CD were included. The average age was 34,5 years [15 - 69 years]. The sex ratio (F/H) was 4.7. Hepatobiliary disorders were noted in 18 cases (16%): 17 women and one man with a mean age of 42.7 years. Liver disease was revealed during the course of CD in 72% of cases, at the diagnostic of CD in 22% of cases and before the diagnosis of CD in 6% of cases.

The different liver disorders associated with CD were: autoimmune hepatitis (AIH) (n=2), primary biliary cholangitis (PBC) (n=1), overlap syndrome (AIH - PBC) (n=2), portal cavernoma due to combined deficiency of protein C and antithrombin III (n=1), nodular regenerative hyperplasia (n=1), hepatic steatosis (n=4) and cryptogenic liver disease (n=7), one of which was at the stage of cirrhosis.

All patients were put on GFD in addition to the specific treatment of the associated liver disease. Liver function tests got back to normal in all cases within an average of 6 months from the start of the treatment.

Conclusion: In our study, 38% of cases of idiopathic liver dysfunction were caused by CD and liver function tests got back to normal after GFD. Consequently, newly onset celiac disease should be rigorously checked for asymptomatic hepatic damage and conversely, any cryptogenic liver disorder, including end-stage liver disease, should be investigated for celiac disease.

Disclosure: Nothing to disclose.

P0169

NUTRITIONAL STATUS, NUTRIENTS IMBALANCES, FOOD-RELATED BEHAVIORS AND DIETARY SUPPLEMENTS USE AMONG PATIENTS WITH CELIAC DISEASES IN LEBANON: A NATIONAL CROSS-SECTIONAL STUDY

M.-M. Bouhairie¹, M. Hoteit², B. Hotayt³, S. Assaf³, Z.I. Chamas³, A. Bahr³

¹Lebanese University - Faculty of Medical Science, Beirut, Lebanon,

²Lebanese University - Faculty of Public Health, Nutrition and

Dietetics, Beirut, Lebanon, ³Lebanese University, Beirut, Lebanon

Contact E-Mail Address: bouhairiemalek@gmail.com

Introduction: Celiac disease (CD) is a chronic autoimmune enteropathy triggered by gluten, occurs in susceptible individuals and is associated with dietary restriction and subsequent nutritional deficiencies.

Aims & Methods: This study investigates the diet quality, the nutrition imbalances and the nutrition status among young children, adolescents and adults with CD who had referred to many hospitals in Lebanon. A cross-sectional study in 50 individuals (31.74 ± 15.64 years) with CD was conducted, using dietary, anthropometric, biochemical parameters, and assessing physical activity.

Results: Out of 50 participants, 38% and 16% were presenting low serum levels of iron and vitamin B12, respectively. The majority of participants were physically inactive and around 40% of them had low muscle mass. A weight loss of 10% to 30% indicating mild to moderate malnutrition were shown in 14% of individuals. The assessment of food related behaviors shows that 80% of participants were reading nutrition labels and 96% of them were following gluten free diet (GFD). Some barriers of which: family ignorance (6%), language on the nutrition labels (20%) and expensive GF products (78%) were limiting the adherence to GFD. Adequacy of the daily energy intake was low and insufficient intakes of calcium and vitamin D were remarked among individuals with CD.

However, protein and iron intake were exceeding the recommendations among all age groups, except in males aged 4-8 years and 19-30 years. Half the study participants were using dietary supplements where 38%, 10%, 46%, 18%, 16% and 4% used vitamin D, vitamin B12, Iron, calcium, folate and probiotics, respectively.

Conclusion: The GFD is the cornerstone of treatment for CD. However, it is not without inadequacies and may result in certain deficiencies such as calcium and vitamin D leading to low bone density as long-term consequence. Dietitians specializing in CD play a critical role in the education and maintenance of the GFD for patients with CD.

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Disclosure: Nothing to disclose.

P0170

QUALITY OF LIFE IN TEENAGERS AND ADULTS WITH COELIAC DISEASE: FROM NEWLY SPANISH COELIAC DISEASE QUESTIONNAIRE VALIDATION TO ASSESSMENT IN A POPULATION-BASED STUDY

D. Sanchez Munoz¹, C. Sousa Marín², M.d.L. Moreno Amador²

¹Instituto Digestivo Sevilla (IDI), Digestive Diseases Department,

Sevilla, Spain, ²Microbiology and Parasitology Department.

University of Sevilla, Sevilla, Spain

Contact E-Mail Address: dsanchezm@digestivosanchezmunoz.com

Introduction: Coeliac disease (CD) is an immune-mediated systemic disorder elicited by the ingestion of gluten in genetically predisposed individuals. Gluten restriction in CD sufferers leads to numerous limitations in various aspects of daily life and can significantly impact quality of life (QoL). The specific and widely used Coeliac Disease Questionnaire (CDQ) is an excellent tool to evaluate QoL in patients with CD, assessing physical, psychological and social domains.

This questionnaire is unavailable in Spain. Therefore, our study is the first to translate, culturally adapt, validate, and apply the Spanish version of CDQ to a representative sample of Spanish teenagers and adults with CD.

Aims & Methods: A total of 153 CD participants with biopsy-proven and self-reported gluten-free adherence were included in the cross-sectional study, which included four stages:

1. translation and retranslation of the French CDQ version into Spanish;
2. cultural adaptation and semantic evaluation;
3. CDQ validation through the internal consistency determination and reproducibility of the QoL; and,
4. application of the questionnaire to Spanish teenagers and adults with CD and estimation of QoL using EQ-5D.

Results: The internal consistency and test-retest reliability of the Spanish CDQ were satisfactory and no ceiling or floor effects were detected. Significant correlations were identified between the CDQ scales and the instrument for validation covering similar dimensions of the QoL were identified. The mean CDQ total score was 131.03±24.1, and the social domain had the highest rating.

There was no correlation between the time spent on a gluten-free diet and QoL. A significantly higher QoL score was reported among males and adolescents in the 15-17 age groups.

Conclusion: The newly Spanish CDQ is an appropriate tool to assess the QoL of teenager and adult patients with CD. This study highlights the importance of identifying the affected scales to address actions to reduce the impact of the gluten-free diet burden of coeliac patients and maintain public health regulations that support patients with chronic diseases such as CD.

Disclosure: Nothing to disclose.

P0171

CLINICAL PRESENTATION AND PROGNOSIS OF SMALL BOWEL ADENOCARCINOMA IN CELIAC DISEASE PATIENTS

O. Chatelana¹, S. Khater¹, J. Bruneau², T. Molina², L. Lhermitte³, C. Brouzes³, A. Bensalah³, B. Rosenbaum¹, D. Sibon³, O. Hermine⁴, C. Cellier¹

¹Hôpital Euopéen Georges Pompidou, Department of Gastroenterology, Paris, France, ²Hôpital Necker-Enfants Malades, Pathology, Paris, France, ³Hôpital Necker-Enfants Malades, Laboratory of Onco-Hematology, Paris, France, ⁴Hôpital Necker-Enfants Malades, Hematology, Paris, France

Contact E-Mail Address: olivier.chatelanaat@hcuge.ch

Introduction: Celiac disease (CD) is associated with an increased risk of small bowel adenocarcinoma (SBA). However, little is known about their clinical features, characteristics and outcome due to the rare cases of SBA.

Aims & Methods: We reviewed all SBA diagnoses in CD patients in our tertiary CD referral center from 2000 to 2022. Data on demographics, clinical features, treatments and outcome were recorded.

Results: Among 1024 CD patients, 8 (0.78%) had SBA. Median age was 64.5 (IQR:57.7-68.5). SBA diagnosis was simultaneous to CD diagnosis in 2 patients and preceded the CD diagnosis in 1. For the 5 other patients, median time between diagnoses was 65 months (IQR:41-101). One patient had a type II refractory CD, and 2 patients had persistent villous atrophy. Localizations of SBA were jejunal (n=6) and duodenal (n=2). Iron deficiency anemia (IDA) (n=4), sub-occlusion (n=1) and ileus (n=2) lead to SBA diagnosis.

All patients had surgical treatment and 3 had an adjuvant chemotherapy for a positive lymph node (N1), a metastatic stage (M1) and a T4N0M0 stage. Molecular biology data are available in 5 patients, showing microsatellite instability (n=3) and KRAS mutation (n=1).

During a median follow-up of 34 months (IQR:15-89.2), only the patient with the metastatic stage died 2 years after the SBA diagnosis and no recurrence occurred in others.

Conclusion: We report one of the largest series of SBA in CD patients and the first SBA in a refractory CD. Frequent microsatellite instability could bring some elements to its pathogenesis.

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Disclosure: Nothing to disclose.

P0172

DIAGNOSTIC YIELD OF CAPSULE ENDOSCOPY AND ENTEROSCOPY IN THE DIAGNOSIS OF INTESTINAL LYMPHOMA IN REFRACTORY CELIAC DISEASE TYPE 2 PATIENTS

A. Aidibi¹, B. Rosenbaum¹, O. Chatelanaat¹, S. Khater¹, J. Bruneau², L. Lhermitte², D. Sibon², O. Hermine², T. Molina², C. Cellier³

¹Georges Pompidou European Hospital, Gastroenterology, Paris, France, ²Necker Enfants Malades Hospital, Paris, France, ³European Georges Pompidou Hospital Dept. of Gastroenterology, Gastroenterology, Paris, France

Contact E-Mail Address: olivier.chatelanaat@hcuge.ch

Introduction: Refractory celiac disease type II (RCD II) is a rare complication of celiac disease (CD) with an increased risk of enteropathy-associated T cell lymphoma (EATL).

Aims & Methods: The aim of this study is to investigate the role of capsule endoscopy (CE) and enteroscopy in the diagnosis of EATL in RCD II patients compared to cross-sectional imaging.

A retrospective review of all RCD II patients was made between 2000 and 2021 including clinical, endoscopic, and imaging data.

Results: 75 patients with RCD II were identified among 1024 celiac patients. 20 CE and 35 upper enteroscopy procedures were performed in these patients. 15 patients (75%) had ulcerative jejunitis (UJ) on CE. The most common location was the proximal jejunum (60%) followed by the distal jejunum (20%) and ileum (20%). Ulcerated stenoses were observed in 13% of patients without capsule retention, and one patient had deep ulcerations.

68% of patients (n=24) had UJ on enteroscopy, five of whom had stenosis. Biopsies performed during enteroscopy confirmed an EATL diagnosis in 31.4% (n=11/35) of patients. Among 14 magnetic resonance enterography (MRE) performed, only 3 pathological aspects were identified (one stenosis, one jejunal thickening, and one mesenteric lymphadenopathy). Only 3 patients showed similarities between the imaging and the endoscopic aspect.

Conclusion: CE and enteroscopy are useful tools to diagnose EATL in RCD II patients and are more relevant than MRE.

Disclosure: Nothing to disclose.

P0173

DUAL X-RAY ABSORPTIOMETRY-DERIVED BONE QUALITY INDEXES IN CELIAC DISEASE

L. Elli¹, E. Filippi², L. Ciceri², F.M. Olivieri³, L. Piodi¹, B. Cesana⁴, L. Roncoroni¹, V. Lombardo¹, A. Scricciolo¹, N. Nandi², M. Topa², L. Scaramella², M. Vecchi²

¹Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico, Center for Prevention and Diagnosis of Celiac Disease, Milan, Italy, ²Università degli Studi di Milano, Department of Pathophysiology and Transplantation, Milan, Italy, ³Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico, Medicina Nucleare, Bone Metabolic Unit, Milan, Italy, ⁴Università degli Studi di Milano, G.A. Maccacaro Unit of Medical Statistics, Biometry, and Bioinformatics, Department of Clinical Sciences and Community Health, Milan, Italy

Contact E-Mail Address: matilde.topa@unimi.it

Introduction: Celiac disease (CeD) is a risk factor for osteopenia and osteoporosis, although the pathogenesis of bone impairment associated with CeD is still unknown. The main etiologies are malabsorption and chronic inflammation; however, the role of intestinal atrophy and its extension is unclear.

Aims & Methods: Our aim was to evaluate the correlation between villous atrophy extension and dual-energy X-ray absorptiometry (DXA) parameters.

We have retrospectively gathered data on 47 celiac patients (36 women and 11 men), aged between 31 and 86 years, treated at Fondazione IRCCS Ca' Granda Ospedale Maggiore in Milan, who underwent videocapsule endoscopy (VCE) and DXA scans from 2004 to 2019. Quantitative and qualitative DXA parameters were derived only from the most recent DXA measurements (since 2015). Different bone parameters were collected, namely quantitative (BMD, T-score and Z-score), qualitative (TBS and BSI) and geometric (BR, CSA, CSMI, Z, HAL and NSA) findings.

Results: Patients were divided into three categories depending on the type of small bowel finding and any extension detected during VCE examination. The first group included those with no lesions (23 patients), the second those with typical lesions (mucosal atrophy, mosaicism and scalloping) in less than one-third of the small bowel (16 patients) and, the third those with typical lesions in more than one-third of the small bowel (7 patients).

One patient was excluded because of missing data. In those patients in whom typical lesions were found in two-thirds or more of the small bowel, bone mineral density seems to be lower in both the lumbar spine and the hip ($p=0.026$ and $p=0.011$, respectively). The deterioration of bone structure in individuals with severe and extended small bowel disease due to CeD seems to be statistically significant ($p=0.032$).

Interestingly, we found that bone density, structure and geometry do not correlate with the duration of a gluten-free diet. Furthermore, autoimmune comorbidities do not affect DXA results.

Conclusion: The main result is that neither endoscopic nor histological atrophy itself can explain the deterioration in bone mineralization and structure, while atrophy extension is mostly responsible for bone impairment. In fact, as villous atrophy becomes more severe and widespread, lumbar and femoral bone density deteriorates. In severe CeD, microarchitectural and textural injury (TBS) increases.

Disclosure: Nothing to disclose.

P0174

COELIAC DIAGNOSIS IN OLDER ADULTS: DOES AGE REALLY MATTER?

O. Fagan¹, G. Madders¹, E. Shannon¹, C. Deane¹, V. Byrnes¹

¹University Hospital Galway, Gastroenterology, Galway, Ireland

Contact E-Mail Address: olgafagan@gmail.com

Introduction: Coeliac disease is being increasingly diagnosed in later life.

Aims & Methods: To assess if the presentation and outcomes of coeliac disease (CD) diagnosed after the age of 65-years differs from that of younger adults.

Chart review of all patients with newly diagnosed CD between January-2012 and December-2021. Variables such as demographics, mode of presentation, TTG-titre and mucosal healing in patients aged > 65 and ≤ 65-years at diagnosis were recorded.

Results: 305 newly diagnosed coeliacs were included, comprising 59 patients >65-years (median age 71 [65-89 years], F:M ratio 2:1), and 247 patients <65-years (median age 36 [16-64 years], F:M ratio 2:1). Abdominal pain/bloating (33% vs 27%, $p=0.22$) and diarrhoea (27% vs 29%, $p=0.4$) were the commonest mode of presentations seen in both older and younger patients.

Weight loss at presentation was numerically more prevalent in the older cohort compared to that of the younger cohort (20% v 12%, $p=0.05$). Anaemia was more prevalent at the time of diagnosis in older patients (36% vs 14%, $p<0.05$). Vitamin-D deficiency at presentation were comparable in older and younger cohort (43% vs 50%, $p=0.25$).

Older patients had lower TTG-titres at diagnosis [33 (range 5-160) v 49 (range 5-840) $p=0.58$] and a higher prevalence of seronegative disease, (12% v 4%, $p<0.05$). The existence of thyroid disease (7% vs 10%, $p=0.3$) and other autoimmune diseases (19% vs 25%, $p=0.16$) were comparable in both groups.

While mucosal recovery was similar in the two groups, (48% v 49%, $p=0.53$), anaemia failed to resolve following 12-months of a GFD (25% v 5%, $p<0.05$) in the older cohort when compared to their younger counterparts. Interestingly, there was an inverse correlation between TTG-titre at diagnosis and poor mucosal healing in both cohorts ($p<0.05$).

Conclusion: Age is just a number. Older patients with CD present similarly to their younger counterparts. The higher rates of anaemia at time of diagnosis in older adults suggests a lower index of suspicion for coeliac disease with advancing age, which may be complicated by the higher rates of seronegative disease in this cohort.

Contrary to prior studies, older adults have equivalent rates of mucosal recovery, which is suggestive of the *de novo* loss of gluten tolerance in this age group as opposed to decades of delayed diagnosis.

Disclosure: Nothing to disclose.

P0175

COELIAC DISEASE (CD) AND CHRONIC INFLAMMATORY BOWEL DISEASE (IBD) ASSOCIATION

D. Azzouzi¹, M. Borahma¹, N. Iagdari¹, M. kadi¹, F.Z. Chabib¹, I. Benelbarhdadi¹, F.Z. Ajana¹

¹Mohamed V University, Gastroenterology C, Rabat, Morocco

Contact E-Mail Address: azzouzidriass.ad@gmail.com

Introduction: The association of coeliac disease (CD) and chronic inflammatory bowel disease (IBD) is rare and has been little studied. CD and IBD are chronic gastrointestinal disorders of inflammatory origin that develop in response to environmental triggers in genetically predisposed individuals.

Aims & Methods: This study aimed to clarify the frequency, anatomical-clinical and evolutionary characteristics, and outcomes of this association. This is a retrospective, descriptive and analytical study of 13 patients between 2005 and 2022. The diagnosis of CD was established based on clinical, serological and histological data. The diagnosis of IBD was based on a combination of clinical, endoscopic, histological and radiological evidence.

Results: 13 cases of CD and IBD association were analysed in a cohort of 341 CD and 1020 Crohn's and 570 ulcerative colitis (UC). The frequency of association was 3.81% in the CD cohort and 0.81% in the IBD cohort. The sex ratio was 5F/M, a predominantly female ratio of 84.6%. The diagnosis of CD preceded that of Crohn's disease in 76.9% ($n=10$), with a mean delay of 32 months (12-72 months).

All patients were put on a gluten-free diet (GFD). Despite good compliance for at least 18 months, the evolution was marked by the persistence of anaemic syndrome and dysenteric syndrome in six cases (60%), diarrhea and abdominal pain of the colonic type in five cases (50%) and by the occurrence of rectal bleeding, anaemic syndrome and dysenteric syndrome in two cases (20%). Given the persistence of symptoms, we first ruled out resistance to GFD. Upper and lower gastrointestinal endoscopy, radiological and histological examination concluded that Crohn's disease was present: isolated colonic in five patients (50%); gastric and colonic in three patients; gastric and oesophageal in one patient; oesophageal in one patient. In 7 cases, the involvement was luminal inflammatory, stenosing in two patients and fistulising in one patient.

The diagnosis of IBD preceded that of coeliac disease in 23% of cases ($n=3$), 2 patients had luminal colonic Crohn's disease and the third had left UC. The diagnosis of CD was clinically retained by the appearance of an anaemic

mic syndrome associated with atypical abdominal pain in 2 cases and a dysenteric syndrome in the other case. Serologically, 2 patients had positive IgA antibodies to transglutaminase and the other was seronegative. Histologically, all three patients had intraepithelial lymphocytosis greater than 30% with subtotal atrophy. The evolution was favourable after the GFD which was always associated with the treatment of IBD, with a good clinical, biological and endoscopic improvement.

Conclusion: Our work shows that the association of CD and IBD is often rare but not exceptional with a strong predominance of CD and Crohn's disease. It should be suspected in the presence of any resistance to GFD or an unusual evolution during the course of IBD despite good therapeutic compliance.

Disclosure: Nothing to disclose.

P0176

CELIAC DISEASE: AN UNUSUAL CAUSE OF PORTAL HYPERTENSION

L. Khalif¹, M. Borahma², M. Kadiri³, F.-Z. Chabib⁴, N. Lagdali¹, C. Berhili¹, I. Benelbarhdadi¹, F.Z. Ajana⁵

¹Mohammed V University, Hepatogastroenterology, Medecine C, CHU Ibn Sina, Rabat, Morocco, ²Mohammed V University, Ibn Sina Hospital, Department of Gastroenterology C, Rabat, Morocco, ³Ibn Sina Hospital, Rabat, Morocco, ⁴Ibn Sina University Hospital, Medical Unit C, Seclin, France, ⁵CHU Ibn Sina, SMMAD, Moroccan Society of Digestif Diseases, Rabat, Morocco

Contact E-Mail Address: dr.ibtissamkhalif@gmail.com

Introduction: Celiac disease (CD) is a chronic autoimmune enteropathy, triggered by ingestion of gluten and other related prolamins in genetically predisposed individuals.

Several liver disorders have been described, and isolated hypertransaminasemia remains the most common hepatic presentation of the CD. The association with portal hypertension (PH) is rare.

The objective of our work was to describe this association, and study the impact of the gluten-free diet on the evolution of portal hypertension signs.

Aims & Methods: It was a retrospective and descriptive study conducted over 26 years, from 1995 to december 2021, collecting twenty patients with the association celiac disease and portal hypertension from a total of 340 celiac patients.

The diagnosis of CD was retained on clinical, serological and histological criteria.

Results: Twenty patients were collected, which represented a prevalence of 5,8%.

The mean age was 34,2 years with extremes ranging from 19 to 60 years. The sex ratio F/M was 3 with a female predominance in 75%.

On the functional level, 2 main symptoms, the abdominal pain and the weight loss were present in 45% of the cases, followed by oedemato-ascitic syndrome in 35% of the cases, chronic diarrhea of the malabsorption type in 30% of the cases, atypical diarrhea in 20% of the cases, vomiting in 15% of the cases, and only one case of upper gastrointestinal hemorrhage made of hematemesis and melena.

Clinical examination revealed an enlarged spleen in 70% of patients and collateral venous circulation in 30% of patients. Liver examination revealed a cirrhotic-looking liver in 20%, and a clinically normal liver in 80% of cases.

Abdominal ultrasound coupled with Doppler showed a homogeneous liver with regular contours in 65% of cases, a heterogeneous liver with spiculated contours in 35% of cases, portal cavernoma in 25% of cases, and one patient only had focal thrombosis of the inferior vena cava. Common causes of chronic liver disease were excluded in all patients.

Liver biopsy was performed in all our patients and the etiological profile was as follows, PH on porto-sinusoidal vascular disease in 40%, PH on celiac cirrhosis in 20%, PH on granulomatous hepatitis associated with celiac disease in 15%, and normal liver histology in 25% of the cases. The PH on portal thrombosis was secondary to hyperhomocysteinemia.

The upper endoscopy found esophageal varices (EV) in 55% of cases.

PH revealed celiac disease in 4 patients and was discovered on average 7.5 years after the diagnosis of PH.

A gluten-free diet (GFD) as well as prophylactic and therapeutic treatment of EV rupture with monitoring were instituted.

The evolution of the patients was marked by the aggravation of EV and the appearance of their complications in 20% of the cases over an average period of 5 years with non-adherence to the GFD. Histologically, 2 patients developed cirrhosis after an initially normal histology, after respectively 4 and 5 years with non-adherence to the GFD.

Conclusion: The association of celiac disease and portal hypertension is rarely reported in the literature, in our series it represented a prevalence of 5.8%.

Celiac disease is responsible for PH by various mechanisms not yet fully elucidated, so its search is systematic during PH. Adherence to a gluten-free diet has a beneficial effect on the evolution and severity of PH.

Disclosure: Nothing to disclose.

P0177

THE USE OF NO-BIOPSY APPROACH FOR DIAGNOSING CHILDREN WITH COELIAC DISEASE IS INCREASING

P. Riznik¹, I. Carnohorski², J. Dolinsek³, N. Dragutinovic⁴, J. Gyimesi Gallisz⁵, A.C. Hauer⁶, T. Kamhi Trop⁷, M. Klemenak¹, I.R. Korponay-Szabó^{5,8}, T. Krencnik¹, M. Masic⁹, Z. Misak¹⁰, V. Pavkov¹¹, A. Popp¹², T. Raba¹³, P. Szitanyi¹⁴, J. Dolinsek^{1,15}

¹UKC Maribor, Clinic for Pediatrics, Maribor, Slovenia, ²CeliVita, Zagreb, Croatia, ³Municipality of Maribor, Project Development Office, Maribor, Slovenia, ⁴University Childrens Hospital, Belgrade, Serbia, ⁵Heim Pal National Paediatric Institute, Coeliac Disease Centre, Budapest, Hungary, ⁶Medical University of Graz, Department of Paediatrics and Adolescence Medicine, Graz, Austria, ⁷University Children's Hospital Ljubljana, Clinical Department of Paediatric Gastroenterology, Hepatology and Nutrition, Ljubljana, Slovenia, ⁸University of Debrecen Faculty of Medicine, Paediatrics, Debrecen, Hungary, ⁹Children's Hospital Zagreb, Pediatric Gastroenterology, Zagreb, Croatia, ¹⁰Childrens Hospital Zagreb, Pediatric Gastroenterology, Zagreb, Croatia, ¹¹Serbian Coeliac Society, Belgrade, Serbia, ¹²IOMC Alfred Rusescu, Department of Pediatrics, Bucharest, Romania, ¹³"Nicolae Testemitanu" State University of Medicine and Pharmacy of the Republic of Moldova, Paediatric Department, Chisinau, Moldova (Republic of), ¹⁴General University Hospital in Prague, Department of Paediatrics and Adolescent Medicine, Prague, Czech Republic, ¹⁵University of Maribor, Faculty of Medicine, Paediatric Department, Maribor, Slovenia

Contact E-Mail Address: tkrencnik@gmail.com

Introduction: European Society for Paediatric Gastroenterology, Hepatology and Nutrition (ESPGHAN) guidelines for diagnosing coeliac disease (CD) in children and adolescents published in 2012 were the first to include the possibility of diagnosing CD without duodenal biopsy.

It has been shown in the following years that paediatric gastroenterologists are often reluctant to use a no-biopsy approach, despite their patients being eligible based on the established criteria (symptoms or signs

suggestive of CD and TGA IgA $\geq 10 \times \text{ULN}$). ESPGHAN guidelines updated in 2020 extended the possibility to use a no-biopsy approach to asymptomatic children belonging to known risk groups.

Aims & Methods: The aim of our study was to assess how often a no-biopsy approach is used in children and adolescents, diagnosed with coeliac disease in 2021 in the Danube region.

A prospective anonymised multi-centre study was conducted in the scope of CD SKILLS project including paediatric gastroenterologists from 8 European countries (Austria, Croatia, Czech Republic, Hungary, Moldova, Romania, Serbia, Slovenia), providing medical data of patients with CD aged ≥ 19 years diagnosed in 2021.

We focused on the presence of symptoms and level of TGA at the time of diagnosis and the used diagnostic approach. The data was compared with the results of the similar study conducted in Central Europe during the Focus IN CD project in 2016.

Results: Data from 284 newly diagnosed CD patients (64.8% female; median age 6.5 years) from 8 European countries were included in the study. 247 children (87%) were symptomatic at the confirmation of the diagnosis. No-biopsy approach was used in 63.7% ($N=181$) of included children (in 70.3% of asymptomatic and in 62.7% of symptomatic children).

Out of 103 children, who were diagnosed using duodenal biopsy, further 19 (18.4%) have also been eligible for the no-biopsy approach based on the very high levels of TGA antibodies. Comparing the data with the similar study conducted in Central Europe in 2016, we found the significant rise in the use of no-biopsy approach (Table 1).

	DANUBE REGION 2021			CENTRAL EUROPE 2016			p-values
	TOTAL	BIOPSY	NO-BIOPSY	TOTAL	BIOPSY	NO-BIOPSY	
CROATIA	61	25 (41%)	36 (59%)	58	54 (93.1%)	4 (6.9%)	<0.001
HUNGARY	85	23 (27.1%)	62 (72.9%)	302	238 (78.8%)	64 (21.2%)	<0.001
SLOVENIA	44	16 (36.4%)	28 (63.6%)	45	28 (62.2%)	17 (37.8%)	0.013
TOTAL	284	103 (36.3%)	181 (63.7%)	653	546 (83.6%)	107 (16.3%)	<0.001

Table 1. The use of no-biopsy approach in countries of Danube region and Central Europe.

Conclusion: In this prospective study it has been shown that the use of no-biopsy approach to diagnose CD in children and adolescents has risen significantly in the recent years. Paediatric gastroenterologists are probably becoming more comfortable with this possibility proposed by both ESPGHAN 2012 and 2020 guidelines for diagnosing CD. Compared to ESPGHAN 2012 guidelines, new 2020 guidelines also allow the use of no-biopsy approach in asymptomatic children.

In our study, the no-biopsy approach was used in 70.3% of asymptomatic children, further indicating that the awareness about possibilities included in ESPGHAN 2020 guidelines and their use among paediatric gastroenterologists in participating countries is high.

Disclosure: Nothing to disclose.

P0178

NUTRITIONAL STATUS ASSESSMENT IN COELIAC DISEASE

D. Maniero¹, I. Marsilio¹, G. Lorenzon¹, E.V. Savarino², F. Zingone²

¹University of Padova, Department of Surgery, Oncology and Gastroenterology, Padova, Italy, ²University of Padua, Division of Gastroenterology, Department Of Surgery, Oncology And Gastroenterology, Padua, Italy

Contact E-Mail Address: dariamaniero@gmail.com

Introduction: Coeliac disease (CeD) is an immune-mediated systemic disorder triggered by the ingestion of gluten in genetically susceptible individuals, which, if untreated, can lead to chronic malabsorption. The mainstay treatment for CeD currently is a gluten free diet (GFD), which some studies have linked to an increased risk of weight gain and the development of metabolic disorders. Most of these studies are focused on the effect of the GFD on the Body Mass Index (BMI).

Aims & Methods: We aimed to evaluate the nutritional status, using different nutritional parameters, in two cohorts of CeD patients at diagnosis and on a GFD compared with healthy controls.

We consecutively recruited CeD patients at diagnosis and on a GFD from June 2020 to April 2022 at our outpatient clinic of the Azienda Ospedale - Università di Padova. Healthy subjects were recruited among family and friends of hospital staff. We collected demographic and clinical data at the time of the recruitment and recorded weight, height, BMI, Hand Grip Strength and bioelectrical impedance. Student t-test and Mann-Whitney test were used to compare parametric and non-parametric variables, respectively. Stata 11 software was used for statistical analysis.

Results: The study population was composed by 28 CeD patients at diagnosis [61% females, mean age 34 (Standard Deviation, SD 12)], 28 CeD patients on a GFD for at least one year [61% females, mean age 33 (SD 14)] and 28 healthy controls [61% females, mean age 34 (SD 11)].

CeD patients at diagnosis had a poorer nutritional status compared with healthy controls; in particular, lower phase angle (PA) ($p<0.001$), body cell mass index (BCMI) ($p=0.006$), fat free mass index (FFMI) ($p=0.007$), and appendicular skeletal muscle index (ASMI) ($p=0.007$). Finally, CeD patients had also a higher percentage of extracellular water (ECW) compared with controls ($p<0.001$).

Considering CeD patients on a GFD, they had only a lower FFMI ($p=0.02$) and ASMI ($p=0.02$) compared with healthy subjects. CeD patients on a GFD had a higher phase angle than CeD patients at diagnosis ($p=0.02$) and lower percentage of ECW ($p=0.02$). Finally, BMI resulted similar among the three groups.

	CeD at diagnosis	CeD on GFD	Controls	CeD diagnosis vs Controls	CeD on GFD vs Controls	CeD diagnosis vs CeD on GFD
BCMI	8.4 (7.8-9.6)	9.3 (8.4-10.4)	9.5 (8.6-10.7)	$p=0.006^{**}$	$p=0.31$	$p=0.06$
FFMI	3 (2-3)	3 (3-3)	4 (3-5)	$p=0.007^{**}$	$p=0.02^{**}$	$p=0.63$
ASMI	2.5 (2-3)	3 (2-3)	3 (3-3)	$p=0.007^{**}$	$p=0.02^{**}$	$p=0.63$
PA	5.7 $\pm$ 0.6	6 $\pm$ 0.6	6.3 $\pm$ 0.6	$p<0.001^{*}$	$p=0.15$	$p=0.02^{*}$
ECW (%)	47.4 $\pm$ 2.8	45.6 $\pm$ 2.7	44.7 $\pm$ 2.5	$p<0.001^{*}$	$p=0.19$	$p=0.02^{*}$

*=Student t-test; **=Mann-Whitney test

Table.

Conclusion: CeD patients at diagnosis have a poorer nutritional status compared with healthy controls, which improves on a GFD, except for FFMI and appendicular skeletal muscle index, which still result statistically significant different between CeD on GFD and controls. Therefore, our study describes a compromised nutritional status at CeD diagnosis

but also a positive effect of a GFD on it for most of the parameters analyzed, underlining the inefficacy to evaluate this aspect only through the BMI evaluation.

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P0179

GENES AND GENOTYPES IN CELIAC DISEASE

R. Nemteanu¹, P. Cianga^{2,3}, I. Girleanu^{4,1}, C. Sfrijan¹, C. Gorincioi¹, S. Butura¹, A. Trifan^{1,4}, A. Plesa^{1,4}

¹Institute of Gastroenterology and Hepatology, Gastroenterology, Iasi, Romania, ²St Spiridon Hospital, Department of Immunology, Iasi, Romania, ³University of Medicine and Pharmacy “Grigore T. Popa”, Immunology, Iasi, Romania, ⁴University of Medicine and Pharmacy “Grigore T. Popa”, Gastroenterology, Iasi, Romania

Contact E-Mail Address: maxim_roxxana@yahoo.com

Introduction: Celiac disease (CD) is considered to have a high heritability. Several studies have indicated that a strong HLA-DQ ‘gene dose’ effect exists with apparent implications on CD development and disease phenotype.

Aims & Methods: A retrospective analysis of medical records was performed using the adult CD patient cohort attending a single tertiary referral centre. The study was carried out between January 2015– December 2019 and included 81 patients. Complete HLA-DQ typing alleles were isolated using genomic DNA extracted from EDTA-anticoagulant peripheral blood according to the manufacturer instructions.

Results: HLA-DQA1*02/DQA1*05 was identified in 49.3%, DQA1*05/DQA1*05 in 21.3% of cases, and HLA-DQB1*02/DQB1*02 in 41.3 % of cases. 8% of patients are DQ2.5 homozygous, 64% are DQ2.5 heterozygous, 24 cases DQ2.5 / DQ2.2, 24 (32%) have the DQ2 genotype 2.5/DQX, 2.67% inherited DQ2.5/DQ7, respectively 1 isolated HLA-DQ2.2 homozygous case. DQX/DQX were identified at 10 (13.33%).

Low frequency was identified for HLA-DQ8. When assessing disease phenotype, the carriage of 2 HLA-DQB1*02 copies was associated with the presence of anaemia ($P=0.024$), but not with the presence of recurrent or chronic diarrhea, loss of weight, infertility or dyspepsia. No differences were detected between the presence of one versus two DQB1*02 copies

and the different Marsh classifications, $P=0.725$. However, the CD patients expressing 2 copies were more likely to have increased IgA-tTG and IgA AGA levels compared to those expressing only one copy.

Conclusion: The number of copies inherited by CD patients influences disease phenotype, but does not interfere with histological involvement. The lack of dosage effect on histological changes suggests that the presence of HLA-DQ heterodimers confers risk of disease, but there are additional factors that determine severity.

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P0180

USEFULNESS OF INTESTINAL ANTI-ENDOMYSIUM ANTIBODIES IN THE DIAGNOSIS OF CELIAC DISEASE IN ADULTHOOD

F. Monica¹, L. De Leo², F. Ziberna³, R. Cannizzaro⁴, S. Maiero⁵, A.M. Baragiotta⁶, P. Brosolo⁷, J. Panos Zamora⁸, M. Zilli⁹, C. Simeth¹⁰, A. visintin¹¹, A. Padoin¹, T. Not¹², C. Zanchi²
¹ASUGI Cattinara Hospital, Gastroenterology, Trieste, Italy, ²IRCCS Burlo Garofolo, Pediatric gastroenterology Department, Trieste, Italy, ³IRCCS Burlo Garofolo, Trieste, Italy, ⁴Centro di Riferimento Oncologico (CRO) Aviano IRCCS, Oncological Gastroenterology, Aviano, Italy, ⁵Centro Riferimento Oncologico SOC Gastroenterology, Aviano, Italy, ⁶Azienda Ospedaliera Pordenone, Gastroenterology, Pordenone, Italy, ⁷Ospedale di Pordenone, Gastroenterology, Pordenone, Italy, ⁸AZ. Osp. Santa Maria Misericordia, Udine, Italy, ⁹AOU SM della Misericordia, Gastroenterology, Udine, Italy, ¹⁰ASUGI Cattinara Hospital, Gastroenterology and digestive endoscopy, Trieste, Italy, ¹¹Cattinara, Centro studi fegato, Gorizia, Italy, ¹²IRCCS Burlo Garofolo, Pediatric Department, Trieste, Italy

Contact E-Mail Address: monifabio@gmail.com

Introduction: Celiac disease (CD) is a systemic immune-mediated disease triggered by gluten ingestion in genetically susceptible individuals, characterized by the presence of a variable combination of clinical manifestations, CD-specific antibodies and enteropathy. The phenotypic expression of the disease has changed over time with a decrease of classical CD and increase of atypical and subclinical phenotype. Moreover, the presence of symptoms is not always related to intestinal injury since CD-patients with a normal mucosa can complain symptoms. This condition is known as potential CD (P-CD) and it is related to people with a normal intestinal mucosa, but presence of serum CD-antibodies.

Recent cohort studies in children at risk of CD showed that P-CD have an increased risk to progress to classical CD. In pediatric patients the presence of CD-antibodies at intestinal level predicts the development of intestinal atrophy and is used to support diagnosis of P-CD. In adult patients intestinal CD-antibodies showed 100% sensitivity in classical CD, while no data are available in adult P-CD and in other gastrointestinal (GI) diseases.

Aims & Methods: We conducted a prospective and multicentric study which involved five-different gastroenterological units in North Italy. The aim of this study was to investigate the sensitivity and the specificity of intestinal CD-antibodies in patients suspected for CD and for other GI disorders in adulthood.

Adult subjects (> 19 years) who performed biopsy for suspected CD or other GI diseases have been prospectively enrolled.

Intestinal CD-antibodies have been investigated by measuring anti-endomysium antibodies (AEA) in the supernatant of intestinal biopsy culture.

Results: Ninety-eight patients were enrolled (63F-35M, median age 33±18y) and divided in 3 groups.

Group A: 18 patients, with CD suspicion and tested positive for HLA DQ2/8 and for serum CD abs. Histological analysis showed villous atrophy in all of them, intestinal AEA were tested positive in biopsy supernatant of 18/18. All these patients were diagnosed as CD patients and put in GFD.

Group B: 5 symptomatic patients, with CD suspicion and tested positive for HLA DQ2/8 and for serum CD abs. The intestinal mucosa was normal in all of them, intestinal AEA were tested positive in biopsy supernatant of 5/5. All these patients were diagnosed as P-CD patients and put in GFD.

Group C: 75 patients underwent GI endoscopy because suffering from other gastrointestinal disorders and 23/75 tested positive for HLA DQ2/8. Intestinal AEA were not detectable in biopsy supernatant of these patients. All controls were negative for serum CD-antibodies.

Sensitivity and specificity of intestinal AEA are absolute (100%).

Conclusion: Intestinal CD-antibodies have shown absolute sensitivity and specificity to detect both CD and P-CD patients. In particular, the detection of these auto-antibodies at intestinal level make prompt diagnosis in symptomatic P-CD patients who may benefit of a well-founded diagnosis reducing both unnecessary medical investigations and delay in diagnosis and treatment.

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P0181

THE KNOWLEDGE ABOUT COELIAC DISEASE AMONG HEALTHCARE PROFESSIONALS IS NOT SATISFACTORY IN THE DANUBE REGION

P. Riznik¹, I. Carnohorski², J. Dolinsek³, N. Dragutinovic⁴, J. Gyimesi⁵, A.C. Hauer⁶, M. Klemenak¹, I.R. Korponay-Szabó^{5,7}, T. Krencnik¹, M. Masic⁸, Z. Misak⁹, V. Pavkov⁹, A. Popp¹⁰, T. Raba¹¹, P. Szitanyi¹², J. Dolinsek^{1,13}

¹University Medical Centre Maribor, Clinic for Pediatrics, Maribor, Slovenia, ²CeliVita, Zagreb, Croatia, ³Municipality of Maribor, Project Development Office, Maribor, Slovenia, ⁴University Childrens Hospital, Belgrade, Serbia, ⁵Heim Pal National Paediatric Institute, Coeliac Disease Centre, Budapest, Hungary, ⁶Medical University of Graz, Department of Paediatrics and Adolescence Medicine, Graz, Austria, ⁷University of Debrecen Faculty of Medicine, Paediatrics, Debrecen, Hungary, ⁸Children's Hospital Zagreb, Pediatric Gastroenterology, Zagreb, Croatia, ⁹Serbian Coeliac Society, Belgrade, Serbia, ¹⁰IOMC Alfred Rusescu Dept. of Pediatrics, Paediatrics, Bucharest, Romania, ¹¹"Nicolae Testemitanu" State University of Medicine and Pharmacy of the Republic of Moldova, Paediatric Department, Chisinau, Moldova (Republic of), ¹²General University Hospital in Prague, Department of Paediatrics and Adolescent Medicine, Prague, Czech Republic, ¹³University of Maribor, Faculty of Medicine, Paediatric Department, Maribor, Slovenia

Contact E-Mail Address: tkrencnik@gmail.com

Introduction: Several studies have shown that the knowledge about coeliac disease (CD) is not satisfactory among healthcare professionals (HCP).

Aims & Methods: The aim of our study was to assess the knowledge of HCPs about CD in the Danube region.

HCPs from 8 countries in the Danube region were asked to complete the web-based questionnaire about CD. The questions were divided into subsections on epidemiology with clinical presentation, diagnostics, and treatment with follow-up. Achieved scores between participating countries and among different specialists managing patients with CD were compared. The scores of HCPs were compared with the results of a similar study conducted in Central Europe within the Focus IN CD project in 2016.

Results: Questionnaire was completed by 799 HCPs from Austria, Croatia, Czech Republic, Hungary, Moldova, Romania, Serbia and Slovenia. Most participants were paediatricians (68.6%), followed by internal medicine specialists (9.5%), general practitioners (6.5%) and other HCPs.

Significant differences ($p < 0.001$) were found between different specialists with paediatricians (mean score: 56.9%) and internal medicine specialists (51.7%) scoring higher than general practitioners (40.4%) and other specialists (37.7%). Comparing paediatricians from different countries, those from Croatia scored the highest, followed by Czech and Slovenian paediatricians.

When comparing gastroenterologists (GE) (paediatric GE (N=72) and internal medicine-GE (N=48)) with primary care physicians (primary care paediatricians (N=362) and general practitioners (N=52)) we found that paediatric GE scored significantly higher than internal medicine-GE, primary care paediatricians (and general practitioners (mean score: 75.3% vs 55.1% vs 53.9% vs 40.4%; $p < 0.001$). Among countries, Slovenian paediatric GE scored the highest, followed by Croatian and Austrian paediatric GE. Comparing the data with the similar study conducted in Central Europe in 2016, we found a significant rise ($p < 0.001$) in the knowledge of paediatric GE (Table 1). Also, overall knowledge of HCPs is slightly higher in the Danube region in 2021 compared to Central Europe in 2016 (52.2% vs 50.9%; NS). We also found that HCPs who previously took part in the Focus IN CD project (N=69), achieved higher score (61.1% vs 50.8%; $p < 0.001$).

CENTRAL EUROPE 2016	GENERAL PRACTITIONERS (N=424)	PRIMARY CARE PAEDIATRICIANS (N=405)	PAEDIATRIC GE* (N=49)	INTERNAL MEDICINE GE (N=20)
Overall mean score	53.4% (SD ±16.5)	53.4%(±15.5)	69.4% (±10.7)	54.2% (±9.4)
Epidemiology and clinical presentation	46.2% (SD±17.5)	46.3% (±17.1)	60.8% (±13.8)	51.7% (±13.6)
Diagnostic procedure	40.4%(SD±26.2)	39.7% (±27.8)	63.3% (±23.3)	34.2% (±14.8)
Treatment and follow-up	67.8%(SD±17.9)	68.1% (±16.2)	80.8% (±15.1)	68.5% (±14.2)
DANUBE REGION 2021	GENERAL PRACTITIONERS (N=52)	PRIMARY CARE PAEDIATRICIANS (N=362)	PAEDIATRIC GE* (N=72)	INTERNAL MEDICINE GE (N=48)
Overall mean score	40.4% (SD ±14.2)	53.9% (±15.9)	75.3% (±13.9)	55.1% (±12.5)
Epidemiology and clinical presentation	32.7% (SD±16.5)	47.8% (±17.6)	69.9% (±18.1)	50.7% (±14.6)
Diagnostic procedure	36.2% (SD±18.6)	49.1% (±22.8)	76.2% (±15.4)	55.4% (±22.3)
Treatment and follow-up	51.7% (SD±19.3)	65.5% (±19.1)	80.6% (±16.5)	59.9% (±14.8)

* p<0,001

Table 1. Results achieved by primary care physicians and gastroenterologists (GE) according to different subsections of the questionnaire in Central Europe and Danube region.

Conclusion: The knowledge about CD among HCPs in Danube region is not satisfactory. However, paediatric GE achieved highest scores, which might be related to a higher awareness about the burden of CD in this group. Also, compared to previous study in Central Europe, there has been a significant rise in the knowledge of paediatric GE, showing the benefit of various awareness raising activities that were carried out, also in the scope of the Focus IN CD project. It has been shown that various learning activities can improve the knowledge of HCPs and reduce the number of unrecognized patients and unnecessary diagnostic delays.

Disclosure: Nothing to disclose.

P0182

IMMUNE RESPONSES TO COVID-19 VACCINES IN CELIAC DISEASE

K.E.A. Lundin¹, J.H. Ibsen², F. Lund-Johansen³

¹K. G. Jebsen Coeliac Disease Research Centre, University of Oslo and Oslo University Hospital, Gastroenterology, Oslo, Norway,

²University of Oslo, Oslo, Norway, ³University of Oslo, Institute of Immunology, Oslo, Norway

Contact E-Mail Address: jostein.ibsen@gmail.com

Introduction: SARS-CoV-2 infection and development of the disease Covid-19 is a serious threat to our society. Effective vaccines have now entered the market, but most patient populations were not included in the registration clinical trials. There is evidence that patients with celiac disease (CeD) have reduced effect of vaccines such as the hepatitis B vaccine. Hence, we investigated the humoral response to COVID-19 vaccines (Chadox1, Corminaty and Spikevax) in CeD patients and healthy controls.

Aims & Methods: Patients with biopsy confirmed CeD diagnosis from patient biobank at Oslo University Hospital (OUH) were invited to donate serum samples before and after vaccination. We sent out 1537 invitations, and received adequate samples from 85 individuals, these were compared with similar samples from 238 healthy controls. Sera were analyzed for

content of antibodies to the Spike protein from SARS-CoV2 and the receptor-binding domain (RBD). The results were then converted into BAU/ml to compare.

Results: Post vaccination analysis showed overlap of antibody levels between CeD and healthy controls. On average, the CeD patient group had 5555.0 binding antibody units per milliliter (330.1 SD) while the average in healthy controls was 5419 (184,7 SD).

Conclusion: The humoral response to SARS-CoV-2 vaccines in CeD patients is similar to that observed in healthy controls.

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P0183

IS THE GLUTEN-FREE DIET A RISK FACTOR FOR FATTY LIVER DISEASE IN CELIAC DISEASE?

A. Ben Mohamed¹, M. Yakoubi¹, M. Medhioub¹, A. Khsiba¹, M. Moufida¹, M.L. Hamzaoui¹, M.M. Azzouz¹

¹Mohame Taher Maamouri Hospital, Gastroenterology, Nabeul, Tunisia

Contact E-Mail Address: asmabenmed2014@gmail.com

Introduction: Fatty liver disease (NAFLD) is a common condition in the general population, and its prevalence during diagnosis of celiac disease (CD) appears to be similar to that of the general population. The contribution of the gluten-free diet (GFD) in its genesis is still a subject of controversy.

Aims & Methods: The aim of our study was to determine the prevalence of NAFLD during CD and to study the role of the GFD in the onset of advanced fibrosis. We conducted a retrospective study including patients with CD among a period of 6 years. Two groups were identified according to the observance of the GFD;

Group 1: Good compliance,

Group 2: Poor compliance.

Compliance was evidenced by clinical, biological and endoscopic remission. Fibrosis was studied by the Fibrosis 4 (FIB 4) score in both groups. Patients with diabetes mellitus, dyslipidemia, excessive alcohol consumption, body mass index > 30, chronic liver disease and those with follow-up less than 12 months were excluded.

Results: The study involved 70 patients middle-aged of the 35-year-old [15- 65] and with a sex ratio M / F of 0.28. The body mass index was less than 20 in 30% of the cases, between 20 and 25 in 54% of the cases and between 25 and 30 in 6% of the cases.

Group 1 contained 72% of the cases and group 2 contained 28% of the cases. The evaluation of Fibrosis by the FIB score 4 in group 1 showed; Absence of fibrosis (FIB 4 <1.30) in 80% of patients, F3 / F4 Fibrosis (FIB 4> 2.67) in 18% of patients, indeterminate fibrosis or gray area in 2% of patients.

In group 2; all patients had an F0 fibrosis score. In analytical study; adherence to the GFD was not correlated with F 3 / F 4 Fibrosis (p = 0.22).

Conclusion: In our series, the prevalence of NAFLD was 18% in patients complying with the GFD. In the analytical study, the GFD was not associated with an increased risk of developing NAFLD, which joins some studies.

Disclosure: Nothing to disclose.

P0184

PREVALENCE AND CHARACTERISTICS OF PEOPLE AVOIDING GLUTEN WITHOUT CELIAC DISEASE: A LONG-TERM POPULATION-BASED FOLLOW-UP STUDY

M. Tiainen¹, K. Kaukinen^{1,2}, T. Jääskeläinen³, N. Kaartinen³, H. Rissanen³, H. Huhtala⁴, K. Kurppa^{1,5,6}, J. Taavela^{1,2}

¹Tampere University, Celiac Disease Research Center, Tampere, Finland, ²Tampere University Hospital, Department of Internal Medicine, Tampere, Finland, ³Finnish Institute for Health and Welfare, Helsinki, Finland, ⁴Tampere University, Tampere, Finland, ⁵Tampere University, Tampere Center for Child, Adolescent, and Maternal Health Research, Tampere, Finland, ⁶University Consortium of Seinäjoki, Seinäjoki, Finland

Contact E-Mail Address: juha.taavela@tuni.fi

Introduction: To evaluate the prevalence, incidence, and characteristics of people avoiding gluten without celiac disease in 2000 and 2011 in a large population-based cohort.

Aims & Methods: Comprehensive health- and diet-related data were collected in nationwide Health 2000 and 2011 surveys comprising 5,978 and 4,268 individuals, forming representative samples for 2,946,057 and 2,079,438 Finnish adults. Samples for transglutaminase antibody (TGA) testing were available from 96.6% and 90.6%, respectively. Altogether 3,424 patients participating in both surveys comprised a prospective follow-up cohort. Non-celiac subjects who were on a gluten-free diet and had no positive TGA formed the study cohort.

Results: The prevalence of non-celiac gluten-avoiding individuals was 0.2% in 2000 and 0.8% in 2011 ($p < 0.001$), with an annual incidence rate of 51 per 100,000 persons in the prospective cohort. These subjects had more frequent visits to the doctor annually (mean 6.2 vs. 3.7, $p = 0.010$), had more often irritable bowel syndrome (6.5% vs. 1.7%, $p = 0.040$) and lactose intolerance (22.6% vs. 7.5%, $p = 0.002$), and maintained lactose-free diet (41.9% vs. 12.0%, $p < 0.001$) and a specific food restriction for allergy (9.7% vs. 2.9%, $p = 0.025$) more often than the gluten-using survey participants. No difference between the groups was seen in demographic data, body mass index or presence of autoimmune diseases.

Conclusion: The number of gluten-avoiding individuals without celiac disease quadrupled within a decade, comprising almost one percent of the population in the end of the study. These subjects had higher use of health-care services and increased prevalence of also other dietary restrictions.

Disclosure: Nothing to disclose.

P0185

SMALL INTESTINAL NEUROENDOCRINE NEOPLASMS WITH PANCREATIC METASTASES

A.C. Milanetto¹, A.-L. Gais Zurcher¹, C. Pasquali¹

¹Università degli Studi di Padova, Department of Surgery, Oncology and Gastroenterology, Padova, Italy

Contact E-Mail Address: acmilanetto@unipd.it

Introduction: Small intestinal neuroendocrine neoplasms (NENs) present in advanced stage with liver or peritoneal metastases. The occurrence of pancreatic metastases has been rarely reported. We reviewed our experience in small intestinal NENs observed from 2006 to 2020 in our Unit to detect a pancreatic involvement in these patients.

Aims & Methods: The objective is to evaluate the results of pancreatic surgery and survival in patients with pancreatic metastases from small intestinal NENs. Among 47 patients with small intestinal NENs (including duodenum) observed, five patients showed a pancreatic involvement. Follow-up to December 2021.

Results: Patients enrolled in the study were 3 F/2 M, averaging 60 years. All the patients but one had a synchronous pancreatic involvement at surgery. The mean primary tumor size was 2.9 (range 1.4-5.5) cm. All patients presented with lymph-node metastases. Only two patients had liver metastases and one had lung metastases.

One patient had a MEN4 syndrome with acromegaly. In one patient the pancreatic lesion was found 8 years after surgery in progressive disease. In one patient the lesion had progression 3 months after surgery and she died shortly after with jaundice and liver failure.

Four patients underwent surgery for the pancreatic metastases: one enucleation, one duodenum-preserving pancreatic head resection, one distal pancreatectomy, and one pancreatico-duodenectomy. Post-operative complications occurred in two patients: a pancreatic fistula (grade B) and an infected abdominal fluid collection which needed reoperation.

Three patients died 3, 34 and 92 months after surgery, respectively. Two patients are still alive with disease 10 and 15 years after surgery, respectively.

Conclusion: Secondary pancreatic lesions in small intestinal NENs are an uncommon finding, but they occurred in up to 11% of cases in our experience. Single pancreatic metastases may be resected with a long-term survival.

Disclosure: Nothing to disclose.

P1026

DISTINCTIVE ENDOSCOPIC FINDINGS PREDICT THE PROGRESSION OF PRIMARY SMALL-BOWEL FOLLICULAR LYMPHOMA

A. Sumioka¹, S. Oka², Y. Matsubara², A. Tsuboi¹, H. Tanaka¹, K. Yamashita¹, H. Takigawa¹, T. Kotachi¹, R. Yuge¹, Y. Urabe³, K. Boda⁴, T. Kohno⁴, H. Okanobu⁴, Y. Kitada⁵, K. Arihiro⁶, S. Tanaka¹

¹Hiroshima University Hospital, Endoscopy, Hiroshima, Japan,

²Hiroshima University Hospital, Gastroenterology and Metabolism,

Hiroshima, Japan, ³Hiroshima University, Regeneration and Medicine Center for Translational and Clinical Research,

Hiroshima, Japan, ⁴Hiroshima Red Cross Hospital & Atomic-Bomb Survivors Hospital, Gastroenterology, Hiroshima, Japan,

⁵Prefectural University of Hiroshima, Health and Science,

Hiroshima, Japan, ⁶Hiroshima University Hospital, Anatomical Pathology, Hiroshima, Japan

Contact E-Mail Address: hikoaki3@hiroshima-u.ac.jp

Introduction: Primary small-bowel follicular lymphoma (FL) is mainly diagnosed as a duodenal lesion in esophagogastroduodenoscopy. Recently with the widespread use of small-bowel endoscopy, FL in the jejunum and ileum can be detected. Most patients with small-bowel FL are diagnosed at the localized stage with the watch and wait policy. However, the predictive factors for the progression of small-bowel FL have not been clarified.

Aims & Methods: This study aims to examine the predictive factors for the progression of primary localized stage small-bowel FL based on the clinicopathologic and endoscopic findings. We enrolled 60 consecutive patients with primary small-bowel FL diagnosed at two tertiary hospitals between January 2005 and December 2020, who have localized stage (clinical stage I-II1 of Lugano classification), low grade (WHO grade 1-2), and low tumor burden (LTB) according to the criteria of *Groupe d'Etude des Lymphomes Folliculaires* (GELF) with the watch and wait policy.

We examined the predictive factors for progression according to the clinicopathologic and endoscopic findings. Endoscopic findings were focused on the color tone (white or similar to the peripheral mucosa), horizontal location of follicular lesions (circumference $\geq 1/2$ or $< 1/2$), fusion of follicular

lesions (fusion [+]) or [-]), and protruded lesion ≥ 6 mm. Progressive disease (PD) was defined as either progression of clinical stage, extension of intestinal lesions, or transformation to diffuse large B-cell lymphoma.

Results: PD was observed in 12 patients (20%), including progression of clinical stage in six patients (10%), extension of intestinal lesions in five patients (8%), and transformation to diffuse large B-cell lymphoma in one patient (2%) (mean observation period 76.9 ± 56.6 months).

In the multivariate analysis, “circumference $\geq 1/2$ ” (OR 8.12, 95% CI 1.34–49.0, $P < 0.05$) and “fusion (+)” (OR 12.46, 95% CI 1.51–102.7, $P < 0.05$) were significant predictive factors for progression. Kaplan–Meier analysis of “circumference $\geq 1/2$ ” and/or “fusion (+)” versus “circumference $< 1/2$ ” and “fusion (-)” showed that progression-free survival was significantly shorter in the “circumference $\geq 1/2$ ” and/or “fusion (+)” groups.

Three out of the 12 patients with exacerbations continued with the watch and wait policy because they met the criteria of GELF for LTB (mean observation period, 82.1 months). The other nine patients received rituximab alone or combined with rituximab chemotherapy. Patients who received rituximab alone or combined with rituximab chemotherapy achieved complete response and had no relapse (mean observation period, 63.5 months).

Conclusion: In the watch and wait policy of patients with primary localized stage small-bowel FL, endoscopic findings of “circumference $\geq 1/2$ ” and “fusion (+)” were the significant predictive factors for progression.

Disclosure: Nothing to disclose.

P0186

HEMORRHAGE POTENTIAL OF SMALL BOWEL ANGIOECTASIAS: CORRELATION WITH HAEMOGLOBIN VALUES

A.I. Ferreira^{1,2,3}, T. Lima Capela^{1,2,3}, V. Macedo Silva^{1,2,3}, C. Arieira^{1,2,3}, S. Xavier^{1,2,3}, P. Boal Carvalho^{1,2,3}, B.J.F. Rosa^{1,2,3}, M.J. Moreira Basto^{1,2,3}, J. Berkeley Cotter^{1,2,3}

¹Hospital Senhora da Oliveira – Guimarães, Gastroenterology Department, Guimarães, Portugal, ²Life and Health Sciences Research Institute (ICVS), School of Medicine, University of Minho, Braga, Portugal, ³ICVS/3B's, PT Government Associate Laboratory, Guimarães/Braga, Portugal

Contact E-Mail Address: tiagolimacapela@gmail.com

Introduction: Small bowel angioectasias often present as overt or occult obscure gastrointestinal bleeding.

Aims & Methods: The aim of this study was to evaluate the characteristics of the angioectasias found in small bowel capsule endoscopy (SBCE) and correlation with patients' haemoglobin value. A retrospective and unicentric study examining SBCE performed during a 3-year period was conducted, selecting those in which angioectasias were reported. Patients' demographic and biochemical data were recorded, as well as the number, size and location of angioectasias. Patients with red spots, erythematous patch or active bleeding without the identification of any lesion were not included.

Results: A total of 62 SBCE reported angioectasias, with half of the patients having angioectasias exclusively in the first tertile. In patients with small bowel angioectasias, as age increases, the mean haemoglobin value decreases ($r = -0.482$, $p < 0.001$). Additionally, as the number of angioectasias in the first tertile increases, the patient's haemoglobin value decreases ($rs = -0.317$, $p = 0.025$), which did not occur in patients with angioectasias in the second or third tertile.

Overall, patients with well filled angioectasias had a lower mean haemoglobin value (8.2 ± 2.5 g/dL) the year before undergoing SBCE, with a mean difference of 1.9 g/dL ($p = 0.016$). This was also observed in patients with angioectasias in the first tertile, who had lower mean haemoglobin value

(7.7 ± 2.0 g/dL) the year before undergoing SBCE, with a mean difference of 2.3 g/dL ($p = 0.003$). However, this was not observed in patients with angioectasias in the second or third tertile. Patients who presented with overt obscure gastrointestinal bleeding (Mdn=4,6) experienced a higher drop in haemoglobin value, $U = 105.50$, $z = -2.41$, $p = 0.016$.

Conclusion: Small bowel angioectasias were more common within the first tertile. A higher number of angioectasias and well filled angioectasias found within the first tertile were associated with lower mean haemoglobin values at presentation. Patients with overt obscure gastrointestinal bleeding had a higher drop in haemoglobin value.

Disclosure: Nothing to disclose.

P0187

CRYPTOGENIC MULTIFOCAL ULCERO-STENOSING SMALL BOWEL ENTEROPATHY (CMUSE): DOES IT EXIST IN CHILDREN?

A. Samanta¹, S.K. Singh¹, M. Sen Sarma¹, A. Srivastava¹, U. Poddar¹, A. Mandelia², V. Agarwal³, S. Kumar Yaccha¹, R. Lal²

¹Sanjay Gandhi Post Graduate Institute of Medical Sciences, Department of Pediatric Gastroenterology, Lucknow, India,

²Sanjay Gandhi Post Graduate Institute of Medical Sciences, Department of Pediatric Surgery, Lucknow, India, ³Sanjay Gandhi Post Graduate Institute of Medical Sciences, Department of Pathology, Lucknow, India

Contact E-Mail Address: arghyasamanta2905@gmail.com

Introduction: Cryptogenic multifocal ulcerous stenosing enteritis (CMUSE) is a rare disease that mimics various chronic inflammatory and ischemic strictures with considerable dilemmas in management.¹ Although it is increasingly reported in adults, literature in children is scarce.¹⁻² We aimed to distinguish characteristics of CMUSE that could differentiate from small bowel Crohn's disease (SBCD) and intestinal tuberculosis (ITB) in children.

Aims & Methods: Confirmed cases of CMUSE presenting to a pediatric gastroenterology referral center with the following criteria were analysed³: (1) unexplained superficial multiple small bowel strictures with or without ulceration; (2) no signs of systemic inflammation (3) not satisfying diagnostic criteria for SBCD and ITB. The clinical details and investigative profile (imaging, small bowel or capsule endoscopy, laparotomy and histopathology) and response to treatment were noted. Poor outcome was defined as progression of diseases despite surgery and or immunosuppression.

Results: CMUSE was diagnosed in 12 of 47 (25%) of isolated small bowel and ileocecal strictures referrals (table 1).

Presentations were obscure gastrointestinal bleeding (83%), protein losing enteropathy (41%), subacute obstruction (75%) and/or short stature (75%). Four children were diagnosed on capsule endoscopy, rest on imaging and laparotomy. Capsule retention occurred in two. Upfront immunosuppression [steroids and azathioprine, median duration 6 months, interquartile range (IQR) 4-17 months] failed in all 6 patients requiring surgery (intestinal resection). Upfront surgery followed by immunosuppression [median duration 24 months, IQR 18-36 months] was required in 6 patients. Two patients each from the above groups ($n = 4$) had ulcer-stricture recurrence requiring repeat intestinal resection.

None of the recurrence patients had change in the phenotypic presentation. Poor outcome was seen in all 4 patients with recurrence. In the total follow-up period of 33 months (IQR 5-216) months, 8 (67%) showed improvement in growth parameters.

Conclusion: CMUSE is an important entity underdiagnosed in children. Characteristic features on enteroscopy, laparotomy and histopathology differentiate this disease from small bowel crohn's disease and intestinal TB. Two-third patients have favorable outcome with combination of surgery and immunosuppression.

Characteristics	CMUSE, n=12	Small bowel crohn's disease, n=6	Intestinal TB, n=21
Age (months), median (IQR)	15 (14-17)	14 (12-16)	14 (12-17)
Disease duration (months), median (IQR)	45 (29-63)	12 (6-17)	9 (4-14)
Disease distribution	Jejunum (67%) Jejunum + proximal ileum (33%)	Jejunum 33%, Mid Ileum 33% Jejunum + mid ileum 34%	Ileo-caecal (66.7%)
Lesion description (enteroscopy or laparotomy)	Multiple, short (1-2 mm) regularly-spaced, mostly superficial, (semi) circumferential ulcers with variable degrees of narrowing.	Deep, linear ulcers, long narrowed segment (15-25 mm), cobblestoning and skip areas	Deep, circumferential or linear ulcers (100%)with ileocecal valve deformity (67%)
Necrotic lymph nodes, n (%)	0	0	11(52%)
Peritoneal involvement and loculated ascites, n(%)	0	0	4(19%)
Upstream dilatation, n (%)	4(33%)	3(50%)	12 (63%)
Comb sign on imaging, n(%)	0	6(100%)	0
Histopathological features on intestinal specimen	Mild mixed inflammatory cell infiltrates in mucosa and submucosa. No granulomatous,transmural or vasculitic changes. No fat creeping.	Transmural inflammation with fat creeping (100%), Non-caseating granuloma(17%)	Caseating granuloma(48%) with Ziel-Neelson stain positivity (42%)

Table 1: Salient features of patients with CMUSE, small bowel crohn's disease and intestinal TB:

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Disclosure: Nothing to disclose.

P1033

ASSOCIATION BETWEEN EUPATILIN AND THE REDUCTION OF SMALL BOWEL BLEEDING IN ASPIRIN USERS: A POPULATION-BASED COHORT STUDY USING NATIONWIDE DATABASE OF NATIONAL CLAIM DATA IN KOREA

J.H. Nam¹, H.S. Lee², D.J. Oh¹, J.-K. Kang¹, H.J. Ahn³, Y.J. Lim¹
¹Department of Internal Medicine, Dongguk University Ilsan Hospital, Dongguk University College of Medicine, Goyang, Korea (Republic of), ²Department of Internal Medicine, School of Medicine, Kyungpook National University, Kyungpook National University Hospital, Daegu, Korea (Republic of), ³Data analytics team, Linewalks Inc., Seoul, Korea (Republic of)

Contact E-Mail Address: drnamesl@gmail.com

Introduction: Aspirin is among the most commonly prescribed oral pills for therapeutic or prophylactic purposes and is often long-term prescribed in clinical settings. Clinical expansion of capsule endoscopy (CE) has revealed that low dose aspirin frequently cause small bowel (SB) injury by disrupting mucosal barrier. Small-sized randomized controlled or cross-over studies have shown that mucoprotective agent (MPA) has a protective effect on SB mucosa in aspirin or NSAID users. However, the relevant evidence is still lacking other than misoprostol, and there are no large-scale studies.

Aims & Methods: We evaluated the protective effect of MPA on SB bleeding in aspirin users using the claim data from the National Health Insurance Service (NHIS).

An aspirin-SB cohort were constructed using the NHIS claim data since CE has been insured. Follow up period was limited to a maximum of 24 months. Suspected SB bleeding was defined as anemia, melena or hematochezia occurred within 4 weeks before and after CE performed. Cox proportional hazard model included sex, age, Charlson comorbidity index (CCI), duration of aspirin use, concurrent use of anticoagulants, MPAs, and acid suppressants such as proton pump inhibitor (PPI) and histamine-2 receptor antagonist (H2RA). Subgroup analyses according to the use of acid suppressants were performed and cumulative hazards were compared among the various categories of gastrointestinal (GI) drugs.

Results: A total of 15,542 aspirin users were included. Multivariate cox model showed that anticoagulant use (HR=3.22), high CCI score (HR=2.10 and HR=3.54, respectively, in score 1 and ≥2), and concurrent use of PPI (HR=2.85) were significantly associated with increased occurrence of SB bleeding. SB bleeding was more frequently occurred in cases with concurrent use of acid suppressants vs. non-use (1.3%, vs. 0.5%).

Whereas, it was inversely associated with eupatilin use (HR=0.35, p=0.013). In subgroup analysis, only eupatilin significantly reduced the risk of SB bleeding among various MPAs in aspirin users with concomitant use of acid suppressant (HR=0.23 vs 1.96 and 2.55).

Conclusion: Eupatilin was associated with reducing the risk of SB bleeding in aspirin users with concomitant use of acid suppressant. Eupatilin use should be considered in aspirin users and especially concomittent users of acid suppressant in patient with high-risk of GI bleeding.

Disclosure: Nothing to disclose.

Poster presentations

Nutrition

Poster Presentations Nutrition

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P0188

THE EVIDENCE REGARDING BODY COMPOSITION PARAMETERS IN PATIENTS WITH NON-ALCOHOLIC FATTY LIVER DISEASE: A SYSTEMATIC REVIEW OF LONGITUDINAL STUDIES AND META-ANALYSIS

D. Mátis¹, S. Váncsa^{1,2,3}, P. Hegyi^{1,3,2}, B. Teutsch^{1,3}, T. Tornai², F. Dembrovszky^{1,3}, B. Erőss², G. Par⁴

¹Semmelweis University, Centre for Translational Medicine, Budapest, Hungary, ²Semmelweis University, Division of Pancreatic Diseases, Heart and Vascular Center, Budapest, Hungary, ³University of Pécs, Institute for Translational Medicine, Szentágotthai Research Centre, Medical School, Pécs, Hungary, ⁴University of Pécs, Division of Gastroenterology, First Department of Medicine, Pécs, Hungary

Contact E-Mail Address: dora.matis@icloud.com

Introduction: Non-alcoholic fatty liver disease (NAFLD) has emerged as one of the most common causes of chronic liver disease worldwide and represents a global public health problem. The most effective treatment for NAFLD is weight loss, however, it has been shown that body composition has a crucial effect on NAFLD resolution. Anyhow, most studies on this topic were cross-sectional and therefore could not demonstrate a causal relationship between certain parameters and NAFLD resolution.

Aims & Methods: In this systematic review and meta-analysis, we aim to evaluate the correlation between different body composition parameter changes and the resolution of NAFLD in longitudinal studies.

This study was registered on PROSPERO under registration number CRD42021278584. A systematic search was performed in Embase, MEDLINE (via PubMed), and Cochrane Central Register of Controlled Trials (CENTRAL) up to September 26, 2021. Studies were eligible if they reported on the correlation between the change of hepatic steatosis state and the change of various body composition parameters in adults with NAFLD. We calculated pooled correlation coefficients (R) with 95% confidence intervals (CIs) using a random-effect model. We separated Spearman's and Pearson's correlation analyses.

Results: Out of 21612 studies after search, altogether we included 14 studies in our quantitative and qualitative synthesis. Based on three studies containing 175 patients we found a moderate correlation between visceral adipose tissue (VAT) decrease and liver fat content reduction (Pearson's R=0.33, CI: 0.19-0.46).

Similarly, in two studies with 85 patients, VAT change showed a moderate correlation with steatosis decrease in Spearman's correlation analysis (R=0.49, CI: 0.22-0.69). On the other hand, subcutaneous adipose tissue (SAT) change showed a moderate correlation with steatosis reduction in two studies (n=163, Pearson's R=0.42, CI: 0.29-0.54).

We also analyzed the correlation between body fat mass, visceral fat rating, skeletal muscle area, and muscle bodyweight ratio change and steatosis reduction, however, we included only one study in each analysis.

Conclusion: We found a moderate correlation between the VAT and SAT content change and liver fat reduction. Body composition parameter measurement should be introduced in the management of NAFLD.

Disclosure: Nothing to disclose.

P0189

MODIFIED HIDA TEST FOR THE DIAGNOSIS OF BILE REFLUX IN PATIENTS WHO UNDERWENT MINI-GASTRIC BYPASS BARIATRIC SURGERY

W. Sbeit¹, A. Mari², M. Faraj³, E. Arnon-Sheleg⁴, T. Khoury⁵

¹Galilee Medical Center, Gastroenterology, Naharia, Israel,

²Nazareth Hospital EMMS, Gastroenterology Department,

Nazareth, Israel, ³The Baruch Padeh Medical Center, Surgery,

Teberia, Israel, ⁴Galilee Medical Center, Department of Nuclear

Medicine and Diagnostic Radiology, Naharia, Israel, ⁵Galilee

Medical Center, Department of Gastroenterology, Naharia, Israel

Contact E-Mail Address: tawfik.khoury.83@gmail.com

Introduction: The mini gastric bypass surgery (MGB) is a relatively simple surgical procedure which is gaining popularity in recent years. Recent studies reported symptomatic biliary reflux gastritis and esophagitis as predominant complications. Hepatobiliary scintigraphy (HIDA) is the test for diagnosis of bile reflux, but there are very few published studies regarding its use for detecting bile reflux after bariatric surgery.

Aims & Methods: The aim of this study was to define an optimized HIDA scintigraphy protocol for demonstrating bile reflux in post MGB patients and demonstrate the prevalence of bile reflux in symptomatic patients with reflux symptoms.

The study was conducted prospectively. Patients after MGB with complaints suggestive of bile reflux, were included. All patients underwent HIDA scintigraphy with a dedicated protocol for demonstrating bile reflux in the Nuclear Medicine Department in the Galilee Medical Center. The presence of the isotope in the stomach or esophagus was reported for each patient as well as the prevalence and severity of bile reflux.

HIDA scan protocol: The patients were instructed to fast for at least 4 hours prior to the scan. mCi eHIDA (commercial details) were injected intravenously. Planar dynamic and static images of the upper abdomen and chest were acquired with the patient in a prone position immediately following the HIDA injection for up to 30 minutes. At this time, the patient was given a small piece of chocolate to eat. If no obvious reflux was seen to the stomach pouch or esophagus, the patient was given a standard meal of a cheese or omelet sandwich (according to patient's preference).

Immediately following the meal, dynamic and static planar images were acquired for up to 30 minutes. If no reflux was seen, reflux encouraging maneuvers were conducted. Immediately following the maneuvers, dynamic and static planar images were acquired for up to 15 minutes. If at any time the isotope was noted in the esophagus on the planar images, SPECT/CT of the upper abdomen and chest was acquired immediately. If no obvious reflux was seen until the end of the scan protocol, SPECT/CT was acquired at the end of the protocol, up to 120 minutes after injection.

Results: Nineteen patients were included. The mean time from surgery to the scan of 22.4 months. Bile reflux into the gastric pouch was documented in 11 patients (53%). In 3 patients the reflux to the stomach pouch was severe (27%), in 2 patients moderate (18%) and in six patients mild (55%). Bile reflux into the esophagus was documented in 4 patients (21%). In 1 patient the reflux was severe (25%) and in the rest mild (75%).

Comparison was conducted between the 11 patients who had bile reflux (group A) as compared to the 8 patients who didn't have (group B). Group A had a significantly higher rate of vomiting and heartburn and regurgitation (63.6% and 100%, P=0.02) as compared to group B (12.5% and 62.5%, P=0.04), respectively.

Moreover, group A had a higher rate of esophagitis (40%), as compared to group B (0), $P=0.02$. On regression analysis to elucidate whether hiatal hernia or resected gallbladder were risk factors for bile acid reflux showed no association with either hiatal hernia (OR 1.28, 95% CI 0.16-10.45, $P=0.81$) and resected gallbladder (OR 0.57, 95% CI 0.09-3.64, $P=0.55$).

Conclusion: The tailored HIDA scan protocol used for this study detected bile reflux in more than half of the post MGB patients included in the study. We believe that the changes introduced to the protocol increase the scans sensitivity while being technically easy to reproduce with good patient tolerability.

Disclosure: Nothing to disclose.

P0190

EVALUATION OF THE EFFICACY AND SAFETY OF ENDOSCOPIC SLEEVE GASTROPLASTY (ESG) IN THE MANAGEMENT OF PATIENTS WITH OBESITY IN A FOLLOW-UP FROM 12 TO 48 MONTHS

B. Queiroz Sander¹, D.T.H. de Moura², L.R. Alberti³

¹Sander Medical Center, Bariatric Endoscopy, Belo Horizonte, Brazil, ²Faculdade de Medicina da Universidade de São Paulo, Gastroenterology Department, São Paulo, Brazil, ³Universidade Federal de Minas Gerais, Surgery Department, Belo Horizonte, Brazil

Contact E-Mail Address: brunosander@hotmail.com

Introduction: According to the World Health Organization (WHO), in 2019, 2.3 billion people were overweight. In Brazil, overweight already affects 52.5% of the adults and this rate only increases every year.

Endoscopic Sleeve Gastroplasty (ESG) is a promising less-invasive technique that allows the suture of the stomach through endoscopy. Its use is increasing, but just short-term follow-up studies are available in the literature.

Aims & Methods: To evaluate the safety and efficacy of ESG, in the short and medium-term follow-up in patients with obesity.

This is a single center retrospective cohort study of prospectively collected data including participants whom underwent ESG between July 2017 and August 2020.

A total of 189 patients were included in the analysis and were divided into different groups, with follow-up times ranging from 12 to 48 months, depending on the interval between procedure and data collection.

All patients were at least 18 years old, had a minimum body mass index (BMI) of 30 kg/m² (grade I obesity) and had not previously undergone bariatric surgery.

Variables that could influence the effectiveness and durability of ESG (Suture patterns, Oversuture, Resuture, Number of threads, Number of bytes, Weight Lost, AWL%, EWL%, Safety, Efficacy, Durability, Argon Plasma Coagulation use and Follow-up with Nutritionist and Psychologist), intra-procedural adverse events (AEs), post-procedure AEs, and follow-up data for up to four years after the procedure, at 12-month intervals, were analyzed.

Results: Regarding safety, there was no intra-procedural AEs. Post-procedural AEs were observed in 7.9% of patients. All AEs were mild and occurred in the first 15 days after the procedure including 33% self-limited gastric bleeding and 67% vomiting.

Regarding efficacy, 87.8% of the patients achieved more than 10% absolute weight loss (%AWL) and more than 25% excess weight loss (%EWL). Mean %AWL was 21.09% with a %EWL of 70.83%. The %AWL values at each time interval were: 16.54% (12M), 20.15% (24M), 19.77% (36M) and 21.09% (48M), and the %EWL were: 56.04% (12M), 69.7% (24M), 70.5% (36M) and 70.8% (48M).

		Weight (Kg)	Weight Lost	% AWL	% EWL	BMI
	Number of Patients	Average	Average	Average	Average	Average
Initial Time	189	99.37 [97.3; 101.44]	...	...	...	36.08 [35.66; 36.5]
12 months	189	82.8 [81.1 ; 84.5]	-16.82 [-17.78 ; -15.87]	-16.54% [-17.78 ; -15.87]	56.04% [53.30% ; 58.78%]	30.13 [29.73 ; 30.52]
24 months	149	78.52 [76.51 ; 80.53]	-20.26 [-21.60 ; -18.92]	-20.15% [-21.60 ; -18.92]	69.69% [65.81% ; 73.58%]	28.67 [28.17 ; 29.16]
36 months	51	78.76 [74.79 ; 82.72]	-20.11 [-22.73 ; -17.49]	-19.77% [-22.73 ; -17.49]	70.54% [64.20% ; 76.89%]	28.41 [27.63 ; 29.19]
48 months	16	76.92 [68.17 ; 85.66]	-21.26 [-26.27 ; -16.24]	-21.09% [-26.27 ; -16.24]	70.83% [61.25% ; 80.42%]	28.66 [27.21 ; 30.10]

Table: Evolution of patients' weight by treatment time

Mean average absolute weight was 99.37 kilos, ending with an average absolute weight of 76.92 kilos, in the 48 months of follow-up group. The BMI presented a reduction from 36.08 kg/m² to 28.66 kg/m². Regarding the 12-month durability, the procedure was effective in 85% of the patients evaluated, with consolidation of fibrosis between the gastric folds, promoting the tubulization of the stomach (a format that mimics the surgical sleeve, with a reduction of more than 40% of the distensibility and gastric diameter, under endoscopic visualization).

Conclusion: ESG is safe and effective in the short and medium-term follow-up, with satisfactory durability of the gastric restriction (Tubulized Stomach). Follow-up with a nutritionist and psychologist has a positive effect on weight loss.

In addition, the use of five or more threads, more than 98 bytes, and the performance of the oversuture as reinforcement, increases the durability of the ESG, in the medium term, by maintaining the tubulized stomach. So, the oversuture U-pattern is more durable and more effective than the U-pattern.

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Disclosure: Nothing to disclose.

P0191

EFFICACY AND SAFETY OF ENDOSCOPICALLY IMPLANTED DUODENAL-JEJUNAL BYPASS LINERS VS. INTRAGASTRIC BALLOONS IN A REAL-WORLD POPULATION – A PROPENSITY SCORE MATCHING ANALYSIS

S. Theodoridou¹, R. Stengel², A. Aksan³, N. Hein⁴, H. Krammer⁵, O. Schröder⁶, J. Stein⁶

¹Obesity Centre, Sana Clinics Offenbach, Offenbach am Main, Germany, ²Internal Medicine Practice, Niesky, Germany, ³Justus-Liebig University, Institute of Nutritional Science, Giessen, Germany, ⁴Obesity Centre, DGD Clinics Sachsenhausen, Frankfurt am Main, Germany, ⁵Gastroenterologische Praxis, Mannheim, Germany, ⁶DGD Clinics Sachsenhausen, Department of Gastroenterology and Clinical Nutrition, Frankfurt am Main, Germany

Contact E-Mail Address: sophiatheodoridou@t-online.de

Introduction: Obesity is a major global health problem associated with comorbidities such as diabetes, cardiovascular disease and cancer. Bariatric surgery is recognised to be the most effective weight loss intervention, but it is highly invasive, costly and can have serious side effects. Intra-gastric balloon (IGB) placement by endoscopy has been shown to be comparatively well tolerated and effective in patients with obesity. The more recently introduced duodenojejunal bypass liner (DJBL) has also been found to induce significant weight loss and dramatically ameliorate type 2 diabetes mellitus (T2DM) by causing nutrients to bypass the duodenum.

Aims & Methods: We aimed to compare the efficacy of DJBL and IGB for induction of weight loss in patients with obesity. In this retrospective, propensity score-weighted observational cohort comparison, participants with a body mass index (BMI) of 30-55 kg/m², aged 18-70 years, were randomized to DJBL or IGB for 12 months. Patients were matched for age, gender and BMI.

Study outcomes were summarised as the changes in percentage excess body weight lost (%EBWL), total body weight lost (TBWL), and percentage total body weight lost (%TBWL).

Results: A total of 140 (70 DJBL, 70 IGB) of the 321 patients screened were matched by propensity score. Mean age was 44.1 ± 10.4 years, and the patients were predominantly female (61.4%). Baseline BMI was 42.0 ± 8.1 kg/m². At month 6, %TBWL in the DJBL group was 11.0 ± 6.5% versus 15.1 ± 9.5% for IGB (*p* < 0.05). After 12 months, %TBWL for the two groups was 12.7 ± 7.5% (DJBL) versus 13.6 ± 9.7% (IGB) (*p* = 0.996). The IGB cohort experienced significantly more adverse events than the DJBL group.

Conclusion: Both IGB placement and DJBL induce clinically meaningful weight loss. Although IGB seems to induce clinically superior weight loss in the first 6 months, after 12 months, the final weight loss was found to be similar. However, DJBL was associated with lower rates of complications and adverse events.

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P0192

COMPARATIVE EFFICACY AND SAFETY OF DIFFERENT INTRAGASTRIC BALLOONS IN A REAL-WORLD POPULATION – A PROPENSITY SCORE MATCHING ANALYSIS

N. Hein¹, S. Theodoridou², A. Aksan³, H. Krammer⁴, O. Schröder⁵, P. Staikov¹, J. Stein⁵

¹Obesity Centre, DGD Clinics Sachsenhausen, Frankfurt am Main, Germany, ²Obesity Centre, Sana Clinics Offenbach, Offenbach am Main, Germany, ³Justus-Liebig University, Institute of Nutritional Science, Giessen, Germany, ⁴Gastroenterological Practice, Mannheim, Germany, ⁵DGD Clinics Sachsenhausen, Department of Gastroenterology and Clinical Nutrition, Frankfurt am Main, Germany

Contact E-Mail Address: nhein@khs-ffm.de

Introduction: The liquid-filled intragastric balloon is an established alternative in the treatment of obesity and has been shown to be well tolerated and effective. However, comparative data on the efficacy and safety of commonly used balloon systems are scarce.

Aims & Methods: The aim of this study was to compare the efficacy and safety of the most commonly used balloon systems in Europe under everyday conditions. In a retrospective, multicentre, observational study (conducted May 2016 to Jun 2021), 202 participants with a BMI of 30-55 kg/m², aged 18-65 years, were followed up for 6 months.

The study outcomes were percentage excess body weight lost (%EBWL), and percentage total body weight lost (%TBWL), the primary endpoint being TBWL% at 6 months; primary and secondary safety endpoints were rates of early balloon removal (within 3 weeks after implantation) and detection of periprocedural complications.

Results: Of 202 patients in total, 68 (57/68 female, 39.1 ± 11.1 years) received a MedSil® balloon (BSB Medical GmbH, Lingen, Germany) and 134 (99/134 female, 41.8 ± 10.5 years) an Orbera® balloon (Apollo Endosurgery, Austin, TX, USA). Mean body mass index (BMI) was similar in each of the two groups at baseline, at 34.2 ± 5.5 kg/m² vs. 36.3 ± 7.2 kg/m², respectively. At month 6, %TBWL was 13.3 ± 9.1% in the MedSil group and 11.7 ± 8.2% in the Orbera group (*p* > 0.05).

When patients were classified according to balloon fill volume (<500 mL, 500-600 mL or >600 mL), no significant volume-related differences in weight loss outcome were observed. However, in those with a greater balloon volume, the rate of adverse events was significantly higher (21.8% vs 36.4%). Early balloon removal occurred in 17.6% of patients with MedSil and 15.8% with Orbera (*p* = 0.483).

Conclusion: Both balloon systems, MedSil and Orbera, induce clinically significant weight loss and have similar outcomes. However, independent of balloon type, the patients with a greater balloon fill volume experienced significantly more adverse effects. Since weight loss outcomes did not differ significantly according to balloon volume, it would appear prudent to decide on fill volumes cautiously in order to minimise complications of balloon therapy.

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P0193

THE IMPACT OF THE DUODENOJEJUNAL BYPASS LINER ON IRON HOMEOSTASIS

S. Hess¹, A. Aksan¹, O. Schröder², L. Tessmer², S. Ulrich-Rückert², J. Stein^{2,3}

¹Justus-Liebig University, Institute of Nutritional Science, Giessen, Germany, ²DGD Clinics Sachsenhausen, Department of Gastroenterology and Clinical Nutrition, Frankfurt am Main, Germany, ³Institute of Pharmaceutical Chemistry, Goethe University, Frankfurt am Main, Germany

Contact E-Mail Address: o.schroeder@em.uni-frankfurt.de

Introduction: Since obesity represents an increasing global concern and is associated with co-morbidities such as type 2 diabetes, hypertension and dyslipidaemia, it also increases the burden on health systems. In patients with severe obesity, bariatric surgery is being increasingly used to achieve both sustainable weight loss and metabolic improvement.

An alternative is the endoscopically inserted Endobarrier® duodenojejunal bypass liner (DJBL), which consists of an impermeable tube that excludes the duodenum and proximal jejunum from digestion. By allowing less fully digested food pulp to make contact with the mucosa only mid-jejunum, weight loss and improved diabetes control can be achieved. However, the question arises as to how this affects absorption of vitamins or essential trace elements such as iron, which is mainly absorbed in the anterior small intestine.

Aims & Methods: We aimed to measure iron parameters over the course of DJBL therapy to assess the impact of DJBL implantation on iron status in patients with obesity. The present study was conducted as a retrospective observational study in patients who underwent DJBL implantation at a specialist obesity centre in Frankfurt, Germany.

Following implantation, the DJBL remained in situ for 12 months. Laboratory parameters were assessed at baseline and after 1, 3, 6, 9 and 12 months, and BMI at baseline, 6 and 12 months. Blood samples were analysed for HbA_{1c}, CBC, blood lipids (LDL, HDL, triglyceride, cholesterol), iron status (serum ferritin, SF; transferrin; transferrin saturation, TSAT) and high-sensitivity CRP (hsCRP) using standard methodology. Inflammation was defined as hsCRP ≥5mg/dL.

Results: 17 patients with obesity (10f,7m; 52,4±10,6y), mean BMI 38.2±8.5 kg/m², were included in the study. Of these, 15 (88%) had been diagnosed with diabetes, 9 (53%) with hypertension and 14 (82%) with dyslipidaemia. DJBL implantation had a significant positive effect on BMI [(40.2 (32.4-65.2) at baseline; 33.1 (28.4-58.1) at month 6; 33.6 (26.7-7.8) at month 12 (p<0.001)] and HbA_{1c} [(8.3 (5.8-12.7) at baseline; 7.5 (5.1-10.5) at month 6; 6.8 (5.3-56.5) at month 12; p<0.001)] over the course of 12 months. During this period, no major changes were observed in levels of Hb, Hct, MCV, MCHC or transferrin. Only MCH showed a slight increase at 12 months (p<0.038).

However, during the implantation period, SF levels decreased consistently (p<0.047). TSAT showed no significant changes, remaining <20% at all time points. Similarly, hsCRP levels remained at ≥5 mg/dL. The observed decrease of ferritin levels <100 µg/L in the absence of changes in CRP concentrations may reflect increasing functional deficiency due to DJBL placement.

Conclusion: Implantation of the DJBL induced a sustained reduction in body weight. However, functional iron deficiency was observed at follow-up 6 months after implantation, with serum ferritin levels showing a constant decrease until the time of device removal.

These results need confirming in larger studies, but indicate a necessity for regular screening of iron parameters in patients undergoing DJBL therapy and consideration of intravenous iron replacement in patients diagnosed with functional iron deficiency.

Disclosure: Sina Hess, Lea Tessmer and Sandra Ulrich-Rückert have nothing to declare.

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Jürgen Stein: Consulting: Abbvie, Bristol Myers Squibb, Dr Schär, Falk, Ferring, Fresenius Kabi, Immundiagnostik, Janssen, Medice, MSD, Pfizer, Pharmacosmos, Shire, Takeda, Thermofisher, Vifor. Board member: Abbvie, Bristol Myers Squibb, Dr Schär, Ferring, Fresenius Kabi, Immundiagnostik, Janssen, MSD, NPS, Pharmacosmos, Takeda, Vifor and Shield. Lecturing fees: Vifor Pharma.

P0194

GHEE BUTTER FROM BOVINE COLOSTRUM ALLEVIATES INTESTINAL INFLAMMATION IN DEXTRAN SULFATE SODIUM-INDUCED COLITIS IN MICE

A. Tarasiuk¹, M. Talar¹, J.B. Krajewska¹, A. Binienda¹, A. Bartoszek¹, A. Fabisiak², P. Mosinska¹, K. Dziedziczak¹, K. Niewinna¹, M. Salaga¹, J. Fichna¹

¹Medical University of Lodz, Department of Biochemistry, Lodz, Poland, ²Medical University of Lodz, Department of Digestive Tract Diseases, Lodz, Poland

Contact E-Mail Address: tarasiuk.aleksandra@gmail.com

Introduction: Nutrition is closely linked to inflammatory bowel disease (IBD). The most recent research indicates that diet and nutrition play an important role in the disease's etiopathogenesis, though their specific role throughout the disease's clinical course is still unknown. Ghee butter from bovine colostrum (GBBC) is a clarified butter produced by heating milk fat to 40°C and separating the precipitating protein. Free fatty acid receptors (FFARs), which are expressed on intestinal epithelial cells, are members of the luminal-facing receptor family that respond to nutrients. As colostrum mainly contains fatty acids (FAs), immunoglobulins, maternal immune cells, we hypothesized that it may exert anti-inflammatory effects through FFARs.

Aims & Methods: Therapeutic activity and mechanism of action of GBBC was investigated in dextran sulfate sodium (DSS) mouse model of colitis, which recapitulates ulcerative colitis in humans. Quantitative biochemical examinations were performed to assess inflammation progress. qPCR was used to determine tight junctions (TJs) mRNA in distal colon samples collected from control, DSS-treated, DDS+GBBC-treated mice, and mice-treated DSS with the combination of GBBC+FFAR 1 or 4 antagonists. Enzyme-linked immunosorbent assays (ELISA) were performed to measure the level of inflammatory cytokines in colon tissue homogenates.

Results: GBBC (*per os*, 100µL/mouse) significantly reduced colon damage score, (myeloperoxidase) MPO activity, stool score, and concentration of fluorescein isothiocyanate (FITC) dextran in serum in comparison with DSS mice. GBBC notably reduced the level of TNFα, IL17, and IL23 while compared to the DSS mice group.

Moreover, administration of the FFAR4 antagonist followed by treatment with GBBC remarkably increased the anti-inflammatory effect of GBBC by reducing the production of IL17 and 23 and the IL6 level in comparison with DSS. Administration of GBBC alone restored the expression of OCLD1 and CLDN1 to the level of control as well as notably increased expression of these TJs mRNA above the basal level. FFAR1 antagonist combined with GBBC significantly potentiated this effect.

Importantly, attenuation of FFAR4 expression reversed the effect of GBBC, thus indicating that FFAR4 receptor may affect the expression of OCLD1 and CLDN 1 in the colon.

Conclusion: Our results suggest that GBBC displays anti-inflammatory effects in the mouse model of DSS-colitis, with the potential involvement of FFARs. This is the first study to show the anti-inflammatory potential of a nutritional supplement derived from GBBC in the colitis animal model.

Disclosure: Nothing to disclose.

P0195

SIGNIFICANT IMPROVEMENTS IN STRESS AND COGNITIVE OUTCOMES WITH BIFIDOBACTERIUM LONGUM 1714 SUPPLEMENTATION – A REAL-WORLD EXPERIENCE PROGRAMME IN ATHLETES

K. Sorensen¹, J. Kupuseravic², J. Jackman²

¹Novozymes, Medical Affairs, Cork, Ireland, ²ART Health Solutions, Science Team, Gateshead, United Kingdom

Contact E-Mail Address: kass@novozymes.com

Introduction: The physical and psychological demands of intense training have been associated with gut dysbiosis in athletes. The implications of this may extend beyond gastrointestinal health, affecting mental wellbeing and cognitive function via the microbiome-gut-brain axis¹. Clinical studies have demonstrated that probiotic supplementation with *Bifidobacterium longum* 1714 may improve perceived stress, energy/vitality and cognitive function^{2,3}. However, real-world data is limited.

Aims & Methods: This experience programme evaluated wellbeing and cognitive outcomes in athletes before and after 8 weeks of probiotic supplementation. Athletes volunteered or were referred to the experience programme by their nutritionist and/or coach, to receive a daily probiotic supplement containing *Bifidobacterium longum* 1714 (1x10⁹ colony-forming units) and B vitamins, for 8 weeks. Perceived sleep quality and energy levels were measured via an online survey prior to starting the programme, and at week 9 (post supplementation).

Perceived stress (Likert scale) and cognitive function including reaction time (Simple Reaction Time test), decision-making (adapted Stroop task), and distractibility (adapted Flanker task) were measured via the Omics™ app at weeks 1, 3, 4, 6 and 8. Data analysis compared the Loading period (weeks 1-4) vs the Observation period (weeks 6-8), including paired samples T-test for perceived stress and cognitive function data. Data are presented as the percentage of athletes who improved, and the average percentage change over time.

Results: 35 athletes completed the programme (75% aged 18-34 years, 25% aged 35-54 years; 81% male, 19% female; 61% team sports, 39% individual sports). During the observation period, 66% of athletes reported improvements in perceived stress (6% average improvement, p=0.015). Improvements in sleep quality and energy levels were reported in 58% and 54% of athletes respectively. Significant improvements in cognitive function were observed for reaction time (63% of athletes; 4% average improvement, p=0.008) and decision-making (72% of athletes; 5% average improvement, p=0.006). Distractibility improved in 43% of athletes (3% average improvement, p=0.196 ns). 87% would recommend the probiotic supplement to others.

Conclusion: These real-world data suggest that supplementation with *Bifidobacterium longum* 1714 may be associated with improvements in wellbeing and cognitive function in athletes, through modulation of the gut-brain axis. This supports the findings of cognitive benefits observed in clinical trials which investigated the bacterial strain without B vitamins in a general, healthy population^{2,3}, suggesting a strain-specific probiotic effect with broader applicability. Further research into the potential mode of action of this strain is warranted.

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Disclosure: K. Sorensen is a registered dietitian and employed by PrecisionBiotics (Novozymes), who developed and manufacture the *Bifidobacterium longum* 1714 strain and funded the programme.

The conduct of the programme, and analysis of results, was undertaken by J. Kupuseravic and J.S. Jackman from ART Health Solutions.

P0196

PATIENTS' EXPERIENCES OF DIETARY CHANGES DURING A STRUCTURED DIETARY INTERVENTION FOR IRRITABLE BOWEL SYNDROME

C. Weznaver¹, S. Nybacka¹, M. Simrén^{1,2}, H. Törnblom¹, S. Störsrud¹, S. Jakobsson³

¹University of Gothenburg / Institute of Medicine, Sahlgrenska Academy, Department of Molecular and Clinical Medicine, Göteborg, Sweden, ²University of North Carolina-Chapel Hill, Center for Functional GI and Motility Disorders, Chapel Hill, United States, ³University of Gothenburg / Institute of Health and care Sciences, Institute of Medicine, Gothenburg, Sweden

Contact E-Mail Address: cecilia.weznaver@vgregion.se

Introduction: Diet plays an important role in both triggering and alleviating gastrointestinal (GI) symptoms in irritable bowel syndrome (IBS). While research has focused on the effects of reducing poorly digested carbohydrates, i.e., the low fermentable oligo-, di-, monosaccharides, and polyols (FODMAP) diet, there are no studies investigating patients' experiences concerning the implementation of required dietary changes.

Aims & Methods: In this study, we aim to highlight the patients' perspectives on undergoing a dietary intervention with the aim to alleviate GI symptoms in IBS.

Within a qualitative design using inductive content analysis, semi-structured interviews were conducted in 19 patients (14 women, 20-68 years) with IBS undergoing dietary interventions. The patients were recruited from two dietary intervention groups in a randomized controlled trial, comparing three treatment options for 4 weeks; a diet low in total carbohydrates, a low FODMAP diet combined with traditional IBS dietary advice, and optimized medical treatment. The interviews were conducted at follow-up visits, 3 and 6 months after the end of the intervention.

Results: The structured dietary intervention was experienced as supportive, motivating, and educational. The IBS patients found the intervention necessary for both initiating and completing the dietary changes.

THEMES	SUBORDINATED CATEGORIES
Supportive, educational, and motivating	- Structured diet support - Support from others - Learnings by eating - For me and others
Multidimensional challenging	- Dominant dietary preferences - Limits in time and energy - Struggles within social contexts
Reflective and developing	- Self-awareness - Individual adjustments and developments

Table. Themes and subordinated categories of patients' experiences of dietary changes during structured dietary interventions in patients with IBS.

Even if the dietary changes could be challenging to implement, competing with many other dimensions of life like dominant dietary preferences, time, and social life, the experiences led to self-awareness and individual dietary adjustments. Reflections made during and after the intervention period helped the participants to develop various new ways to manage and implement the new diet in daily life. (Table)

Conclusion: Patients living with IBS experienced structured dietary support as being effective for implementing the dietary changes. Furthermore, the achieved self-awareness contributed to individual dietary adjustments that were not only related to alleviating GI symptoms but also functional solutions in everyday life. This study supports previous knowledge about the importance of providing support and education in health-care for patients living with IBS.

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HT has served as an advisory board member/consultant and/or speaker for Takeda, Tillotts, Biocodex, Dr. Falk Pharma GmbH.

P0197

ABSORPTION AND METABOLIZATION OF THE NATURALLY OCCURRING SWEETENERS ERYTHRITOL AND XYLITOL IN HUMANS: A DOSE-RANGING STUDY

V. Bordier^{1,2}, F. Teyssie^{1,2}, F. Senner³, G. Schlotterbeck³, J. Drewe⁴, C. Beglinger^{1,2}, B.K. Wölnerhanssen^{1,2}, A.C. Meyer-Gerspach^{1,2}

¹St. Clara Research Ltd at St. Claraspital, Basel, Switzerland,

²University of Basel, Faculty of Medicine, Basel, Switzerland,

³FHNW University of Applied Sciences and Arts Northwestern

Switzerland, Muttens, Switzerland, ⁴Department of Clinical Pharmacology and Toxicology, University Hospital Basel, Basel, Switzerland

Contact E-Mail Address: valentine.bordier@unibas.ch

Introduction: Erythritol and xylitol are naturally occurring bulk sweeteners. Erythritol is absorbed at high rates in the intestine and excreted unchanged in the urine. Recently, a conversion of erythritol into erythronate in human cells has been proposed [1]. Xylitol is absorbed at about 50% in the small intestine and fermented at about 50% in the colon.

Aims & Methods: The aim of this study was to determine the absorption and metabolism of different concentrations of erythritol and xylitol. Seventeen healthy normal weight participants (10 women, BMI mean±SD: 21.6±1.3, range: 19.4-24.0 kg/m², age: 26±6, range: 18-41 years) received intragastric (i.g.) solutions of 10, 25 or 50g erythritol (arm 1) or 7, 17 or 35g xylitol (arm 2) on three study days in this parallel trial. Within each arm, the trial was randomized, double-blind and crossover for the doses administered. Plasma samples were collected at fixed time intervals to assess the concentrations of erythritol, xylitol and erythronate with gas chromatography-mass spectrometry. Data were analyzed using linear mixed model.

Results: A dose-ranging absorption of erythritol was found. The erythritol plasma concentrations increased in response to the three i.g. loads (AUC₁₈₀: 10g vs. 25g, p<0.001; 10g vs. 50g, p=0.006; 25g vs. 50g, p=0.034). We found also a dose-ranging metabolism of erythritol into erythronate (AUC₁₈₀: 10g vs. 25g, p<0.001; 10g vs. 50g, p=0.001; 25g vs. 50g, p=0.024). The metabolic ratio AUC_{erythritol}/AUC_{erythronate} was highest with 10g erythritol and decreased with higher doses. Absorption of xylitol was low and could not be detected in any of the subjects after the low dose, but

in some subjects after the medium dose and in all subjects after the high dose. No erythronate levels could be detected in any of the subjects after any dose of xylitol.

Conclusion: In this study we showed that:

- Erythritol is absorbed in a dose-ranging manner;
- Erythritol is metabolized into erythronate in a dose-ranging manner, confirming previous reports;
- The decreasing metabolic ratio with higher doses of erythritol indicates that an increasing fraction of erythritol is metabolized into erythronate;
- There is no evidence that xylitol is metabolized into erythronate.

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Disclosure: Nothing to disclose.

P0198

COOKING METHODS ONLY NEGLIGIBLY AFFECT DIETARY FIBER CONTENT AND COMPOSITION

J. Wellens¹, S. Hoeckx¹, J. Vanderstappen¹, E. Vissers², J. Raes³, S. Vermeire¹, J. Sabino¹

¹Leuven University Hospitals, Gastroenterology and Hepatology

department, Leuven, Belgium, ²Catholic University of Leuven,

Translational Research Center for Gastrointestinal Disorders,

Leuven, Belgium, ³Rega Instituut, Microbiology, Immunology and

Transplantation department, Leuven, Belgium

Contact E-Mail Address: joao.sabino@uzleuven.be

Introduction: Dietary fibers are indigestible by the human host, but fermented by the gut microbiota. Emerging evidence supports the importance of dietary fibers in maintaining gut health and a beneficial gut microbial composition and function.

However, if and how cooking methods affect dietary fiber content has been greatly overlooked, but may represent an important confounder in dietary studies and gut microbial research.

Aims & Methods: We aimed to study the effect of cooking methods on dietary fiber content and composition in commonly used food products using standard cooking methods and contemporary analytical methods. Potato, onion, oats, and broccoli were selected, and processed using standard cooking techniques (raw, cooking, steaming, baking, and frying). Aliquots of 250 g to 500 g were stored at -20°C. We combined the ISO 17025 validated AOAC 2011.25 and AOAC 2017.17 method to estimate dietary fiber content and composition, using enzymatic gravimetric liquid chromatography (Eurofins, the Netherlands).

Since samples may have taken up fat and water content might change after exposure to the different cooking methods, additional tests and calculations in dried and defatted material were performed to account for this. Only the oats samples did not undergo defatting as the fat content was not expected to exceed 10%.

Results: After food processing, the total dietary fiber (DF) and fractions of insoluble high molecular weight DF, soluble high molecular weight DF and low molecular weight DF remained fairly constant (table 1).

The main difference within a product type was for the onion samples where insoluble high molecular weight DF was lower and soluble high molecular weight DF higher after both cooking methods.

Furthermore, when overlaying the chromatograms, a decrease of fructose was seen in the pan-fried samples, possibly due to the involvement of these sugars in Maillard or caramelization reactions. A higher variation was also noted in the potato samples, possibly related to changes in resistant starch (RS2) and the formation of resistant starch (RS3).

Sample type	Oats - Raw	Oats - Cooked	Oats - Oven baked	Broccoli - Oven baked	Broccoli - Steamed	Onion - Raw	Onion - Steamed	Onion - Pan-fried	Potato - Pan-fried	Potato - Oven baked	Potato - Steamed
Insoluble High Molecular Weight DF	8.4	9.7	9.4	43.5	40.9	16.5	12.2	10.4	8.0	10.4	8.3
Soluble High Molecular Weight DF	4.3	4.4	2.7	16.1	15.6	4.1	10.2	9.6	5.5	5.9	4.7
Low Molecular Weight DF	0.8	0.8	0.8	1.4	2.0	20.9	20.3	29.5	2.2	2.6	1.8
Total DF	13.5	14.9	12.9	61.1	58.4	41.6	42.8	49.5	15.7	18.9	14.8

Table 1: Dietary fiber (DF) results reported on % w/w in the total carbohydrate content of the dried and/or defatted samples.

Conclusion: Cooking methods only negligibly affect dietary fiber content and composition, and should therefore not be taken into account as a major confounder in dietary and gut microbial studies.

Disclosure: Nothing to disclose.

P0199

THE BURDEN OF DISORDERS OF GUT-BRAIN INTERACTION IN OBESITY AND THE EFFECT OF DIFFERENT TREATMENTS ON QUALITY OF LIFE

E. Colomier^{1,2}, J. Halminen¹, G. Höskuldsdóttir¹, K. Mossberg³, M. Engstöm^{4,5}, B. Eliasson¹, L. Fandriks^{5,6}, H. Törnblom¹, M. Simrén^{1,7}

¹Institute of Medicine, Sahlgrenska Academy, University of Gothenburg, Molecular and Clinical Medicine, Gothenburg, Sweden, ²Translational Research Center for Gastrointestinal Disorders (TARGID), Chronic Diseases, Metabolism and Aging (CHROMETA), KU Leuven, Leuven, Belgium, ³Institute of Medicine, Sahlgrenska Academy, University of Gothenburg, Public Health and Community Medicine, Gothenburg, Sweden, ⁴Institute of Health and Care Sciences, Sahlgrenska Academy, University of Gothenburg, Gothenburg, Sweden, ⁵Region Västra Götaland, Sahlgrenska University Hospital, Surgery, Gothenburg, Sweden, ⁶Institute of Clinical Sciences, Sahlgrenska Academy, University of Gothenburg, Surgery, Gothenburg, Sweden, ⁷Center for Functional GI and Motility Disorders, University of North Carolina-Chapel Hill, Chapel Hill, United States

Contact E-Mail Address: esther.colomier@kuleuven.be

Introduction: Obesity has a negative impact on many health outcomes. We aimed to identify the prevalence of gastrointestinal symptoms compatible with one or more of the specified disorders of gut-brain interaction (DGBI) among patients with obesity, and to study the effect of three obesity treatments on Quality of life (QoL).

Aims & Methods: We used baseline and two-year follow-up data from a prospective non-randomized cohort study including 1121 patients with BMI ≥ 35 kg/m² referred for treatment of obesity in Region Västra Götaland, Sweden, between May 2015 and November 2017, the BARIatic surgery SUBstitution and Nutrition (BASUN) study. Patients completed the Rome III diagnostic questionnaire before being treated with Roux-en-Y gastric bypass (RYGB), sleeve gastrectomy (SG), or medical treatment (MT) including a period with very low energy diet according to clinical guidelines and the patient's preference.

Additional measures used to characterize the cohort included validated questionnaires assessing anxiety (BAI), depression (PHQ-9), and quality of life (QoL) (EQ-5D VAS scale). The effect of treatment on QoL in patient

with vs. without DGBI diagnoses at baseline was assessed using Two-way repeated measures ANOVA. Data are presented as mean $\pm$ SD, percentage (95%CI), or mean difference (95% CI for difference).

Results: In total, 911 patients (75% female, 44 $\pm$ 13 years, 42 $\pm$ 5 kg/m², 40% RYGB, 21% SG 39%, MT) completed the Rome III questionnaire at baseline and 660 patients (32 $\pm$ 6 kg/m²) at follow-up. The proportion of obese patients fulfilling diagnostic criteria for one or more DGBI at baseline and at follow-up was 61.8% (58.7%, 64.8%) and 55.3% (51.5%, 59.1%), respectively. Details about the prevalence of the different DGBI diagnoses per GI region at baseline and follow-up are given in the table.

In both patients with and without a DGBI at baseline, the QoL significantly improved over time across all treatment groups (Within-Subjects treatment*time effect: F(2, 387)=14.7, p<0.001 (with DGBI) and F(2, 237)=9.2, p<0.001 (without DGBI)).

However, only in patients with a DGBI at baseline, the main effect of treatment on average QoL scores across time was statistically significant (Between-Subject treatment effect: F(2, 387)=8.5, p<0.001 (with DGBI) and F(2, 237)=1.3, p=0.27 (without DGBI)). Bonferroni adjusted pairwise comparisons showed that patient with a DGBI at baseline had significantly more improvement of QoL when receiving RYGB compared to MT (Mean difference of EQ-5D vas scale of 7.7 (3.2, 12.1)).

Disorder of gut-brain interaction	Baseline			2-year follow-up		
	Roux-en-Y gastric bypass	Sleeve gastrectomy	Medical treatment	Roux-en-Y gastric bypass	Sleeve gastrectomy	Medical treatment
Esophageal disorders	29.2 (24.5, 34.3)	22.4 (16.5, 29.3)	18.5 (14.5, 23.1)	12.9 (8.9, 17.8)	21.7 (14.6, 30.4)	13.6 (9.3, 18.9)
Gastroduodenal disorders	27.2 (22.6, 32.2)	19.0 (13.4, 25.6)	27.1 (22.4, 32.1)	29.0 (23.4, 35.2)	22.4 (15.2, 31.1)	20.2 (15.1, 26.1)
Bowel disorders	39.0 (33.8, 44.3)	39.1 (31.8, 46.8)	36.0 (30.9, 41.3)	38.0 (31.9, 44.5)	35.3 (26.7, 44.8)	28.6 (22.9, 34.9)
Anorectal disorders	10.7 (7.6, 14.4)	11.6 (7.2, 17.2)	7.7 (5.1, 11.1)	9.1 (5.8, 13.5)	9.6 (4.9, 16.5)	6.0 (3.2, 10.1)

Data are presented as percentages (95%CI).

Conclusion: The majority of patients suffering from obesity fulfil criteria for one or more DGBI. After treatment to reduce weight, the proportion of patients having a DGBI has mostly decreased, but in some treatment arms, the proportion of patients having a gastroduodenal disorder has increased. In patients with a DGBI before treatment, the QoL of patients receiving RYGB improved significantly better compared to MT.

Disclosure: Nothing to disclose

P0200

COMPREHENSIVE ANALYSIS OF NUTRITIONAL PARAMETERS IN PATIENTS WITH IDIOPATHIC ACHALASIA: A PROSPECTIVE STUDY

Z. Nabi¹, M.R. Goud², S. Priya², N. Cheripelli², P. Inavolu², S. Darisetty², D.N. Reddy¹

¹Asian Institute of Gastroenterology, Gastroenterology, Hyderabad, India, ²AIG Hospitals/Asian Institute of Gastroenterology, Clinical Research, Hyderabad, India

Contact E-Mail Address: rajashaig761@gmail.com

Introduction: Achalasia cardia is characterized by absence of normal peristalsis and relaxation of lower esophageal sphincter leading to dysphagia and variable degree of weight loss. As a consequence, cases with achalasia are at significant risk of malnourishment.

Aims & Methods: In this study, we aimed to perform a comprehensive nutritional assessment of untreated cases with achalasia and compare them with cases with functional bowel diseases.

This is a prospective study including consecutive cases diagnosed with achalasia at a tertiary care centre (December 2021 to April 2022). The diagnosis of achalasia was established using standard protocol. Nutritional assessment was performed using biochemical parameters (hemoglobin, serum albumin, serum pre-albumin, serum iron, serum calcium, serum vitamin D and B12), triceps fold thickness (TSF), mid-arm circumference (MAC), mid-arm muscle circumference (MAMC), hand grip strength.

Subjective global assessment (SGA) was used to characterize these patients into well nourished, moderately malnourished and severely malnourished groups. Cases diagnosed as functional bowel diseases (functional dyspepsia, irritable bowel syndrome, functional constipation) and matched for age and gender served as controls. Multivariate analysis was performed to assess for the risk factors formalnourishment in cases with achalasia.

Results: 118 cases (41.2±13.9 years, 61% males) were diagnosed with achalasia during the study period and compared with 200 matched controls (43.4±11.9 years, 69% males). The subtypes of achalasia included type I in 20 (16.9%), II in 90 (76.3%) and III in 8 (6.8%).

Overall, 53 (44.9%) cases with achalasia were moderately (38.1%) or severely (6.8%) malnourished. The mean symptom duration was non-significantly higher in the malnourished cohort (26.8±26.4 vs 24.5±20.9 months; $p=0.604$). Mean Eckardt score was significantly higher in the malnourished cases with achalasia (6.8±1.8 vs 5.9±1.8; $p=0.014$). The proportion of malnourished patients (SGA) were significantly higher in type I achalasia as compared to type III (60% vs 14.3%; $p=0.038$).

As compared to controls, the mean values were significantly lower in cases with achalasia for serum albumin (4.3 vs 4.7; $p=0.024$), pre-albumin (19.4 vs 25.2; $p=0.001$), serum calcium (8.6 vs 9.7; $p=0.012$), vitamin D (17.6 vs 25.2; $p=0.001$), serum iron (58.2 vs 78.4; $p=0.001$), triceps fold thickness (9.2 vs 10.2; $p=0.002$) and hand grip strength (21.5 vs 27.4; $p=0.001$). On multivariate analysis, symptom severity (Eckardt score) was a significant predictor of malnourishment in cases with achalasia.

Conclusion: Cases with achalasia are at significant risk of malnourishment as compared to those with functional bowel diseases. Increased symptom severity is an independent risk factor for malnourishment in these cases. (NCT05161923)

Disclosure: Nothing to disclose.

P0201

ORTHOREXIA NERVOSA IS MORE PREVALENT IN PATIENTS WITH IRRITABLE BOWEL SYNDROME COMPARED TO HEALTHY CONTROLS

C. Tuck¹, M. Foyster¹, N. Sultan¹, M. Tonkovic¹, A. Govus¹, J. Biesiekierski^{1,2}

¹La Trobe University, Department of Dietetics, Nutrition and Sport, Bundoora, Australia, ²Monash University, Department of Nutrition, Dietetics and Food, Notting Hill, Australia

Contact E-Mail Address: C.Tuck@latrobe.edu.au

Introduction: Concern has been raised that use of restrictive dietary interventions, such as the low fermentable carbohydrate diet in irritable bowel syndrome (IBS), or nutrition for peak sport performance may increase the risk of disordered eating. Orthorexia nervosa is a form of disordered eating where people restrict their diet based on its quality rather than quantity, becoming so obsessed with eating healthily that it leads to malnutrition or impaired daily functioning. Little is known about the prevalence and risk factors of orthorexia in these proposed at-risk groups.

Aims & Methods: The aim of this cross-sectional survey was to measure the prevalence of orthorexia in participants with IBS, athletes, people with eating disorders (ED), and healthy controls (HC). Participants with IBS (Rome IV), athletes (minimum 5 hours training per week), ED partici-

pants (assessed via DSM-5 with mild-moderate symptoms in past 5 years), and healthy controls were recruited via online advertisement. Orthorexia was assessed utilising the 'Sick, Control, One-stone, Fat, Food' (SCOFF, ≥ 2 indicating disordered eating) and eating habits questionnaire (EHQ). Additional questionnaires assessed gastrointestinal symptoms (IBS-severity symptom score), and the eating motivations survey (TEMS). Data was analysed using one-way ANOVA as appropriate.

Results: Two hundred and four IBS, 54 athletes, 34 ED participants, and 112 healthy controls completed the study. Significantly more orthorexic traits were exhibited in the IBS and ED cohorts compared to athletes and healthy controls when measured by the SCOFF (IBS, ED, athletes, and HC respectively, 54% vs 71% vs 41% vs 31%, $p<0.01$) and in all 3 groups compared to the healthy controls when measured by the EHQ (IBS, ED, athletes and HC respectively, mean±SD, 75±20 vs 73±22 vs 76±17 vs 60±19, $p<0.01$). There were no significant differences between IBS and ED for either the SCOFF or EHQ. Participants with one or more food intolerance rated higher on the EHQ compared to those with none (95% CI: [6, 14], $t(245)=-4.62$, $p<0.01$). Using the TEMS, 'health' ($r=0.32$ (95% CI [0.21, 0.42])), 'natural concern' ($r=0.42$ (95% CI [0.31, 0.51])) and 'weight control' ($r=0.44$ (95% CI [0.34, 0.52])) were motivations positively associated with orthorexia.

Conclusion: These findings suggest that orthorexia is a significant concern, especially in IBS where more than half of patients are displaying orthorexic traits, with similar prevalence to those with a known eating disorder. Presence of food intolerances, and motivations of healthfulness and weight control may be predictors of higher tendency towards orthorexia.

Clinicians should be aware of orthorexia and consider if a restrictive diet is appropriate in individuals with IBS. Future prospective studies should further evaluate orthorexia traits within this patient group, particularly those using restrictive dietary therapies.

Disclosure: No conflict of interest to declare.

P0202

THE EFFECT OF RIBOFLAVIN SUPPLEMENTATION ON THE SYSTEMIC REDOX STATUS IN HEALTHY VOLUNTEERS: A POST-HOC ANALYSIS OF THE RIBOGUT TRIAL

A.T. Otten¹, A.R. Bourgonje¹, M. Sadaghian Sadabad², J.Z.H. von Martels¹, M.L.C. Bulthuis³, K.N. Faber¹, H. van Goor³, G. Dijkstra¹, H.J.M. Harmsen²

¹University Medical Center Groningen, Gastroenterology and Hepatology, Groningen, Netherlands, ²University Medical Center Groningen, Medical Microbiology, Groningen, Netherlands,

³University Medical Center Groningen, Pathology and Medical Biology, Groningen, Netherlands

Contact E-Mail Address: a.t.otten@umcg.nl

Introduction: Riboflavin (vitamin B₂) is a redox-active vitamin that plays a pivotal role in human energy metabolism. Riboflavin may have beneficial health effects by increasing extracellular antioxidant capacity, thereby alleviating oxidative stress. Reduced levels of free thiols in blood reflect systemic oxidative stress, since they are readily oxidized by reactive species. In this study, we aimed to investigate the potential of riboflavin supplementation to improve the systemic redox status in healthy volunteers.

Aims & Methods: This study was a post-hoc analysis of the Ribogut study, a randomized, double-blind, placebo-controlled human intervention trial that investigated the effect of riboflavin supplements on the gut microbiota composition of healthy individuals. Serum free thiols were quantified before and after intervention and adjusted to serum albumin levels. Changes in albumin-adjusted free thiols were analyzed, as well as potential associations with routine laboratory parameters and fecal bacterial quantification by fluorescence in-situ hybridization (FISH).

Results: A total of 99 participants were randomized for a two weeks intervention of either placebo ($n=34$), riboflavin 50 mg daily ($n=32$), or riboflavin 100 mg daily ($n=33$). At baseline, no significant differences in albumin-adjusted serum free thiols were observed.

After intervention with either placebo or riboflavin, albumin-adjusted serum free thiols did not significantly change ($P>0.05$), however, observed changes were inversely associated with changes in C-reactive protein (CRP) levels ($r=-0.22$, $P<0.05$). At baseline, albumin-adjusted serum free thiols were positively associated with fecal relative abundances of *Faecalibacterium prausnitzii* ($P<0.01$).

Conclusion: Riboflavin did not change the systemic redox status in healthy individuals. Observed changes in albumin-adjusted free thiol levels were negatively associated with changes in CRP levels, confirming that inflammation and oxidative stress are two highly associated processes. Strikingly, albumin-adjusted free thiols were independently associated with relative abundances of fecal *F. prausnitzii*, which may suggest a potential host redox-microbiota interaction.

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P0203

GUT MICROBIOTA AND ITS ASSOCIATION WITH SMALL INTESTINAL BACTERIAL OVERGROWTH IN PATIENTS WITH HYPERLIPIDEMIA

K. Kvit¹, N. Kharchenko²

¹Danylo Halytsky Lviv National Medical University, Therapy №1 and Medical Diagnostics, Lviv, Ukraine, ²Shupyk National Healthcare University of Ukraine, Gastroenterology, Dietology and Endoscopy, Kyiv, Ukraine

Contact E-Mail Address: akskris88@gmail.com

Introduction: The variety of microbes colonizing the human gut is almost 10 times more than the total cells in a human. Current evidence suggests that the intestinal microbiota is involved in cardiovascular disease occurrence with the host-microbe interaction regulating metabolic pathways. Recent studies suggest that the characteristics of the gut microbiota are altered in hyperlipidemia patients, and also, that small intestinal bacterial overgrowth (SIBO) contributes to the pathogenesis of this condition. However, such associations remain poorly investigated and characterized. The LPS from intestinal flora bacteria can induce a chronic subclinical inflammatory process with further atherosclerosis development. Additionally, microbiota injuries through activation of TLR4 pathway could impact on lipid metabolism in the liver.

Aims & Methods: The aim of this study was to examine the composition of gut microbiota and its correlation relationship with SIBO in patients with hyperlipidemia. TLR4 serum level was examined as one of the proinflammatory factors that could play a substantial role in gut-liver-cholesterol axis.

105 patients with hyperlipidemia (average age 42.52 ± 2.6) with an average BMI of 26.08 ± 0.81 were examined in Danylo Halytsky Lviv National Medical University (Lviv, Ukraine). 52 control subjects (average age 37.38 ± 2.6), an average BMI of 24.01 ± 0.75 . All control subjects had normal lipid range and no history of coronary disease. Determination of microbial composition at the level of major microbial phyla was carried out by identification of Bacteroidetes, Firmicutes, and Actinobacteria DNA with quantitative real-time PCR (qRT-PCR), using gene-targeted primers. The examination of lactulose breath test was proved to patients of both groups. Quantitative detection of TLR4 in the serum was realized by using the Cusabio Elisa kit.

Results: The composition of microbiota was significantly different in separate groups of species between patients with and without hyperlipidemia. Bacteroidetes in main group amounted to $40.70\pm25.43\%$, Firmicutes –

$39.43\pm23.77\%$, Actinobacteria – $8.95\pm9.41\%$, while in the control group - Bacteroidetes $52.98\pm13.62\%$, Firmicutes $33.85\pm12.47\%$, Actinobacteria – $5.36\pm1.76\%$. Firmicutes/Bacteroidetes index in the main group averaged 2.98 ± 1.61 , in control – 0.75 ± 0.54 . Negative correlation between Bacteroidetes and Firmicutes ($r=-0.84$), Bacteroidetes and Actinobacteria ($r=-0.52$), and Bacteroidetes and Firmicutes/Bacteroidetes index ($r=-0.74$) was marked in patients of the main group. Additionally, there was a positive correlation between triglycerides, cholesterol and Actinobacteria ($r=0.48$). SIBO prevalence was 58,5% in main group, while in control - 31%. TLR4 serum level was 2.67 ± 1.05 ng/mL in hyperlipidemia group, 1.23 ± 0.99 ng/mL in controls (normal range 1,25-2,5 ng/mL).

Conclusion: There is an essential role of microbiota in lipid metabolism due to the fact of SIBO prevalence in patients with hyperlipidemia in comparison with the control group (58,5% vs. 31%). Moreover, the TLR4 serum level that is usually activated by LPS as the result of SIBO was higher more than the normal range in patients with hyperlipidemia (2.67 ± 1.05 ng/mL).

Additionally, the composition of the microbiota was different between both groups - Actinobacteria and F/B index were significantly higher in patients with hyperlipidemia. Actinobacteria was in correlational relationship with triglycerides and cholesterol level.

Disclosure: Nothing to disclose.

P0204

IDENTIFYING ARFIDS IN SEVERE DGBIS WHO PRESENT TO TERTIARY CARE GI PSYCHOLOGY AND DIETETICS

L.D. Martin^{1,2}, K. MartinKova³, C. Perrin², C. Brugaletta², A. Emmanuel², N. Zarate-Lopez²

¹University College London Hospital, Nutrition & Dietetics, London, United Kingdom, ²University College London Hospital, GI Physiology Unit, London, United Kingdom, ³University College London, London, United Kingdom

Contact E-Mail Address: lee.martin1@nhs.net

Introduction: Avoidant Restrictive Food Intake Disorder (ARFID) is an eating disorder associated with anxiety and food avoidant/restrictive behaviours which are also commonly observed in Disorders of Gut Brain Interaction (DGBI). ARFID diagnostic criteria defined in the Diagnostic and Statistical Manual of Mental Disorders, 5th edition (DSM-5) is open to clinical interpretation, making identification difficult.

We therefore aimed to identify patients with a severe DGBI who presented with DSM-5 ARFID and examine their psychological and nutritional characteristics compared to Non-ARFID presentations.

Aims & Methods: The cohort under investigation included all patients with a Rome IV diagnosed DGBI ($n=33$, 88% female, mean age 39 ± 15 years, 42% Irritable Bowel Syndrome, 39% Functional Dyspepsia). Severity was defined as requiring both GI Psychology and Neurogastroenterology Dietitian input in tertiary care over an 18 month period (May 2018 to October 2019). Medical notes were retrospectively reviewed and a diagnosis of ARFIDs was applied if the DSM-5 Criteria was met along with severity cut offs chosen by our unit for Criteria A as follows:

- A1. Weight loss (severely or very severely underweight (BMI $\leq 17\text{kg/m}^2$) and/or experienced $>10\%$ weight loss),
- A2. Nutritional Deficiency (defined as eating ≤ 5 foods and/or laboratory assay),
- A3. Dependence on enteral tube feeding (ETF) or oral nutrition supplements (ONS) (defined as $\geq 50\%$ of daily caloric intake from ONS or any ETF not required by a concurrent medical condition),
- A4. Psychosocial impairment (defined as symptoms that impact on usual daily activities).

ARFID sub type was also ascribed. Characteristics measured included dietary restrictions (if specific diets were followed or specific foods were avoided), medical conditions, severe anxiety (≥ 15 on GAD-7), severe depression (≥ 15 on PHQ-9) and high somatic burden (≥ 13 on PHQ-12).

Results: 11 patients (33%) met DSM-5 ARFID diagnostic criteria. 100% had the concern of aversive consequences subtype. Applied severity Criteria A was met as follows; A1(weight loss)=82% (n=9), A2(Nutritional Deficiency)=9% (n=1), A3(ONS/ETF Dependence)=54% (n=6), A4(Psychosocial)=100% (n=11).

When comparing ARFID vs Non-ARFID a non-significant higher percentage of severe anxiety (83% vs 45%), severe depression (57% vs 50%) and high somatic symptoms (50% vs 30%) were observed in ARFID.

ARFIDs were more likely to have a chronic pain disorder (0=0.016), and ≥ 3 medical conditions ($p=0.026$). In non-dependent ONS/ETF ARFID (n=5/11) 60% had BMI $\leq 17\text{kg/m}^2$ and 20% BMI $\leq 18\text{kg/m}^2$, however there were no differences in dietary restrictions compared to Non-ARFID (n=22), none of whom were underweight (BMI $\leq 18.5\text{kg/m}^2$).

Conclusion: ARFIDs is present in one third of severe DGBIs who require both dietetic and psychological tertiary care support, and awareness of DSM-5 criteria is essential. In particular suspicion of ARFID should be raised in those who present with aversive consequences of eating associated with significant weight loss ($\geq 10\%$), BMI ≤ 17 and/or dependence on ONS or ETF.

Psychosocial impairment is perhaps of less relevance in identifying ARFID as it is already recognised as part of diagnostic criteria in DGBIs. Despite no differences in dietary restrictions between Non-ARFID and non-dependent ONS/ETF ARFID, 80% were underweight indicating restriction of volume rather than variety is an important dietary factor to consider.

The findings of significant chronic pain conditions in ARFIDs, which shares similar fear avoidance behaviours, plus the high prevalence of severe anxiety indicate factors to explore further.

Disclosure: Nothing to disclose.

P0205

RISK STRATIFICATION, PREVENTION AND OCCURRENCE OF REFEEDING SYNDROME IN ADULTS USING A COMPUTER-BASED TOOL: A PROSPECTIVE COHORT STUDY

L. Duez¹, F. Défossez^{2,3}, A. Hadeff¹, S. Ruiz Maymo⁴, A. Ballarin⁴, J. Thomas⁴, A. Szalai⁵, R. Aglave⁵, M. Odent⁵, J.C. Preiser⁶, M. Arvanitakis¹

¹ERASME University Hospital, Université Libre de Bruxelles, Gastroenterology Department, Brussels, Belgium, ²University of Mons, Chemical and Biochemical Process Engineering Department, Mons, Belgium, ³UMR CNRS 7331, University of Reims, Group of Molecular and Atmospheric Spectroscopy, Reims, France, ⁴ERASME University Hospital, Université Libre de Bruxelles, Nutritional Support Unit, Brussels, Belgium, ⁵ERASME University Hospital, Université Libre de Bruxelles, Dietetic Department, Brussels, Belgium, ⁶ERASME University Hospital, Université Libre de Bruxelles, Biomedical Research and Clinical Teaching, Brussels, Belgium

Contact E-Mail Address: alia.hadeff@gmail.com

Introduction: Refeeding syndrome (RS) is defined as severe fluid and electrolyte shift during oral, enteral (EN) or parenteral nutrition (PN). Incidence can reach 30%, according to the risk prevalence (1). Prevention includes identification of individuals at risk, controlled nutritional intake, and vitamin/electrolyte replacement. (2) The aim of this prospective cohort study is to assess the occurrence of RS based on computer-based risk stratification and application of a systematic nutrition protocol.

Aims & Methods: All consecutive, adult patients requiring medical nutrition therapy with EN or PN outside the ICU were considered. Exclusion criteria included other reasons for electrolyte shifts (ex renal failure), indications for EN or PN apart malnutrition (ex stroke with swallowing disorders, acute abdominal surgery) and an estimated length of stay (LOS) < 5 days. Patients were classified according to a computer-based risk stratification application in low, moderate and high RS risk and medical nutrition modalities were applied accordingly regarding initial protein-caloric intake and progressive increase in administration rate.

All patients received electrolyte supplementation (phosphate and magnesium) or correction of preexisting electrolyte disturbance (hypokalemia), as well as intravenous thiamine administration prior to initiating EN or PN. Imminent RS (electrolyte shift such as hypophosphatemia, hypokalemia and/or hypomagnesemia) and manifest RS (electrolyte shift AND clinical criteria such as oedema/tachycardia/tachypnea) was recorded according to predefined criteria. Descriptive statistics were expressed in median (min-max) and %.

Results: : From 1/02/21 to 1/02/22, 213 patients were screened and 172 were included; 91 men (53%), age: 62,5 (17-92), body mass index: 20,3 kg/m² (11,4-42) and serum prealbumin: 0,12 gr/L (0,05-0,38). Eighty-four (48,8 %) patients had cancer, 56 (32,6%) benign digestive disorders and 10 (5,8%) psychiatric disease (eating disorders).

Computer-based risk stratification for RS identified a high or moderate risk in 166 (96,5%) and 6 (3,5%) patients, respectively. Seventy-seven (44,8 %) patients received EN, 89 (51,7 %) PN and 6 (3,5 %) had both. Imminent RS was identified in 38/172 (22,1%) patients and managed by electrolyte supplementation and adapting nutrition intake.

One patient (0,6%) presented manifest RS, requiring interruption of PN and administration of diuretics. LOS was 19 days (5-58) and 43 (25%) patients were still hospitalized 30 days after admission. Medical nutrition could be stopped in 72 (41,8 %) patients because of sufficient oral intake. Twenty-one (12,2%) patients died during the 30-day period following admission.

Conclusion: Computer-based risk stratification combined with application of a systematic nutrition protocol including thiamine and electrolyte supplementation and/or correction prior to medical nutrition, as well as adapting medical nutrition administration, may help in mitigating RS.

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Disclosure: Nothing to disclose.

P0206

COMPLICATIONS OF PERCUTANEOUS ENDOSCOPIC GASTROSTOMY (PEG) TUBE PLACEMENT BY PROVIDER TRAINING: A RETROSPECTIVE ANALYSIS

P. Ziegler¹, B. Schwartz¹, A. DeMeo², J.-M. Hermes¹, G. Swanson³
¹Rush University Medical Center, Internal Medicine, Department of Gastroenterology, Chicago, United States, ²Rush University Medical Center, Department of Gastroenterology, Chicago, United States, ³Rush University, Department of Gastroenterology, Chicago, United States

Contact E-Mail Address: patricia_ziegler@rush.edu

Introduction: Percutaneous endoscopic gastrostomy (PEG) is well established as a minimally invasive method of supplementing nutrition in patients with a variety of clinical presentations and nutrition requirements. In recent years, this endoscopic technique has been widely adopted in a multidisciplinary fashion and enteral nutrition is often preferable to starting parenteral nutrition due to complications and expense. Although PEG tube insertion is usually considered a safe procedure, complications can occur at a variable rate based on the study population.¹

One of the challenging aspects of evaluating the existing literature might be due to the variability of studies as each study defines complications differently. PEG tubes are placed by both gastroenterologists and surgeons alike and there have been no studies, to our knowledge, that have examined differences in outcomes, nor have they commented on the benefit of extended formal endoscopic training.

This study aims at assessing the overall complications of PEG tube placement according to endoscopic training in both surgical and gastroenterology sub-specialties.

Aims & Methods: This was a single-center retrospective chart review study examining PEG tube placement by provider specialty with gastroenterology or general surgery over two years. Peri-procedural complication rates were compared within 30 days of endoscopy.

Disease severity was compared using the American Society of Anesthesiology (ASA) classification. A total of 330 patients were included in the study; 70 of these patients underwent PEG tube placement by gastroenterology and 260 patients underwent placement with general surgery.

Results: At baseline, ASA class scores (gastroenterology mean 3.14, standard deviation 0.601 (n=69, one absent ASA class documentation event) vs surgery (n=260) mean 3.138, standard deviation 0.485) were not statistically significantly different between the gastroenterology and surgery groups by Mann-Whitney U-test (p=0.8186). Gastroenterology PEG tubes were associated with statistically significantly lower rates of overall complications (12.86% vs 28.85%, p=0.005) as well as major bleeding events (0% vs 6.92%, p=0.017) and peri-stomal leakage or exudate (0% vs 5.77%, p=0.047).

There were no statistical differences in rates of necrotizing fasciitis, internal organ injury, aspiration pneumonia, buried bumper syndrome, sepsis, peri-stomal infection, or gastric outlet obstruction between gastroenterology and surgery.

Conclusion: These results suggest that there may be differences in rates of PEG tube placement complications between gastroenterology and general surgery based on the endoscopic training of the operating physician.

This study could provide insight into the importance of more extensive endoscopic training, post gastrostomy follow-up, and management of PEG procedures.

Given this was a single-center retrospective study, further review of larger populations will provide a better understanding of the differences in complication rates between different provider specialties to continue to improve outcomes and deliver quality care.

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Disclosure: Nothing to disclose.

P0207

MALNUTRITION WITH LOW MUSCLE MASS IS COMMON AFTER WEANING OFF HOME-PARENTERAL NUTRITION FOR CHRONIC INTESTINAL FAILURE

L. Wauters^{1,2}, S. Dermine², B. de Dreuille², J. Bettolo², C. Hutinet², E. Lecoq², L. Billiauw², A. Nuzzo², C. Stefanescu², X. Treton², O. Corcos², Y. Bouhnik², F. Joly²
¹University Hospitals Leuven, Leuven, Belgium, ²APHP Beaujon Hospital, Clichy, France

Contact E-Mail Address: lucas.wauters@kuleuven.be

Introduction: Although a formal definition and classification of intestinal failure (IF) was proposed [1], the differences in nutritional outcomes are still unclear. Weaning off home-parenteral nutrition (HPN) is more likely in short bowel syndrome (SBS) patients with a colon-in-continuity and/or use of GLP2-analogues, but the impact has not been compared to other subgroups.

Aims & Methods: Differences in outcomes were studied between subgroups of adult IF patients who were followed and weaned off HPN at a single tertiary care center (2019-2022). IF was classified as temporary (small bowel >2m after continuity surgery) or definite SBS (enterostomy or small bowel <2m with colon-in-continuity), dysmotility, mucosal disease and fistulas. Nutritional markers included BMI, body composition using bioimpedance analysis (fat free mass index or FFMI) and serum albumin levels. Functional markers included handgrip strength (HGS). Changes during HPN and follow-up (FU) after weaning were compared between groups and proportions of malnutrition defined using the Global Leadership Initiative on Malnutrition (GLIM)-criteria [2].

Results: In total, 87 patients (46 female, median (IQR) age 58 (47;70) years) were included, with similar demographics between groups. Duration of HPN significantly differed and temporary (n=23) or definite SBS (enterostomy (SBS-I, n=8), jejuno-colonic (SBS-JC, n=23) or jejuno-ileo-colonic (SBS-JIC, n=14) anastomosis) and dysmotility (n=11) were most common (table), followed by mucosal disease (n=5) and fistulas (n=3) which were excluded from subgroup analyses. Changes in BMI during HPN differed between groups (table), with no change in temporary SBS but significant increases in definite SBS and dysmotility (all p<0.01) patients.

In contrast, albumin levels increased in both temporary (p<0.0001) and definite SBS or dysmotility (all p<0.01) patients with no between-group differences (table).

Period/ changes	Temporary SBS (n=23)	SBS-JC (n=18)	SBS-JIC (n=14)	SBS-I (n=8)	Dysmotility (n=11)	p-value
HPN (weeks)	11 (8;23)	42 (28;66)	29 (15;79)	79 (35;134)	47 (16;109)	<0.0001
BMI (kg/m ²)	0.2 (-1.8;1.4)	1.9 (1.2;9)****	1.4 (0.1;2.9)**	4.5 (2.4;6.4)**	1.7 (0.8;4.7)**	0.005
albumin (g/L)	12.9 (3.7;20.9)****	10.6 (2.7;17.3)**	11.9 (5.3;18.6)**	11.5 (4.5;12.4)**	8.4 (4.8;13.9)**	0.73
FU (weeks)	31 (15;45)	34 (11;76)	27 (13;83)	41 (10;55)	45 (18;79)	0.25
BMI (kg/m ²)	1.5 (-0.4;2.8)	-1.6 (-2.9;-0.6)*	-0.4 (-1.6;1)	-0.3 (-1.4;0.3)	2.5 (0.3;6)*	<0.001
albumin (g/L)	2.3 (-1.3;6.9)	2.7 (0.7;4.9)	3.6 (2.1;9.7)	-0.7 (-2.1;0.7)	1.2 (-3.6;4.8)	0.3

Legend: p-values given for between-group analysis, within-group: *p<0.05, **p<0.01, ***p<0.001, ****p<0.0001

Table.

Duration of FU was similar between groups and differences in BMI were explained by a significant decrease in SBS-JC ($p=0.01$) but increase in dysmotility ($p=0.02$) patients with stable albumin levels (table). Malnutrition (GLIM) was present in 41.7% of all patients, of which 86.7% with reduced muscle mass (FFMI). Of note, BMI remained stable in SBS-JC patients on GLP2-analogues ($n=5$), of which none were malnourished.

Finally, HGS significantly increased (median 4 (0.1;8.4) kg, $p<0.0001$) during FU in all patients, including SBS-JC (median 7.1 (2.9;9.4) kg, $p=0.03$).

Conclusion: Malnutrition is common after weaning off HPN for chronic IF, with alterations in body composition including low muscle mass. Despite significant weight loss in SBS-JC patients after weaning, the nutritional and physical implications are rather limited considering the increased muscle strength. Compared to the beneficial outcomes with GLP2-analogues, close follow-up is needed in SBS patients after weaning off HPN.

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Disclosure: Nothing to disclose

P0208

DOES A NURSE-LED PERCUTANEOUS ENDOSCOPIC GASTROSTOMY OUTPATIENT CLINIC HAS IMPACT IN PATIENT'S OUTCOME?

H. Vilar¹, R. Pinheiro¹, R. Cerqueira¹, M. Correia¹, M. Sousa¹, I. Pita¹, V. Coelho¹, S. Ferreira¹, C. Leite¹, R.F. Veloso¹, N. Sá¹
¹Centro Hospitalar de Entre Douro e Vouga, Gastroenterology, Santa Maria Feira, Portugal

Contact E-Mail Address: helder.vilar@chedv.min-saude.pt

Introduction: Percutaneous endoscopic gastrostomy (PEG) related complications usually occur shortly after hospital discharge and sometimes motivate readmission for inpatient treatment. Mild local infections at the tube insertion site have been reported in approximately 11% of cases and require only local treatment. Recent studies have reported severe complications (acute and during feeding) in 3.8%–10% of PEG patients (1).

A prospective study has shown that in the absence of adequate gastrostomy aftercare, 6-month hospital readmission rates are as high as 23% (2).

Aims & Methods: The aim of this study was to assess the rate of complications and hospital readmissions in PEG patients. Demographic data, early and unscheduled PEG replacements and gastrostomy complications and readmission rates were retrospectively collected from a cohort of discharged gastrostomy patients regularly observed in an outpatient nurse clinic over a 4-year period, from January 2018 until December 2021.

Major complications were defined as those who required intravenous or oral drug treatment, tube dysfunction and endoscopic intervention or hospital readmission.

Results: One-hundred and twelve patients (32.1% women), age range [23-91] generated 968 consultations. The main indications for PEG were neurodegenerative (63.4%) and oncological diseases (26.8%).

There were 226 PEG replacements: 18.1% unscheduled; 35.8% early replacements. We detected 167 complications: 75 (44.9%) stoma-related and 92(55.1%) tube-related. Forty three (25.7%) major complications were observed: 7 (4.2%) stoma related and 36 (21.5%) tube-related.

All tube-related major complications and six (85.7%) of the major stoma ones were solved in a single clinical visit. There were no hospital readmissions.

Conclusion: This study demonstrates that a dedicated nurse-led outpatient clinic for PEG patients may, in a single visit, treat most PEG-related complications and therefore avoid hospital readmissions. Nevertheless, the persisting high rate of major complications leaves room for improvement of gastrostomy aftercare.

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Disclosure: Nothing to disclose.

Poster presentations

IBD

IBD

P0209

PROTEOMIC PROFILE OF SERUM AND URINE IN NEWLY DIAGNOSED PATIENTS WITH INFLAMMATORY BOWEL DISEASE: NEW APPROACH FOR BIOMARKER DISCOVERY

M. Baldan Martín¹, M. Azkargorta², I. Iloro², L. Ortega Moreno¹, L. Aldars-García¹, I. Soletto¹, C. Ramírez¹, S. Riestra Menéndez³, M. Rivero Tirado⁴, A. Gutierrez Casbas⁵, I. Rodríguez-Lago⁶, L. Fernández Salazar⁷, D.S. Ceballos Santos⁸, J.M. Benítez⁹, M. Aguas¹⁰, I. Bastón-Rey¹¹, F. Bermejo¹², M.J. Casanova¹, R. Lorente Poyatos¹³, Y. Ber Nieto¹⁴, V. Royo Escosa¹⁵, M. Esteve Comas¹⁶, F. Elortza², J.P. Gisbert¹, M. Chaparro Sanchez¹

¹Hospital Universitario de La Princesa, Instituto de Investigación Sanitaria Princesa (IIS-Princesa), and Centro de Investigación Biomédica en Red de Enfermedades Hepáticas y Digestivas (CIBERehd), Madrid, Spain, ²Proteomics Platform, CIC bioGUNE, BRTA (Basque Research & Technology Alliance), CIBERehd, ProteoRed-ISCIII, Derio, Spain, ³Hospital Universitario Central de Asturias and Instituto de Investigación Sanitaria del Principado de Asturias (ISPA), Oviedo, Spain, ⁴Hospital Universitario Marqués de Valdecilla and Instituto de Investigación Marqués de Valdecilla IDIVAL, Santander, Spain, ⁵Hospital General Universitario Alicante, ISABIAL and CIBERehd, Gastroenterology, Alicante, Spain, ⁶Hospital de Galdakao-Usansolo, Gastroenterology, Vizcaya, Spain, ⁷Hospital Clínico Universitario de Valladolid, Valladolid, Spain, ⁸Hospital Universitario de Gran Canaria Doctor Negrín, Las Palmas de Gran Canaria, Spain, ⁹Hospital Universitario Reina Sofía and IMIBIC, Córdoba, Spain, ¹⁰Hospital Universitari i Politècnic La Fe and CIBERehd, Gastroenterology Unit, Valencia, Spain, ¹¹Hospital Clínico Universitario de Santiago de Compostela, Gastroenterology and Hepatology, Santiago de Compostela, Spain, ¹²Hospital Universitario de Fuenlabrada and IDIPAZ, Gastroenterology, Madrid, Spain, ¹³Hospital General Universitario de Ciudad Real, Ciudad real, Spain, ¹⁴Hospital San Jorge, Huesca, Spain, ¹⁵Hospital Universitari Son Espases, Palma de Mallorca, Spain, ¹⁶Hospital Universitari Mutua Terrasa and CIBERehd, Barcelona, Spain

Contact E-Mail Address: mbaldanm@gmail.com

Introduction: Currently, endoscopy is the gold standard for the evaluation of disease activity and inflammation in clinical practice. However, it is an invasive procedure for the patient, costly and time-consuming. Therefore, there is an urgent need to identify non-invasive biomarkers with the potential clinical utility to diagnose inflammatory bowel disease (IBD) patients, improve the patient's quality of life and increase efficiency in the Health Systems.

Aims & Methods: The identification of non-invasive biomarkers in blood and urine through a proteomic approach for early and differential diagnosis of Crohn's disease and ulcerative colitis. Integration of proteomic and clinical results to clarify the molecular mechanisms involved in the development of these diseases.

A label-free quantitative proteomics method was used to profile the urinary and serum proteomes of 100 patients with newly diagnosed IBD, before starting any treatment [50 patients with Crohn's disease (CD) and 50 patients with ulcerative colitis (UC)] and 50 healthy controls (HC). The

resulting peptides were separated by NanoLC (EVOSEP ONE) and coupled online by electrospray to Trapped Ion Mobility Spectrometry (TIMS) TOF Pro for tandem mass spectrometry analysis. Mass spectrometry data were processed and analyzed with MaxQuant and Perseus software.

Proteins with $p \leq 0.05$ and ratio > 1.5 in any sense, were considered as significantly dysregulated. Bioinformatic analysis of differentially expressed proteins was performed to characterize involved biological processes, molecular functions, cell locations and proteins pathways (PANTHER and STRING v11.5).

Results: A total of 2,500 proteins were identified in the urine, and 468 proteins were identified in the serum with at least two different peptides at FDR $< 1\%$. Of the urine proteins, 110 were significantly changed in UC versus HC, 50 proteins were differentially expressed between CD and HC, and a total of 31 proteins were significantly changed in CD compared with UC patients. In serum samples, a total of 45 differentially expressed proteins were identified in the comparison between UC and HC groups, 32 proteins significantly expressed in CD versus HC, and 12 proteins in CD compared with UC.

Finally, biological information analysis was performed according to these differential proteins. The molecular functions, biological processes, and pathways enriched mainly involved the neutrophil degranulation, complement and coagulation cascades and immune system responses.

Conclusion: Proteome profiling revealed significant differences in newly diagnosed patients with CD or UC. Both serum and urine seem to be appropriate biological matrices for this approach. Next steps of our research will be to understand the role of candidate proteins as well as to validate those with potential as biomarkers in independent cohort.

Disclosure: Nothing to disclose.

P0210

SURGICAL RESECTIONS FROM IBD PATIENTS EXHIBIT DIFFERENT METABOLITE-SENSING GPCRS EXPRESSION, METABOLIC PROFILES AND MICROBIAL DYSBIOSIS

C. Bauset¹, M. Carda-Diéguez², E. Buetas², L. Lis-López¹, D. Ortiz-Masia³, Á. Mira^{2,4}, J. Cosin-Roger^{5,6}

¹Universitat de València, València, Spain, ²FISABIO, Genomics and Health Dept., València, Spain, ³CIBERehd-Univ. de Valencia, Dept. de Medicina, Valencia, Spain, ⁴CIBERESP, Network of Epidemiology and Public Health, Madrid, Spain, ⁵Unidad Mixta Facultad de Medicina-Hospital Dr Peset, FISABIO, Pharmacology, València, Spain, ⁶CIBERehd, Liver and Digestive Diseases, Madrid, Spain

Contact E-Mail Address: cristina.bauset@uv.es

Introduction: Inflammatory Bowel Disease (IBD) is a chronic inflammatory autoimmune disease which affects the gastrointestinal tract. Among other alterations, microbiota dysbiosis and altered metabolomic profiles have been reported in IBD patients. Recently, G-protein coupled receptors (GPCRs) have been identified as promising pharmacological targets.

Aims & Methods: We aim to characterize the tissular metabolite-sensing GPCRs expression, metabolomic patterns and microbiota composition of IBD patients.

Intestinal resections from Ulcerative colitis (UC) (n=18), Crohn's Disease (CD) (n=21) and non-IBD (n=32) were obtained. Metabolomic analysis was performed by Nuclear Magnetic Resonance and UPLC Q-ToF Mass Spectrometry. Results are expressed as μg metabolite/g tissue. Gene

expression was analyzed by qPCR and data expressed as fold induction (mean±SEM). Microbiota characterization was performed by 16S rRNA gene Illumina Miseq sequencing. Bioinformatic analysis of sequencing data was performed using constrained correspondence analysis and non-parametric Wilcoxon test to compare species proportions. Bacterial load was estimated by qPCR.

Results: Differential expression of metabolite-sensing GPCRs were found in both UC and CD patients, as summarized in the table.

	GPR 35	TAAR1	CaSR	GPR 91	GPR 81	GPR 109a	GPR 109b	GPR 43	GPR 41	GPR 84	GPR 40	GPR 120	GPR 119	TGR 5
Non- IBD (colon)	1.83 ±0.44	2.05 ±0.55	1.58 ±0.35	1.51 ±0.27	2.63 ±0.67	1.39 ±0.24	1.60 ±0.44	1.39 ±0.25	1.18 ±0.14	1.70 ±0.38	2.08 ±0.52	4.59 ±1.09	1.92 ±0.47	1.30 ±0.26
UC	0.52 ±0.11	45.46 ±26.68	1.66 ±0.76	13.24 ±5.65	3.04 ±0.97	19.05 ±5.30	42.30 ±29.01	21.52 ±9.06	4.7 ±3.17	6.73 ±2.03	6.55 ±1.81	0.88 ±0.31	0.62 ±0.18	2.41 ±0.91
Non- IBD (ileal)	6.59 ±2.07	48.13 ±17.58	23.22 ±8.35	5.59 ±1.25	11.98 ±4.85	28.50 ±13.89	20.07 ±8.06	6.33 ±1.78	44.27 ±15.18	1.04 ±0.26	4.43 ±1.13	0.46 ±0.13	1.47 ±0.32	6.16 ±1.38
CD	1.74 ±0.28	814.2 ±283.5	123.7 ±34.47	63.29 ±22.71	77± 21.24	400.6 ±130.6	295.7 ±53.41	118.7 ±35.88	269.5 ±90.24	11.64 ±5.17	40.43 ±9.50	0.23 ±0.10	82.52 ±29.8	10.47 ±2.48

Table.

Next, the following results were obtained in the metabolomic analysis of intestinal resections from non-IBD (colon), UC, non-IBD (ileum), CD: aspartic acid (20.3±1.88;33.93±3.08;54.82±6.49;66.08±5.98), phenylalanine (5.16±0.54;8.77±1.55;12.09±1.59;25.09±3.21), glutamic acid (98.42±9.44;13 6.30±10.82;150.20±23.05;185.20±17.95) succinic acid (7.29±0.94;7.97±0.8 8;7.17±0.83;14.06±1.70), b-hydroxybutyric acid (6.18±0.47;8.28±0.85;9.0 5±0.88;13.13±1.07), lactic acid (204.70±27.77;297.50±34.66;125.70±30.22 ;303.20±35.78), propionic acid (4.71±0.74;7.71±1.13;4.09±0.44;7.82±0.97) , acetic acid (7.72±0.88;7.47±0.80;10.81±1.33;16.01±1.82), butyric acid (1. 21±0.20;1.77±0.49;3.54±0.26;4.28±0.42), undecanoic acid (0.24±0.01;0.32 ±0.02;0.41±0.01;0.42±0.01), decanoic acid (1.01±0.24;4.47±0.90;0.27±0.07 ;0.79±0.33), eicosapentaenoic (2.59±0.38;3.73±0.54;0.49±0.08;0.86±0.20) , docosahexaenoic (17.73±3.50;25.90±3.15;7.99±2.60;10.43±2.02), α-linoleic acid (11.73±2.74;23.12±4.02;3.66±1.15;4.11±1.44), oleic acid (927.60±209.5 0;1208.00±204.70;186.50±42.82;164.80±25.93), N-oleylethanolamide (0.07 ±0.01;0.06±0.01;0.08±0.01;0.08±0.01) and myristic acid (25.52±5.72;64.53± 8.73;13.7±4.68;19.62±8.03).

Finally, microbiota characterization revealed a reduction in bacterial diversity and load in UC, whereas no differences were found in CD. Next, significant differences at genus and species level between UC, CD and its respective non-IBD controls were also detected. For instance, *Cellulosimicrobium NA* was increased in UC patients while *Escherichia NA* was decreased. Regarding CD, *Ruminococcus bromii* and *Faecalibacterium prausnitzii* were decreased in CD patients.

Conclusion: Altered levels of several metabolites, metabolite-sensing GPCRs expression and microbial dysbiosis is detected in intestinal resections from IBD patients pointing new promising protagonists which need to be further studied.

Disclosure: Nothing to disclose.

P0211 PROPIONATE AMELIORATES DSS-INDUCED COLITIS BY M2A MACROPHAGE POLARIZATION AND SECRETING INTERLEUKIN-10 VIA HISTONE DEACETYLASE

X. Wang¹, X. Cao¹, H. Huang², J. Zhao¹, G. Kang², Z. Feng¹, Y. Ye¹
¹Tianjin Medical University General Hospital, Department of Gastroenterology and Hepatology, Tianjin, China, ²Tianjin University, Department of Biochemical Engineering, School of Chemical Engineering and Technology, Key Laboratory of Systems Bioengineering, Ministry of Education, Tianjin, China

Contact E-Mail Address: wangxiaolli@tmu.edu.cn

Introduction: As a member of short-chain fatty acids, propionate has been proved to be able to regulate host metabolism and immunity and also exert anti-inflammatory effects in many diseases, but its role and mechanism on intestinal inflammation remain largely unknown.

Aims & Methods: In this study, the dextran sulfate sodium (DSS) -induced colitis model was used to explore the protective effect of propionate in vivo. Bone marrow-derived macrophages (BMDM) and RAW264.7 cell line were used to explore the effect and mechanism of propionate on the polarization of macrophages in vitro. Real-time polymerase chain reaction (RT-PCR) was performed to detect the expression of macrophage markers and cytokines in colon tissue and cells.

Enzyme-linked immunosorbent assay (ELISA) was used to detect the level of interleukin-6, interleukin-10, and tumour necrosis factor (TNF)-α. Immunofluorescent Staining and flow cytometry were used to evaluate the ratio of macrophage polarization. Western bolt was used to detect histone deacetylase protein levels. ChIP assay was used to determine the mechanism of IL-10 transcription.

Results: The in vivo results showed that the propionate group had less barrier damage and less inflammatory infiltration than the control indicating it could ameliorate DSS-induced colitis. Propionate promoted the production of anti-inflammatory cytokine IL-10 and reduced the production of IL-6 and TNF-α in DSS-induced mice and cells.

To explore the mechanism of IL-10 production, we found that propionate promoted the polarization of M2 macrophages by upregulating the expression of M2 marker ARG1 and CD206.

Further investigation revealed increased cell surface markers CD301 and IL-1R, which are expressed by the M2a macrophage subtype. Flow cytometry analysis showed increased proportion of M2a macrophages in colon tissue and bone marrow of mice.

Moreover, propionate inhibited histone deacetylase 2 (HDAC2) expression, and HDAC inhibitor trichostatin A (TSA) played a similar role to propionate in promoting IL-10 production and surface markers expression.

Furthermore, we analyzed the mechanism of propionate regulating IL-10 production at the gene level and showed that propionate promoted histone H3K9 acetylation and drove transcription of IL-10, thus increasing the production of IL-10.

Conclusion: Propionate ameliorated DSS-induced colitis by promoting the polarization of M2a macrophages and produced robust amounts of interleukin (IL)-10, thus regulating the intestinal immune homeostasis, and could be a promising immunological intervention for ulcerative colitis.

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Disclosure: Nothing to disclose.

P0212

AN INSIDE OUT APPROACH TO IDENTIFY PERIPHERAL PATIENT PATHOTYPE-SPECIFIC BIOMARKERS FROM A HIGH-CONTENT, MULTI-DIMENSIONAL DATASET OF HETEROGENOUS IBD POPULATIONS

J. Saini¹, C. Jiang², F. Baribaud², N. Raghupathy³, E. Holzinger⁴, Y. Luo⁵, R. Gaur⁶, W. Gonsiorek², T. Wang⁴, Q. Xiao⁷, M. Turchin⁴, R. Naik¹, A. Dongre⁷, J. Maranville⁴, M. Osterman⁸, F. Ramirez-Valle⁶, D. Greenawalt¹, L. Menard², A. Hall⁶

¹Bristol Myers Squibb, Early Development Predictive Sciences, Princeton, United States, ²Bristol Myers Squibb, Immunology Cardiovascular and Fibrosis Translational Early Development, Princeton, United States, ³Bristol Myers Squibb, Informatics and Predictive Sciences, Princeton, United States, ⁴Bristol Myers Squibb, Informatics and Predictive Sciences, Cambridge, United States, ⁵Bristol Myers Squibb, Immunology Cardiovascular and Fibrosis Translational Medicine, Lawrenceville, United States, ⁶Bristol Myers Squibb, Immunology Cardiovascular and Fibrosis Translational Early Development, Summit, United States, ⁷Bristol Myers Squibb, Discovery and Translational Proteomics, Cambridge, United States, ⁸Bristol Myers Squibb, Immunology and Fibrosis Development, Lawrenceville, United States

Contact E-Mail Address: aisling.hall@bms.com

Introduction: A critical goal for the treatment of inflammatory bowel diseases (IBD) is to identify biomarkers which allow optimization of therapeutic dose and response. Indeed, molecular characterization from diseased tissues coupled with clinical measures of IBD therapeutic responders and non-responders has identified patient pathotypes enabling future tailoring of treatments to disease-driving mechanisms.

As such, our ability to identify biomarkers tied to patient subtypes and pathways is critical in understanding how best to treat patients. Most existing clinical datasets do not pair gut and peripheral samples and focus on well-defined IBD populations.

Therefore, the generation of content-rich datasets from heterogeneous IBD populations is an outstanding effort worth pursuing. A high-content dataset containing matched gut and peripheral samples with extensive multi-omics data dimensions associated with clinical metadata would help address this unmet need.

Aims & Methods: Endoscopic biopsies were obtained from 39 Crohn's disease (CD) patients, 59 Ulcerative colitis (UC) patients, and 15 non-IBD donors from multiple matched colon and ileum sites. RNA and protein were co-extracted from the biopsies for RNAseq and mass spectrometry-based proteomics (LC-MS). Peripheral whole blood was used for generating donor genotype, RNA, and protein followed by RNAseq, LC-MS proteomics along with untargeted SOMAscan plasma proteomics.

Differential expression analysis was done on transcriptome and proteome from gut and peripheral samples, using linear regression model (LIMMA package in R). Genotyping (Illumina Infinium Human Omni2.5-8 v1.3 array) was completed; eQTL and pQTL analysis is ongoing.

Results: This IBD cohort had patients in remission or with mild, moderate, or severe disease activity as defined by Mayo UC endoscopic scores or SES CD scores. Principal component analysis showed distinct tissue-based clustering for colon and ileum and for lesional (L) vs. non-lesional (NL) biopsies. No separation in CD vs. UC donors was observed in biopsy and blood data. The colon and ileum biopsies revealed significantly up-regulated metabolic and immune pathways in both L vs. NL disease, and in IBD vs. non-IBD controls for both gene and protein expression. Differentially expressed changes from biopsies overlapped when comparing both proteomics and genomics data, while in the periphery the changes were less pronounced and concentrated on neutrophil and immune markers.

We identified biomarkers in tissue and blood that tracked with disease severity, allowing for development of a panel to predict IBD severity. Correlation with other disease-related biomarkers and clinical metadata is ongoing, along with analyses to identify key drivers of IBD using co-expression network approaches to address patient heterogeneity in the cohort.

Conclusion: Here, we focused on paired gut to peripheral samples and on IBD patients with a range of disease pathotypes. Data analyses did not distinguish between UC and CD; rather, we identified tissue location and involvement changes related to metabolic and immune pathways and a panel predicting IBD severity.

Therefore, the generation of content-rich datasets from these IBD populations will further the molecular classification of IBD patients, as well as the correspondence of diseased tissues to blood in addition to clinical measures. These findings will help characterize patient pathotypes enabling future tailoring of therapies to disease-driving mechanisms.

Disclosure: All authors are current or former employees of Bristol Myers Squibb.

P0213

EFFECTS OF ANTI-TNFA AND ANTI-A4B7 DRUGS ON CIRCULATING DENDRITIC CELLS MIGRATORY CAPACITY IN INFLAMMATORY BOWEL DISEASE

I. Soletó^{1,2}, S. Fernández-Tomé³, I. Mora-Gutierrez⁴, M. Baldan-Martin^{1,2}, C. Ramirez^{1,2}, C. Santander^{1,2}, J.A. Moreno-Monteagudo^{1,2}, M.J. Casanova^{1,2}, F. Casals^{1,2}, S. Casabona^{1,2}, I. Becerro^{1,2}, M. Chaparro Sanchez^{1,2}, D. Bernardo⁵, J. Gisbert^{1,2}

¹Instituto de Investigación Sanitaria Princesa, Gastroenterology Unit, Madrid, Spain, ²Centro de Investigación Biomédica en Red de Enfermedades Hepáticas y Digestivas (CIBERehd), Madrid, Spain, ³Facultad de Farmacia, Universidad Complutense de Madrid, Departamento de Nutrición y Ciencia de los Alimentos, Madrid, Spain, ⁴Biobanco del Sistema de Salud de Aragón, Zaragoza, Spain, ⁵Instituto de Biomedicina y Genética Molecular (Universidad de Valladolid-CSIC), Immunology, Valladolid, Spain

Contact E-Mail Address: irenesoletof@gmail.com

Introduction: Inflammatory bowel disease (IBD) is an idiopathic and chronic disorder that includes ulcerative colitis (UC) and Crohn's disease (CD). Both diseases are different but show an uncontrolled intestinal immune response that generate tissue inflammation. Dendritic cells (DC) are antigen presenting cells that play a key role in the tolerogenic maintenance of the gastrointestinal mucosa.

It has been reported that DC are recruited by intestinal mucosa in a CCR2 dependent manner and in IBD patients, this recruitment is more prominent than in healthy controls (HC), but the specific migration mechanism is still unknown. Taking in account this, we decide to study if anti-TNFA and anti-α4β7 drugs modify the GI mucosa recruitment capacity of DC in the same manner.

Aims & Methods: This is a cross-sectional observational post-marketing study where the modulatory effect of different biologic treatments on samples from patients with endoscopic diagnosis of IBD and HC was studied *ex vivo*.

Peripheral blood mononuclear cells were obtained from 15 patients per group (HC, UC active and quiescent, CD active and quiescent). After that, the expression of homing markers and the migratory capacity of circulating DC toward CCL2, CCL25 and MadCam1 from the different study groups were determined.

Then, cells were cultured in presence of anti-TNF α or anti- α 4 β 7, following culture, surface markers expression was determined hence assessing the differential effect of biological drugs (if any) over the DC subset in the different groups.

Finally, we evaluated the DC migratory capacities in presence of biological drugs or with culture media alone.

Results: Our data reveal that cDC2 (CD11c⁺ CD1c⁺) express more surface markers than other DC subsets, in addition, the expression of CCR9 within this subset was expanded in both quiescent groups (UC and CD).

According to the treatment with biologic drugs only integrin β 7 was modulated by anti- α 4 β 7 but not by anti-TNF. Focus on DC migratory capacities CCL2 showed a clear chemoattract but it was not modulated by biological drugs. In this sense, surprisingly, anti-TNF increased the migratory capacities in almost all groups.

Conclusion: We described for the first time a cDC2 subset as a potential diagnostic marker in IBD. Circulating DC from IBD patients express a different migration pattern than HC, being the expression of these molecules modulated by anti- α 4 β 7 in a different manner in UC and CD. CCR9 seem to elicit a protective function over IBD. The migratory capacity of circulating DC to migrate towards CCL2 is higher than towards culture media not being diminish by any biological drug.

Disclosure: Nothing to disclose.

P0214

THE OVERLAP BETWEEN CANNABINOID AND NOCICEPTIN SIGNALING AND ITS ROLE IN INTESTINAL INFLAMMATION – A PILOT STUDY

M. Wołyniak¹, K. Owczarek¹, M. Zielinska¹, A. Mokrowiecka², E. Małeczka-Wojcieszko², A. Fabisiak²

¹Medical University of Lodz, Department of Biochemistry, Lodz, Poland, ²Medical University of Lodz, Department of Digestive Tract Diseases, Lodz, Poland

Contact E-Mail Address: maria.wolyniak@stud.umed.lodz.pl

Introduction: Due to the loss of efficiency and adverse events of the current drugs in colitis, novel therapeutical options are needed. Both, the endogenous cannabinoid system (ECS) and nociceptin receptor (NOP) have been implicated in the pathogenesis of the inflammatory bowel diseases (IBD). Based on functional similarities between the ECS and NOP systems and anti-inflammatory effects exerted by their ligands, we hypothesize that there is an interaction between cannabinoid receptors 1 and 2 (CB1 and CB2) and NOP during colitis.

Aims & Methods: Our aim was to investigate the potential cross-talk between the cannabinoid receptors and NOP in chemically-induced model of colitis in mice. Colitis was induced by dextran sodium sulfate (DSS). NOP agonist (SCH 221510, 3 mg/kg), CB1 antagonist (AM 6545, 3mg/kg) or CB2 antagonist (AM 630, 5mg/kg) were given intracolonicallly, twice daily, alone or in combination.

On day 8 the mice were sacrificed, macroscopic scoring was performed and colonic samples were taken for further studies. The protein level of extracellular signal-regulated kinase (ERK) 1/2 was measured using Western blot. The expression of genes encoding CB1 and CB2 receptors was determined in the mouse colon using real time RT-PCR. One-way ANOVA followed by the Newman-Keuls post-hoc test was used for analyses of multiple treatment means. Data are showed as mean $\pm$ SEM.

Results: We observed an initial increase in total colon damage score in DSS-treated mice as compared to control group (6.40 $\pm$ 1.52 vs. 1.20 $\pm$ 0.46, respectively), which decreased after treatment with SCH 221510 (4.10 $\pm$ 0.50). Interestingly, addition of AM 6545, AM 630 or combination of both drugs significantly increased a total damage score as compared to mice treated with SCH 221510 alone (11.83 $\pm$ 0.44 vs. 4.10 $\pm$ 0.50, (P<0.01) for AM 6545,

9.12 $\pm$ 1.54 vs. 4.10 $\pm$ 0.50 (P<0.05) for AM 630 and 8.57 $\pm$ 0.86 vs. 4.10 $\pm$ 0.50 (P<0.05) for combination of both antagonists). Similar trend was found in comparison of myeloperoxidase activity in tissues of these groups (14.69 $\pm$ 5.84 vs. 13.96 $\pm$ 3.67, 18.97 $\pm$ 2.40 vs. 13.96 $\pm$ 3.67, and 17.60 $\pm$ 3.31 vs. 13.96 $\pm$ 3.67, respectively).

We found a significant reduction in protein level of ERK 1/2 in the colon collected from mice treated with NOP agonist and CB2 antagonist as compared to mice treated with SCH 221510 alone (1.30 $\pm$ 0.16 vs. 1.89 $\pm$ 0.31, P<0.01). Real time RT-PCR analyses showed that SCH 221510 increased the relative expression of cannabinoid receptors as compared to mice treated only with AM 630 (23091 $\pm$ 3050 vs. 5021 $\pm$ 1794, respectively for CB1 expression and 24488 $\pm$ 8316 vs. 2800 $\pm$ 1050, respectively for CB2 expression).

Conclusion: We obtained promising results suggesting the existence of cross-talk between the CB and NOP receptors. Fully elucidating this phenomenon could aid in developing novel treatment options for patients with IBD based on the modulation of activity of ECS or NOP receptors.

Disclosure: Nothing to disclose.

P0215

IFN γ -TREATED MACROPHAGES INDUCE EMT THROUGH THE WNT PATHWAY: RELEVANCE IN CROHN'S DISEASE

M.M. Edo¹, M. Mendoza-Ballesteros¹, D.C. Macias-Ceja², M. Seco³, L. Lis-López⁴, C. Bauset⁴, J. Cosin-Roger³, S. Coll⁴, S. Calatayud⁵, M.D. Barrachina⁵, D. Ortiz-Masia²

¹Universitat de Valencia, Departamento de Medicina, Valencia, Spain, ²CIBERehd-Universidad de Valencia, Departamento de Medicina, Valencia, Spain, ³Unidad Mixta Facultad de Medicina-Hospital Dr Peset, FISABIO, Pharmacology, Valencia, Spain, ⁴Universitat de València, Departamento de Farmacología, Valencia, Spain, ⁵CIBERehd-Univ. de Valencia, Departamento de Farmacología, Valencia, Spain

Contact E-Mail Address: cristina.bauset@uv.es

Introduction: Fibrosis is a common complication of Crohn's disease (CD) in which macrophages play a central role. Epithelial mesenchymal transition (EMT) and the WNT pathway have been associated with fibrosis.

Aims & Methods: We aimed to analyze the relevance of the tissue microenvironment in macrophage phenotype and the EMT process. Intestinal surgical resections were obtained from control and CD patients with stenotic or penetrating behavior. Cytokines expression, macrophages phenotypes, EMT markers and WNT signalling pathway were determined by WB, RT-PCR, ELISA or Cytometry. U937 cells were treated with IFN γ , TNF α , IL1 β , IL4 or IL10 and co-cultured with HT29 cells, and were treated, in some cases, with XAV939 or miFzd4. The expression of macrophage, EMT and WNT pathway markers in U937 or HT29 cells was analyzed by WB or RT-PCR.

Results: IFN γ , WNT6, CD16 and CD86 were increased in intestinal tissue from CD patients. U937 cells treated with IFN γ increased significantly the protein expression of WNT2b (1,3 $\pm$ 0,07 N=13* vs vehicle), CD86 (1,425 $\pm$ 0,1194 N=19* vs vehicle) and CD16 (1,459 $\pm$ 0,1355 N=12* vs vehicle). IFN γ -U937 co-cultured with HT29 increased significantly the protein expression of EMT markers, β CATENIN, WNT2b and WNT6 in HT29 cells (VIMENTIN: 2,7 $\pm$ 0,3 N=6* vs vehicle-HT29; SNAIL1: 1,5 $\pm$ 0,1 N=5* vs vehicle-HT29; β CATENIN: 1,4 $\pm$ 0,09 N=5* vs vehicle-HT29; WNT2b: 2,0 $\pm$ 0,3 N=8* vs vehicle-HT29; WNT6: 1,742 $\pm$ 0,2503 N=4* vs vehicle). Treatment HT29 cells with XAV939 (VIMENTIN: 1,4 $\pm$ 0,4 N=6 vs vehicle-HT29 XAV; SNAIL1: 1,0 $\pm$ 0,1 N=5 vs vehicle-HT29 XAV; β CATENIN: 0,8 $\pm$ 0,1 N=5 vs vehicle-HT29 XAV) or with miFzd4 (VIMENTIN: 0,3 $\pm$ 0,07 N=12* vs IFN γ -HT29 mock; SNAIL1: 0,5 $\pm$ 0,06 N=12* vs IFN γ -HT29 mock; β CATENIN: 0,6 $\pm$ 0,04 N=12* vs IFN γ -HT29 mock; FZD4: 0,5 $\pm$ 0,04 N=12* vs IFN γ -HT29 mock) partially reversed the increases produced by IFN γ -U937 in HT29 cells.

Conclusion: IFN γ -treated macrophages may stimulate the expression of WNT ligands in an autocrine and paracrine manner. The expression of WNT ligands at the epithelial level could favor mesenchymal epithelial transition through WNT2b and WNT6 ligand and FZD4 receptor.

Disclosure: Nothing to disclose.

P0216

DECODING THE TAXONOMIC AND FUNCTIONAL PROFILES OF MICROBIOTA IN INFLAMMATORY BOWEL DISEASES—A MULTI-OMICS APPROACH

Y. Eb-Levadoux¹, L. Khachatryan¹, M. Porchet¹, A. Fennouri¹, S. Dijon¹, C. Nury¹, O. Lavrynenko¹, M. Auberson¹, D. Peric¹, D. Bornand¹, R. Dulize¹, E. Guedj¹, N. Sierro¹, B. Titz¹, N. Ivanov¹, J. Hoeng², G. Lo Sasso¹

¹Philip Morris Products S.A, Pre-Clinical Science and Toxicology, Neuchatel, Switzerland, ²Philip Morris Products S.A, External Innovation Officer, Neuchatel, Switzerland

Contact E-Mail Address: giuseppe.losasso@pmi.com

Introduction: Inflammatory bowel disease (IBD) is a collective term used for describing two main conditions, Crohn's Disease (CD) and ulcerative colitis (UC), characterized by chronic inflammation of the gastrointestinal tract (GI), and associated with genetic susceptibility and alterations in the intestinal microbiome of the host. Standard approaches linking host-microbiome relationship with disease activity and progression mostly focus on metagenomic data.

However, the changes in the host-associated proteome in response to IBD are crucial for disease diagnostics and have led to the investigation of new disease biomarkers, such as calprotectin. Meta-proteomics analyses would allow simultaneous elucidation of microbiome- and host-associated translational profiles.

Thus, a multi-omics data integration approach may provide insights on both host and microbiome functional profiles, which is essential to guide therapeutic care and develop personalized treatment for IBD.

Aims & Methods: We aimed to identify novel protein, gene, and lipid biomarker signatures in fecal samples from IBD patients, using a comprehensive multi-omics analytical and data integration approach, involving metagenomics, metaproteomics, and lipidomics analyses.

We mapped the reads derived from the metagenomics analyses to those from the Integrated Gene Catalog (IGC) and the Unified Human Gastrointestinal Protein (UHGP-95) catalogs. We used gene abundance and coverage profiles to determine differentially abundant genes and build an in-house spectral gene library.

Metaproteomics data-independent acquisition was carried out by high-resolution mass spectrometry (MS); we processed the obtained raw data and spectral libraries against the in-house gene library using Spectronaut. Lipid profiling of the fecal samples was performed using high-resolution MS direct infusion analysis; targeted MS assays were applied on a broad panel of 196 lipid mediators and 47 bile acids.

Results: We performed multi-omics analysis of human fecal samples from 14 and 11 patients with UC and CD, respectively, and 12 healthy donors. All the samples were purchased from The Biocollective (Colorado, USA). As a result of metagenomics analysis over 20,000 genes were found to be differentially abundant in IBD cases compared to that in healthy groups, for both gene catalogs.

We generated in-house IGC and UHGP-95 databases (2.4 M and 3.1 M protein sequences, respectively) from the metagenomics reads and found 17 differentially abundant host proteins, including calprotectin, in IBD patients. Moreover, we identified 36 lipid mediators, 370 structural lipids, 4 ceramides, and 29 bile acids host specific. To investigate any potential

disease-associated switch for translational regulation, we compared abundance gene profiles (metagenomics) with their metaprotein product intensities. Through Multi-Omics Factor Analysis (MOFA), we were able to highlight common disease effects and particular trends in disease subgroups, which provided an integrative perspective.

Conclusion: We developed a multi-omics approach and applied it for the analysis of genes, proteins, and lipids in fecal samples from IBD patients, highlighting specific disease-related signatures.

Disclosure: The research described in this abstract was sponsored by Philip Morris International.

P0217

HUMAN INTESTINAL CD103+SIRPA+ CONVENTIONAL DENDRITIC CELLS FROM PATIENTS WITH CROHN'S DISEASE PRIME IL-17+ T-CELLS

E. Arribas Rodríguez¹, C. González de Castro¹, A. Fiz López², Á. De Prado Santos², L. Fernández Salazar³, J. Barrio Andrés⁴, S. Izquierdo³, F.J. García-Alonso⁴, B. De Andrés⁵, J.M. García Abril⁶, A. Romero De Diego⁵, J. Sánchez González⁶, J.A. Garrote Adrados¹, E. Arranz Sanz¹, D. Bernardo¹

¹Instituto de Biología y Genética Molecular (Universidad de Valladolid-CSIC), Gut Immunology Research Lab, Valladolid, Spain, ²Instituto de Biología y Genética Molecular. University of Valladolid, Gut Immunology Research Lab, Valladolid, Spain, ³Hospital Clínico Universitario de Valladolid, Servicio de Gastroenterología, Valladolid, Spain, ⁴Hospital Universitario Río Hortega, Servicio de Gastroenterología, Valladolid, Spain, ⁵Hospital Clínico Universitario de Valladolid, Servicio de Cirugía, Valladolid, Spain, ⁶Hospital Universitario Río Hortega, Servicio de Cirugía, Valladolid, Spain

Contact E-Mail Address: d.bernardo.ordiz@gmail.com

Introduction: Human intestinal conventional dendritic cells (cDC) maintain the balance between immunity and tolerance. However, their specific function in patients with Crohn's disease (CD) is scarce. Hence, we hereby decided to assess their phenotype in the inflamed and non-inflamed tissue from patients with CD referred to non-inflamed controls.

Aims & Methods: Tissue resections from patients with ileocolonic CD and controls (healthy tissue from patients with proximal colonic cancer) were obtained, being subsequently enzymatically digested. Total intestinal cDC were identified within singlet viable leukocytes as CD14-CD64-HLA-DR+CD11c+.

Three cDC subsets were sorted based on the expression of CD103 and SIRPα+ (CD103-SIRPα+, CD103+SIRPα+, CD103+SIRPα-) while total macrophages were sorted as CD14+CD64+HLA-DR+. cDC subsets and macrophages were further cultured with allogeneic CD4+ naïve T-cells to assess their Th1, Th17 and Treg phenotype.

Results: All 3 intestinal cDC subsets from controls stimulated naïve T-cells as opposed to intestinal macrophages. Indeed, cDC stimulated T-cells produced IL-10 and co-expressed FoxP3, being this capacity increased in both CD103+ subsets (CD103+SIRPα- and CD103+SIRPα+).

Moreover, all three ileal cDC subsets stimulated T-cells more efficiently than their paired colonic counterparts, although the acquired T-cell profile did not differ among tissues. None of the cDC subsets, on the contrary, induced the expression of IFN γ or IL-17 on the stimulated T-cells. Referred to CD patients, all three colonic cDC subsets were more stimulatory than their counterparts from the control tissue, while CD103+SIRPα+ cDC from the inflamed ileum primed the generation of IL-17+ responding T-cells.

Conclusion: We have demonstrated that all human intestinal cDC prime the generation of Tregs, being this capacity increased in CD103+ cDC. Indeed, ileal cDC were more stimulatory than their paired colonic coun-

terparts, suggesting an increased capacity of the ileum to generate Tregs. Nevertheless, this process was dysregulated in the inflamed tissue from patients with CD where CD103+SIRPα+ cDC seem to have been reprogrammed by the tissue microenvironment to prime the generation of Th17 T-cells hence driving disease progression.

Disclosure: Nothing to disclose.

P0218

EXCLUSIVE ENTERAL NUTRITION DRIVES PROTECTIVE MICROBIOME MODULATION IN PEDIATRIC CROHN'S DISEASE

D. Häcker^{1,2}, K. Siebert^{3,2}, A. Metwaly¹, H. Hölz³, F. De Zen³, N. Köhler⁴, J.K. Pauling⁴, M. Matchado⁵, M. List⁵, T. Schwerdt^{3,2}, D. Haller^{1,6,2}

¹Technical University Munich (TUM), Chair of Nutrition and Immunology, Freising, Germany, ²Both authors contributed equally to this work, Germany, ³Dr. von Hauner Children's Hospital, University Hospital, LMU Munich, Department of Paediatrics, Munich, Germany, ⁴TUM School of Life Sciences, Technical University of Munich, LipiTUM, Chair of Experimental Bioinformatics, Freising, Germany, ⁵Technical University of Munich (TUM), Chair of Experimental Bioinformatics, Freising, Germany, ⁶Technical University of Munich, ZIEL-Institute for Food and Health, Freising, Germany

Contact E-Mail Address: deborah.haecker@tum.de

Introduction: Exclusive enteral nutrition (EEN) is a first-line induction therapy for pediatric Crohn's disease (CD). Although the protective mechanisms remain unclear, previous studies showed substantial changes in microbiome composition in response to EEN.

Aims & Methods: The aim of the study is to assess the protective function of EEN and its impact on gut microbiome signatures in pediatric CD. We prospectively followed 20 newly diagnosed paediatric CD patients who received EEN. Patients were treated according to international guidelines including EEN therapy for 6-8 weeks, followed by a gradual re-introduction of solid food and concomitant start of maintenance treatment.

Disease activity and inflammatory biomarkers were monitored during 12-months follow-up. 16S rRNA gene sequencing and targeted/untargeted metabolomics was performed on stool samples collected weekly during EEN and monthly thereafter (n = 289).

Dietary modulation and clinical activity of patient-derived stool microbiota were studied by *ex vivo* continuous faecal culturing and after faecal microbiota transplantation (FMT) and subsequent dietary intervention in germ free (GF) IL10-deficient (*Il10^{-/-}*) mice.

Results: All patients achieved remission with EEN therapy but 7/20 had recurrent CD activity within 6 months. Microbiota profiling of patient-derived fecal microbiota before and after EEN confirmed the heterogeneity of gut microbiome composition and identified two bacterial community clusters dominated either by the two phyla Firmicutes and Bacteroidetes or the two phyla Firmicutes and Proteobacteria.

Longitudinal microbial profiling showed highly individualized responses to EEN without a coherent EEN-specific signature. Despite the individual variations, integrated microbiota and metabolite profiles resulted in better separation and the selection of bacterial taxa associated with certain metabolites (mostly long-chain fatty acids) improved the diagnostic classification of CD patients based on the diet (EEN vs. post-EEN).

FMT into GF mice showed that humanized mice recapitulated the phenotypic and the dysbiotic features of their respective human donors. FMT using patient-derived baseline fecal microbiota after exposure to *ex vivo* continuous culturing with EEN media showed no colonic inflammation. In contrast, mice colonized with fermented baseline microbiota following

the exposure to fiber rich (FR) media developed inflammation associated with substantial changes in gut microbiota composition, confirming that *ex vivo* fermentation can simulate EEN-induced remission by driving microbial shifts.

Interestingly, EEN-like diet maintained the disease inactive behaviour of EEN remission-associated microbiota but induced inflammation in the *Il10^{-/-}* mice when fermented under FR media. In contrast, EEN-like diet failed to mitigate the aggressive behaviour of relapse microbiota in both *ex vivo* culture and FMT experiments. Transfer of the same microbiota in the mouse model together with pre-treatment with an EEN-like purified diet reduced inflammation severity, suggesting that fiber might play a role in provoking inflammation after EEN cessation.

Conclusion: Our data show that clinical efficacy of EEN in pediatric CD is accompanied by temporal and individual gut microbial and metabolite changes but regardless of individual variations, integrated multi-omics data analysis identified diet-related microbiome signatures.

Findings from continuous culture and gnotobiotic mouse models point towards a direct impact of diet on the composition and metabolic activity of patient-derived microbiota and on regulating intestinal inflammation.

Disclosure: Nothing to disclose.

P0219

MUCOSAL AND PLASMA METABOLOMES IN NEW-ONSET PAEDIATRIC INFLAMMATORY BOWEL DISEASE: CORRELATIONS WITH DISEASE CHARACTERISTICS AND PLASMA INFLAMMATION PROTEIN MARKERS

N. Nyström¹, S. Prast-Nielsen^{2,3}, M. Correia⁴, D. Globisch^{4,3}, L. Engstrand^{2,3}, I. Schuppe Koistinen^{2,3}, J. Halfvarson⁵
¹Uppsala University, Women's and Children's Health, Uppsala, Sweden, ²Karolinska Institutet, Microbiology, Tumor and Cell Biology (MTC), Stockholm, Sweden, ³Karolinska Institutet, Centre for Translational and Microbiome Research, Stockholm, Sweden, ⁴Uppsala University, Chemistry, Uppsala, Sweden, ⁵Örebro University, Gastroenterology, Faculty of Medicine and Health, Örebro, Sweden

Contact E-Mail Address: niklas.p.nystrom@akademiska.se

Introduction: Metabolomics can advance the understanding of inflammatory bowel disease (IBD) pathophysiology, and children with new-onset IBD without concomitant disease or medication are in many ways an ideal study population for metabolomic research. However, most studies have examined adult populations and few have addressed the intestinal mucosa where the primary inflammation occurs.

Aims & Methods: To explore the metabolomic profiles of children with IBD, we compared the mucosal and plasma metabolomes in new-onset paediatric IBD patients and symptomatic non-IBD paediatric controls, and correlated plasma inflammation markers and disease characteristics with the altered metabolites.

Paired colonic and ileal biopsies and plasma from 67 treatment-naïve children with incident Crohn's disease (CD; n=47), ulcerative colitis (UC; n=9), and non-IBD controls (n=11) were analysed using ultra-performance liquid chromatography-mass spectrometry (UPLC-MS/MS). Inflammatory plasma proteins (n=92) were assessed.

Results: The metabolomes in inflamed mucosal biopsies differed between IBD patients and controls. In CD, mucosal levels of several lysophospholipids (lysophosphatidylcholines, lysophosphatidyletanolamines, lysophosphatidylinositols, and lysophosphatidylserines) were decreased, correlating with various plasma metabolites, including amino acid analogues and *N*-acetylated compounds. In both CD and UC, mucosal sphingolipids, including ceramide (d18:2/24:1, d18:1/24:2), lactosyl-*N*-palmitoyl-sphingosine (d18:1/16:0), behenoyl sphingomyelin (d18:1/22:0), lig-

noceroyl sphingomyelin (d18:1/24:0), and/or sphingomyelin (d18:1/24:1, d18:2/24:0) were increased, correlating with sphingolipids, bile acids, and/or *N*-acetylated metabolites in plasma. Among proteins associated with CD, interleukin-24 correlated with plasma metabolites, including lactosyl-*N*-palmitoyl sphingosine (d18:1/16:0) and phosphatidylethanolamine (18:1/18:1), haemoglobin, and faecal-calprotectin. In UC, interleukin-24, interleukin-17A, and C-C motif chemokine 11 correlated with several plasma metabolites, including *N*-acetyltryptophan, tryptophan, glycerate, and threonate, and with the paediatric ulcerative colitis activity index, C-reactive protein, and faecal-calprotectin.

Conclusion: In this study we demonstrate specific patterns of metabolomic alterations in the inflamed mucosa of children with new-onset IBD compared with symptomatic non-IBD controls. Perturbations of lysophospholipids and sphingolipids characterized the mucosal metabolome in IBD and correlated with plasma metabolites.

By integrating plasma metabolomics data with inflammatory proteins and clinical data, we identified clinical and inflammatory markers associated with metabolomic signatures for IBD. Further studies are warranted for confirmation and to determine the role for these bioactive lipid classes in IBD.

Finally, this study demonstrates that exploration of mucosal metabolomes provides a foundation for improving the understanding of IBD pathogenesis and for future diagnostic biomarker discoveries in paediatric IBD.

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All other authors declare no conflicts of interest.

P0220

LOW DRUG LEVELS ARE IMMUNOGENIC: EXCESS INFLIXIMAB COMPETES WITH IFX/TNF COMPLEXES TO DECREASE COMPLEX-INDUCED IMMUNOGENICITY

S. Pressman^{1,2}, A. Blatt^{2,1}, S. Gerassy Vainberg^{2,1}, S. Freilich^{2,3}, H. Bar-Yoseph^{2,4}, Y. Chowers^{2,1,4}, IIRN

¹Rambam Health Care Campus, Clinical Research Institute, Haifa, Israel, ²Rambam Health Care Campus, Department of Gastroenterology, Haifa, Israel, ³Technion Israel Institute of Technology, Faculty of Biotechnology and Food Engineering, Haifa, Israel, ⁴Technion Israel Institute of Technology, Rapaport School of Medicine, Faculty of Medicine, Haifa, Israel

Contact E-Mail Address: sigal.pressman@gmail.com

Introduction: The efficacy of Anti-TNF therapy is hampered by anti-drug antibodies (ADA) formation. Complexes formed between the bivalent Infliximab (IFX) and the trimeric TNF molecule were shown to drive ADA formation in a mouse model and to activate human innate blood cells. However, the relation between drug/TNF ratios and immunogenicity is still not clear.

Aims & Methods: We aimed to assess the effect of drug/TNF ratio on complex size and consequential immune activation and immunogenicity. Whole blood was incubated with IFX/TNF complexes formed at a range of molar ratios (0.25-32 IFX/TNF) keeping TNF at a constant concentration.

Cellular response was evaluated by TNF mRNA expression.

Size exclusion chromatography (SEC) was used to assess IFX/TNF complex size distribution and to collect high molecular weight fractions for cellular induction.

C57B6 mice were injected with complexes prepared with constant TNF and increasing IFX concentrations, or with excess of an IgG isotype control. Human-TNF transgenic mice were injected with IFX in different dosages. Serum ADA were quantified by ELISA.

Fcg receptors activation was assessed using Jurkat cells expressing FcgR with a downstream NFAT-driven luciferase reporter. Cells were incubated with IFX/TNF complexes and luciferase activity was measured.

Results: Whole blood incubation with complexes formed at different IFX/TNF ratios led to the induction of TNF mRNA expression. Gradual addition of IFX increased TNF expression to a maximal value, beyond which further IFX addition caused a dose-dependent reduction of TNF mRNA expression. A similar phenomenon was observed in the mouse model. Lower ADA levels were observed upon increasing the IFX/TNF ratio of injected complexes beyond an optimal ADA inducing ratio. In human-TNF transgenic mice, increasing IFX dosage also led to reduction in ADA formation. SEC analysis demonstrated that similar high molecular weight complexes were formed regardless of IFX/TNF ratio and that addition of IFX led to the accumulation of free IFX.

Pre-incubation of whole blood with IFX, or addition of an IgG isotype control instead of excess IFX, reduced complex-induced TNF mRNA expression, suggesting competition between the complexes and free drug/IgG.

Mice were injected with IFX/TNF complexes at a 4:1 and 16:1 molar ratio, or with the 4:1 complex supplemented with an IgG control. ADA levels exhibited a similar reduction with IgG and excess IFX.

A reporter cell-based assay demonstrated that Fcg receptor activation by the complexes was reduced when increasing the IFX/TNF ratio. Induction by high molecular weight fractions alone demonstrated that at the high IFX/TNF ratios, free IFX antagonized the complex inducing effect.

Conclusion: IFX/TNF complexes induce immunogenicity by innate cell activation via receptor binding. High molecular weight drug/target complexes form regardless of drug concentrations. Free IFX and IgG compete with drug/target complex binding to Fcg receptors, thereby reducing immune activation both *in vitro* and *in vivo*. The finding suggests that low anti-TNF levels are immunogenic secondary to lack of competition of receptor complex binding by free IFX. Therefore, high dose anti-TNF therapy may serve as a strategy for the reduction of immunogenicity.

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Shiran Gerassy-Vainberg declares CytoReason advisory fees for the last 3 years.

P0221

THE SOLUTE CARRIER SLC22A4/OCTN1 AS A NOVEL IBD DETERMINANT AT THE MICROBE-HOST INTERFACE

L. Masi¹, V. Petito¹, M. Fidaleo², I. Palucci³, F. Del Chierico⁴, V. Ivagnes³, A. Mercuri⁵, C. Graziani¹, L.R. Lopetuso¹, A. Armuzzi¹, A. Gasbarrini¹, G. Pani⁵, F. Scaldaferri¹

¹Fondazione Policlinico Universitario A. Gemelli IRCCS, Dipartimento di Gastroenterologia e Medicina Interna, Rome, Italy,

²Università La Sapienza, Dipartimento di Biologia e Biotecnologie, Rome, Italy, ³Fondazione Policlinico Universitario A. Gemelli IRCCS, Dipartimento di Microbiologia, Rome, Italy, ⁴Ospedale Pediatrico Bambino Gesù IRCCS, Unità Microbiota Umano, Rome, Italy,

⁵Università Cattolica del Sacro Cuore, Dipartimento di Medicina Traslazionale, Rome, Italy

Contact E-Mail Address: letizia.masi94@gmail.com

Introduction: The putative Ergothioneine Transporter, SLC22A4/OCTN1, is expressed in the intestine and in monocytes/macrophages, and its widely represented missense variant L503F (0.4 Minor Allele Frequency in Caucasians) has been found to be associated with Crohn's disease, sporadic colorectal cancer in early age and ulcerative colitis (UC) patients.

The leucine-to-phenylalanine substitution at amino acid 503 affects OCTN1 capacity to transport ergothioneine, acetylcholine and likely other substrates of endogenous or microbial origin; however, whether this defect contributes to inflammatory bowel disease (IBD) pathogenesis, and the mechanistic underpinnings, remain elusive.

Aims & Methods: In order to gain mechanistic insight on the role of SLC22A4 in IBD, we first analyzed primary monocytes from healthy donors and UC patients of varying OCTN1 genotypes. Then we stably knocked-down or overexpressed OCTN1 and its disease-associated variant in the monocytic cell line THP-1. Finally, we compared wild type and OCTN1 knockout C57BL/6 mice in a chemical colitis paradigm in vivo.

Results: Primary adherent monocytes from healthy donors homozygous for the IBD-associated allele (TT) displayed a significant enhancement of interleukin 1 beta (IL-1β) response to peptidoglycan (PGN) compared to the other genotypes. Likewise, cells from UC patients bearing the 503F variant released more IL-1β in response to live bacteria and displayed reduced expression of autophagy markers (e.g. p62, LC3), compared to patients negative for the variant.

In agreement with these findings, OCTN1-deficient THP-1 macrophages secreted reduced amounts of IL-1β when challenged in vitro with PGN or live bacteria. Most relevant, THP1 cells engineered to overexpress the 503F variant of OCTN1 displayed a much stronger IL-1β response to muramyl dipeptide and PGN challenge, compared to cells transduced with the "wild type" transporter.

Also consistent with a role for OCTN1 variants in inflammatory cascades relevant to IBD, *in vivo* studies revealed a milder DSS-induced colitis in OCTN1 knockout mice compared to wild type animals, both at the peak of disease severity and at the end of the recovery period.

Conclusion: Collectively our initial evidence supports the view that OCTN1 may have a causative role in IBD via deranged bacterial sensing and cytokine production, with 503F likely behaving as a gain-of-function variant. Thus, targeting OCTN1 variant may provide unprecedented opportunities for the personalized treatment of IBD patients and a better understanding of disease pathogenesis.

Disclosure: Nothing to disclose.

P0222

DISTINCT MUCOSAL HOST-MICROBE INTERACTIONS IN RELATION TO CLINICAL PHENOTYPES IN INFLAMMATORY BOWEL DISEASE

A.R. Bourgonje¹, S. Hu^{1,2}, R. Gacesa^{2,1}, B.H. Jansen¹, J.R. Björk¹, A. Bangma¹, I.J. Hidding^{1,2}, E.A.M. Festen^{1,2}, H.M. van Dullemen¹, M.C. Visschedijk¹, K.N. Faber¹, G. Dijkstra¹, H.J.M. Harmsen³, A. Vich Vila^{1,2}, L.M. Spekhorst¹, R.K. Weersma¹

¹University Medical Center Groningen, Gastroenterology and Hepatology, Groningen, Netherlands, ²University Medical Center Groningen, Genetics, Groningen, Netherlands, ³University Medical Center Groningen, Medical Microbiology, Groningen, Netherlands

Contact E-Mail Address: a.r.bourgonje@umcg.nl

Introduction: Host intestinal immune gene signatures and microbial dysregulations expose potential mechanisms in the pathogenesis of inflammatory bowel diseases (IBD). Profiling of mucosa-attached microbiota allows the understanding of locally present microbial communities and their immediate impact on the host. This study evaluated interactions between host mucosal gene expression and intestinal mucosa-attached microbiota in IBD.

Aims & Methods: Intestinal mucosal bulk RNA-sequencing data was combined with mucosal 16S rRNA gene sequencing data from 696 intestinal biopsies derived from 337 patients with IBD (181 with Crohn's disease [CD] and 156 with ulcerative colitis [UC]) and 16 non-IBD controls. Hierarchical all-against-all associations testing (HALLA) was used to assess factors affecting host gene expressions and microbiota. Sparse canonical correlation analysis (sparse-CCA) was used to identify inflammation-related gene-microbe components. Intestinal cell type enrichments were predicted by RNA-seq deconvolution. Linear mixed interaction models were used to investigate host-microbiota interactions, while adjusting for age, sex, BMI, disease location, tissue inflammation, medication use and batch effects.

Results: In total, 15,934 intestinal genes and 113 microbial taxa were identified and included in subsequent analyses. Host intestinal gene expressions were characterized by tissue- and inflammation-specificity, whereas intraindividual variability of the mucosal microbiota dominated over disease location and inflammation effects. Using sparse-CCA, six distinct inflammation-related pathways were modulated by the intestinal microbiota (FDR < 0.05), covering 94% of individual gene-bacteria associations.

Notably, higher expression of host fatty acid metabolism pathway genes was associated with increases of *Bifidobacterium*, while metallothionein signaling pathway genes were affected by the presence of *Bacteroides*. Mucosal abundance of *Erysipelotrichaceae* was inversely associated with genes involved in collagen biosynthesis.

Further, we observed a loss of a *Lachnospirillum*-dominated gene-bacteria networks in non-stenotic intestinal tissue of patients with fibrostenotic CD. Patients using TNF-α-antagonists demonstrated *Ruminococcaceae*-associated gene interactions related to fatty acid metabolism.

In addition, gene-bacteria associations were dependent on the degree of mucosal dysbiosis. Furthermore, the identified gene-bacteria associations showed high concordance in an independent replication cohort from the integrative Human Microbiome Project (HMP2).

Finally, deconvolution of bulk RNA-seq data revealed that mucosal microbiota significantly contributed to the variation (up to ~10%) in intestinal epithelial cells, macrophages and NK-cells.

Conclusion: Our results demonstrate a complex and heterogeneous interplay between the mucosal microbiota and gene expressions in context of IBD phenotypes. Multiple novel mucosal host-microbe interactions were exposed, which could aid in guiding drug development and foster precision medicine in IBD.

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P0223

MUCUS COMPOSITION ALTERATIONS IN INFLAMMATORY BOWEL DISEASES

H. Abu-Taha^{1,2}, K. Kaboub^{1,2}, E. Brook³, I. White⁴, N. Wasserberg⁴, S. Ben-Shachar^{1,5}, D. Navaro⁶, A. Levy Barda⁷, I. Dotan^{1,2,6}, K.M. Rabinowitz^{6,2}

¹Sackler Faculty of Medicine, Tel Aviv University, Petah Tikva, Israel, ²The Felsenstein Medical Research Center, Rabin Medical Center and Tel-Aviv University, Petah Tikva, Israel, ³Department of Pathology, Beilinson Campus, Rabin Medical Center, Petah Tikva, Israel, ⁴Department of Surgery, Beilinson Campus, Rabin Medical Center, Petah Tikva, Israel, ⁵Clalit Research Institute, Ramat-Gan, Petah Tikva, Israel, ⁶Division of Gastroenterology, Rabin Medical Center, Petah Tikva, Israel, ⁷Biobank, Rabin Medical Center, Petah Tikva, Israel

Contact E-Mail Address: kawsarkaboub@gmail.com

Introduction: Intact mucus layer is crucial for intestinal mucosal barrier function. Mucins, mucus layer building blocks, are secreted by goblet cells and composed of glycans that are essential for resisting bacterial interactions. Mucins composition alterations may contribute to intestinal inflammation such as that in inflammatory bowel diseases (IBD).

Aims & Methods: Our aim is to assess intestinal mucus expression and composition in IBD, and inflammation-induced alterations.

Patients with IBD and non-IBD controls were recruited prospectively and mucosal samples were obtained by endoscopy and from surgical specimens, respectively. Hierarchical clustering of MUCs gene expression was assessed in intestinal biopsies from 52 subjects; 32 patients with IBD (Crohn's disease [CD], ulcerative colitis [UC] and pouchitis) and 20 non-IBD controls, using gene expression data to generate a heatmap.

To study mucus composition, Carnoy's-fixed and paraffin embedded mucosal biopsies from patients with CD, were stained with PNA (Galactose-binding lectin), using immunofluorescence. Human intestinal organoids (HIOs) obtained from surgically resected intestines of non-IBD controls were differentiated to enrich goblet cells and increase mucus secretion. Following treatment with pro-inflammatory cytokines glycan-binding lectins, and MUCs mRNA levels were assessed by flow cytometry, and RT-PCR, respectively.

Results: Hierarchical clustering analysis revealed significant increase in MUC1, MUC4, MUC6 expression and slight increase in MUC2 expression in patients with IBD with active inflammation compared to non-IBD controls. Galactose expression was lower in inflamed compared to the non-inflamed mucosal explants of patients with CD (n=4). Also, galactose expression was reduced in HIOs treated with cytokines mix (IFN- γ , TNF- α and IL-2). MUC1 RNA levels were upregulated following treatment with IL-22, or IL-6 in HIOs (p<0.001, and p<0.05, respectively, n=3). MUC4 RNA levels were upregulated in HIOs treated with IFN- γ , IL-22, or IL-6 (p<0.0001, p<0.0001, and p<0.05, respectively, n=3). Additionally, MUC6 RNA expression levels were upregulated in HIOs treated with IL-13 or IL-4 (p<0.001, n=3).

Conclusion: Upregulated MUC1, MUC2, MUC4 and MUC6 expression in the inflamed mucosa suggest mucins potential importance in the pathophysiology of IBD. Reduced galactose expression in inflamed mucosal explants,

and HIOs treated with cytokines mix, stresses the effect of inflammation on mucins composition. Moreover, inflammation-induced alterations in MUC genes expression, indicates that mucus layer modifications may be immune-mediated. HIOs may serve as a platform for studying alterations in mucus layer characteristics.

References: S Ben-Shachar et al. Inflamm Bowel Dis- 2013

Disclosure: Nothing to disclose.

P0224

CHARACTERIZATION OF THE CYTOKINE EXPRESSION IN HUMAN COLON ORGANIDS FROM INFLAMMATORY BOWEL DISEASE PATIENTS

T. Molnár^{1,2}, B. Jójárt^{1,2,3}, T. Resál¹, K. Szántó¹, D. Kata⁴, I. Földesi⁴, T. Molnár¹, J. Maléth^{1,2,3}, K. Farkas¹

¹University of Szeged, Szent-Györgyi Albert Medical School, Department of Medicine, Szeged, Hungary, ²Hungarian Academy of Science, University of Szeged Momentum Epithelial Cell Signaling and Secretion Research Group, Szeged, Hungary, ³Hungarian Centre of Excellence of Molecular Medicine, University of Szeged Molecular Gastroenterology Research Group, Szeged, Hungary, ⁴University of Szeged, Szent-Györgyi Albert Medical School, Institute of Laboratory Medicine, Szeged, Hungary

Contact E-Mail Address: moltunde93@gmail.com

Introduction: Inflammatory bowel diseases (IBD) are chronic inflammatory disorders of the gastrointestinal tract. IBD is associated with hyperactivation of immune cells and imbalanced pro- and anti-inflammatory cytokines. Anti-TNF- α treatment is widely used, but 10-30% of the patients are primarily not responding to the treatment or lose response over time.

In vitro organoid cultures (OCs) generated from tissue specific adult stem cells can mimic cellular diversity and function of the organ of origin and may be utilized as a predictive model. However, the lack of knowledge of the OC's cytokine pattern and characteristics limit the possible use of the OCs as an *ex vivo* model.

Aims & Methods: Our aims were to characterize the cytokine profiles of the IBD colon organoids and compared them to the colon biopsies they were originated from and to control colon organoids.

In this study 20 IBD and 8 non-IBD patient sample were used. The biopsies were taken during colonoscopy from inflamed part of the colon of IBD patients. To establish colon organoid cultures crypts were isolated from the biopsy samples. Cytokine Array was used to determine cytokine expression patterns in our samples.

After first passage the gene expressions of control and IBD OCs were determined by qPCR. TNF- α concentrations was determined by ELISA and immunostainings, respectively in control and IBD organoids. To determine therapeutic response OCs were treated with anti-TNF- α therapy.

Results: We didn't observe any significant difference between the biopsies and the organoid's cytokine pattern until the first passage. Major pro-inflammatory cytokines such as IL-6 and IL-8 were detected both in biopsies and organoids. After the second passage the cytokine expression decreased or disappeared in OCs. ELISA showed that TNF- α was expressed in the organoid cultures, however a similar decrease was observed, which was also confirmed by immunofluorescence staining.

Increased gene expression of TNF- α , IL-1 β and IL-6 were detected in IBD organoids compared to controls. ELISA also showed higher TNF- α concentration in organoids from inflamed origin compared to healthy controls. After anti-TNF- α treatment we detected a decrease in the IL-6 gene expression in treated OCs.

Conclusion: Our results suggest that colon OCs maintain the cytokine expression *ex vivo* until the 2nd passage. Furthermore, *in vitro* treatment induces detectable changes in the cytokine expression. Based on these results patient-derived organoids may be utilized as an *ex vivo* model to predict therapeutic response of IBD patients.

Disclosure: Nothing to disclose.

P0225

ELEVATED ADAPTIVE IMMUNE RESPONSES TO MULTIPLE *LACHNOSPIRACEAE* BACTERIAL FLAGELLINS IN THERAPY-NAIVE PEDIATRIC CD PATIENTS ARE ASSOCIATED WITH DISTINCT IMMUNE PATHOLOGY

D.M.H. Barendregt¹, M.E. Joosse¹, K.L. Alexander², L.M.M. Costes¹, I. Tindemans¹, Y. Simons-Oosterhuis¹, M. Aardoom³, R. Klomberg³, M. Heredia¹, D.H. Hulleman - van Haaften¹, B. Tuk¹, S. Nugteren¹, M. Doukas⁴, J.C. Escher³, L. de Ridder³, C.O. Elson², J.N. Samsom¹
¹Erasmus University Medical Center, Lab of Pediatrics, div. Gastroenterol & Nutrition, Rotterdam, Netherlands, ²University of Alabama at Birmingham, Department of Medicine, div. Gastroenterology and Hepatology, Birmingham, United States, ³Erasmus MC - Sophia Children's Hospital, Department of Pediatric Gastroenterology, Rotterdam, Netherlands, ⁴Erasmus University Medical Center, Department of Pathology, Rotterdam, Netherlands

Contact E-Mail Address: d.barendregt@erasmusmc.nl

Introduction: In inflammatory bowel disease (IBD), including Crohn's disease (CD) and ulcerative colitis (UC), inflammatory CD4⁺ T cell responses to microbial antigens drive chronic intestinal inflammation in a genetically susceptible host. The phenotype, function and specificity of these inflammatory CD4⁺ T cells remains unknown. Previously, IgG antibodies to commensal *Lachnospiraceae* bacteria-derived flagellins were detected in a subgroup of adult CD patients with complicated disease.

However, whether these IgG responses already occur in therapy-naïve pediatric patients and whether they relate to insufficient or hyperactive anti-microbial innate immunity is unknown.

Moreover, as IgG antibody responses require CD4⁺ T cell help, IgG specificity may serve as a proxy for T-cell specificity, providing a way to study the specificity and phenotype of anti-microbial T-cell responses.

Therefore, we hypothesize that a subgroup of pediatric CD patients has IgG responses to *Lachnospiraceae* flagellins and concomitant flagellin-reactive T-cell responses that are inflammatory and detectable at the therapy-naïve stage.

Aims & Methods: Plasma IgG reactivity to 20 flagellins from *Lachnospiraceae* bacteria that colonize mouse and human gut was measured in therapy-naïve pediatric IBD patients (CD: n=49; UC: n=16), non-IBD controls (n=12) and age-matched healthy controls (HC: n=17). CD patients were divided into two groups: 'flagellin-high' (elevated IgG responses to 11-20 flagellins) and 'flagellin-low' (elevated IgG responses to 0-10 flagellins), whose immunological and clinical profiles were compared.

Results: The proportion of flagellin-high patients was higher in CD patients (41%) compared to UC (6%), non-IBD (8%) and HC (6%). Flagellin-high CD patients more often had ileocolonic disease, while flagellin-low CD patients more often had isolated ileal disease. Clinical disease activity score, CRP and ESR did not relate to flagellin-high or -low reactivity. In the blood, flagellin-high patients had significantly increased frequencies of CD38⁺ (CD62L^{neg}CD4⁺) effector T cells, which are enriched for gut-homing properties, compared to flagellin-low patients. These gut-homing T cells had similarly increased frequencies of proliferative Ki67⁺ and decreased frequencies of regulatory TIGIT⁺ cells in flagellin-high and -low patients

compared to HC. After antigen-specific peripheral blood re-stimulation with recombinant flagellins, flagellin-high patients had higher frequencies of flagellin-reactive CD4⁺ T cells than flagellin-low patients.

Surprisingly, the increase in flagellin-reactive and inflammatory gut-homing T cells in flagellin-high patients associated with less histological disease activity, i.e. reduced neutrophilic and mononuclear infiltration and epithelial damage, and less phosphorylated NFκB in colonic biopsies compared to flagellin-low patients. In addition, the plasma concentration of EN-RAGE, a protein produced by neutrophils, was decreased in flagellin-high compared to flagellin-low patients.

Conclusion: In conclusion, a subgroup of pediatric therapy-naïve CD patients has high IgG reactivity to *Lachnospiraceae* flagellins at diagnosis. Although these flagellin-high patients have increased frequencies of circulating gut-homing and flagellin-specific CD4⁺ T cells, they have lower colonic histological disease activity and reduced NFκB activation, suggesting less innate immune cell activation and/or infiltration.

Together, our data raise the question whether elevated anti-*Lachnospiraceae* adaptive immune responses are related to insufficient anti-microbial innate immune responses in the colon.

Disclosure: Nothing to disclose.

P0226

DIFFERENTIAL EXPRESSION OF MIR-424-5P AND MIR-378C IN STENOTIC AND PENETRATING LESIONS OF CROHN'S DISEASE ASSOCIATES WITH ALTERED TRANSCRIPTION OF GENES INVOLVED IN VASCULAR REGULATION

S. Coll¹, M. Seco-Cervera¹, C. Bauset¹, L. Lis-López¹, J. Cosin-Roger², D. Ortiz-Masia³, L. Gisbert-Ferrandiz¹, M.D. Barrachina¹, S. Calatayud¹

¹Universidad de Valencia, Pharmacology, Valencia, Spain,

²Unidad Mixta Facultad de Medicina-Hospital Dr Peset, FISABIO, Pharmacology, Valencia, Spain, ³CIBERhd-Univ. de Valencia, Dept. de Medicina, Valencia, Spain

Contact E-Mail Address: sandra.coll@uv.es

Introduction: Crohn's disease (CD) is often complicated by the appearance of intestinal stenosis (B2 behaviour) or fistulas (B3 behaviour), and the factors determining the pattern of disease and the etiology of these lesions, both associated with fibrosis and requiring surgery, are poorly defined.

Aims & Methods: Our aim has been to detect transcriptomic alterations in intestinal tissues affected by stenosis or fistulas, and have centred our attention in genes affecting vessel formation and function as potential contributors to these lesions. We conducted a small RNA sequencing profiling on ileal surgical resections from CD patients with B2 (n=10) or B3 (n=10) behaviour. We obtained a sample from affected tissue and the paired non-affected ileum from each patient.

Results: Tissues affected by stenotic or penetrating lesions present a differential expression of two pro-angiogenic miRNAs (miR-378c and miR-424-5p), and an increased expression of genes associated with vascular regulation, and both alterations are more pronounced in penetrating lesions. The expression of this set of genes shows a generalized and significant correlation with that of the pro-angiogenic miRNAs (negative with the down-regulated miR-378c, positive with the up-regulated miR-424-5p), especially in the affected tissue.

Conclusion: Ileal tissues from CD patients affected by stenosis or penetrating injuries present a local alteration in the expression of miRNAs with pro-angiogenic functions that probably contributes to the up-regulation of genes associated with vessel formation and to the modification of the vascular compartment in these lesions.

Disclosure: Nothing to disclose.

P0227

ACCUMULATION OF PRO-INFLAMMATORY CD4⁺ T CELLS AND ACTIVATED TCR V δ 1⁺ T CELLS IN INFLAMED GUT TISSUE OF CROHN'S DISEASE PATIENTS

J. Devan¹, V. Nosi^{1,2}, J. Spagnuolo¹, A. Beshirova¹, A. Chancellor¹, J.H. Niess³, L. Mori¹, R. Calogero², G. De Libero¹, P. Hruz^{4,1}

¹University of Basel, Department of Biomedicine, Basel, Switzerland, ²University of Torino, Department of Molecular Biotechnology and Health Sciences, Torino, Italy, ³Clarunis - University Center for Gastrointestinal and Liver Diseases Basel, Gastroenterology and Hepatology, Basel, Switzerland, ⁴Universitätsspital Basel, Abt. Endoskopie, Basel, Switzerland

Contact E-Mail Address: jan.devan@unibas.ch

Introduction: Crohn's disease (CD) is a chronic immune mediated disorder of the gastrointestinal tract. Wide screening-based studies revealed that immune cell subsets with unique plasticity and immune-regulatory properties accumulate in CD patients.

Aims & Methods: To investigate the presence of unique T cells in the intestinal mucosa phenotype and functional studies were performed on inflamed and not-inflamed biopsies from patients with CD and healthy controls. We established an anti-CD45 mAbs-based barcoding approach to simultaneously analyze hundreds of surface-molecules expressed on cells isolated from intestinal tissue of CD patients.

Using 31 color flow-cytometry and phenograph clustering analysis, unique T cell populations were detected in inflamed tissue. Functional capacity was studied by intracellular staining with anti-cytokine mAbs after *in vitro* T cell activation.

Results: In intestinal tissue we found mutually exclusive expression of CD39 and CD73 ectonucleotidases on CD4⁺T cells and CD39 and CD45RA on TCR V δ 1⁺ T cells, defining phenotypically and functionally distinct populations.

In inflamed tissue of patients with CD, we observed:

- Augmented proportion of effector memory CD4⁺T cells;
- Accumulation of activated CD4⁺CD39⁺T cells producing IL-17 and IL-21;
- Increased frequency of terminally differentiated TCR V δ 1⁺ T cells producing TNF- α and IFN- γ and;
- Decreased frequency of T-effector memory TCR V δ 1⁺CD39⁺ T cells producing IL-9 and IL-6. No major alterations in CD8⁺T cells and MAIT cells were found.

Conclusion: The inflamed areas of intestinal tissue in CD patients showed significant changes of CD4⁺ and TCR V δ 1⁺ T cell populations, each secreting different types of pro-inflammatory cytokines, thus indicating their non-overlapping contribution to inflammation. The abnormal accumulation of TCR V δ 1⁺ T cells with phenotype of terminally differentiated T cells implicates continuous activation in inflamed tissue.

Disclosure: Nothing to disclose.

P0228

THE HEALTH DATA RESEARCH HUB FOR INFLAMMATORY BOWEL DISEASE - GUT REACTION- 3 YEARS ON

L. Pele^{1,2}, M. Avery^{3,4}, A. Ullrich⁵, D. Yuchun⁵, N. Walker⁵, N. Kingston⁵, J. Bradley^{5,6}, M. Parkes^{1,2,6}

¹NIHR IBD BioResource, Cambridge, United Kingdom, ²University of Cambridge, Department of Medicine, Cambridge, United Kingdom, ³Eastern AHSN, Cambridge, United Kingdom, ⁴Cambridge University Health partners, Cambridge, United Kingdom, ⁵NIHR BioResource, Cambridge, United Kingdom, ⁶NIHR Cambridge Biomedical Research Centre, Cambridge, United Kingdom

Contact E-Mail Address: laetitia.pele@bioresource.nihr.ac.uk

Introduction: Inflammatory Bowel Disease (IBD), comprising Crohn's disease (CD) and ulcerative colitis (UC), affects ~500,000 people in the UK, causing relapsing intestinal inflammation. Long-term management often requires costly drug treatments and major surgery. While recent advances in 'omics' technologies have improved our understanding in IBD pathogenesis and outcomes, their full potential will only be realised if allied to routinely collected clinical data.

For this purpose, the Health Data Research (HDR) Hub for IBD - Gut Reaction was launched in 2019 after a successful bid to HDR UK. Gut Reaction is led by Cambridge University Hospitals NHS Foundation Trust and Eastern AHSN in partnership with the NIHR BioResource, UK IBD Registry, Crohn's & Colitis UK, thirteen NHS Trusts and three technology partners.

Aims & Methods: Building a multidimensional data resource: We are developing methodologies to link data assets from ~36,000 NIHR IBD BioResource participants to centrally-held data at NHS Digital and electronic healthcare record data for a subset of ~11,000 patients recruited from thirteen participating NHS Trusts. In particular, we are working toward integrating genomic data with structured phenotypic data and routinely collected longitudinal healthcare data including laboratory test results; histopathology, endoscopy and radiology results, digitised radiology and histopathology images (where applicable), prescribing data, clinic letters and commissioning data sets.

Accessing the multidimensional data resource: Since NIHR IBD BioResource participants have consented to their medical records being accessed for research purposes, the resulting built-in Gut Reaction data 'panel' is open to any investigators, from science or industry, to facilitate studies requiring access to integrated real world IBD patient data. Working in partnership the Gut Reaction Patient Advisory Committee, the NIHR BioResource Data Access Committee and the Scientific Advisory Board review research applications based on scientific merits and projected benefit to patients and, upon approval, provide integrated data using secure cloud research environments.

Results: Almost 3 years on, Gut reaction has received > 20,000 standard files, and > 11 million 'records' from participating Trust including >6 million test results, >28,000 radiology images and >98,000 radiology reports and ~3 million correspondence, to name a few.

The aspirations of Gut Reaction have generated a lot of interest from industry and academia alike, and to date the HDR Hub for IBD has been able to facilitate two commercial and two academic use cases:

- Exploring association differences across multiple sub-phenotypes of CD and UC.
- Turning samples into data by providing access to de-identified health data and gut biopsy samples from clinically phenotyped UC and CD patients.
- Developing a tool to predict clot risk in IBD.
- Assessing whether immunosuppressant / biologic therapies do or do not increase Covid risks, and whether vaccines are or are not effective in patients on these medications.

Conclusion: Gut Reaction is on course to deliver a world-class multidimensional integrated data resource for research and innovation. Its success may be recapitulated across other disease areas to benefit other patient communities.

Disclosure: Nothing to disclose.

P0229 WITHDRAWN

P0230

THE IMPACT OF VITAMIN D DEFICIENCY ON COVID-19 INFECTION AND RESPONSE TO VACCINATION

J. Doherty¹, N. O'Morain², R. Stack³, D.J. Daghfal⁴, P. Doran⁵, C. O'Morain⁶, R. Inzitari⁵, G.A. Doherty⁷

¹St Vincent's Hospital, Dublin, Ireland, ²St. Vincent's University Hospital, Gastroenterology, Dublin, Ireland, ³St Vincent's University Hospital, Centre for Colorectal Disease, Dublin, Ireland, ⁴Abbott Laboratories, Abbott Diagnostics, Lake Forest, IL 60045, United States, ⁵University College Dublin, Dublin, Ireland, ⁶Trinity College Dublin - Faculty of Health Sciences, Trinity College Dublin; Dublin/IE, Faculty of Health Sciences, Dublin, Ireland, ⁷University College Dublin, Gastroenterology, Dublin, Ireland

Contact E-Mail Address: jaynedoherty@hotmail.com

Introduction: Accelerated vaccine development and mass vaccination campaigns have been conducted to induce protective immunity against SARS-CoV-2. Although data is conflicting, certain agents with the ability to regulate the immune response, such as vitamin D have been shown to prevent and improve outcomes in respiratory illnesses including COVID-19 infection [1].

Aims & Methods: Determine the impact of vitamin D deficiency in patients with inflammatory bowel disease (IBD) on Spike Protein (SP) immunoglobulin (Ig) G levels post-vaccination against COVID-19 and the impact on rates of COVID-19 infection.

IBD patients and healthy controls (HC) were recruited prospectively from five hospitals and quantitative antibody responses and vitamin D levels assessed following COVID-19 vaccination. Infection with COVID-19 was defined by a positive polymerase-chain-reaction or antigen test.

Results: 485 participants had vitamin D samples analysed (331 patients, 154 controls). 319 had SP IgG levels analysed post two doses of COVID-19 vaccine. 231 (47.3%) participants were male. Median age was 39.5 years. A significant diurnal variation was found in median vitamin D levels between the winter and summer period ($p < 0.001$). Vitamin D levels were significantly higher in IBD patients compared to HCs (27.8 ng/ml versus 18.1 ng/ml, $p < 0.001$) with 56.9% of IBD patients being vitamin D deficient compared to 74.7% of HCs ($p < 0.001$). Vitamin D levels did not correlate with SP IgG levels post-vaccination against COVID-19 (Correlation coefficient -0.41, $p = 0.47$). Median vitamin D levels were significantly lower in participants who were previously infected with COVID-19 compared to those who were not infected (16.4 ng/ml versus 27.0 ng/ml, $p < 0.001$).

	Healthy controls (n=154)	IBD cohort (n=331)	p - value
Median age (IQR)	40.6 (30.0 - 49.4)	34.8 (28.3 - 49.6)	0.1
Male gender (%)	27 (17.5%)	204 (61.6%)	<0.001
Previous COVID-19 infection (%)	48 (31.2%)	25 (7.5%)	<0.001
Median Vitamin D levels	18.1	27.8	<0.001

Table.

Conclusion: Vitamin D deficiency has no impact on response rates to COVID-19 vaccination. However vitamin D deficiency was more prevalent in participants who had experienced COVID-19 infection. Vitamin D deficiency was common and replacement may not alter vaccine response but along with vaccination may modify risk of COVID-19 disease in the population.

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Disclosure: None.

P0231

TRANSCRIPTOME CHANGES IN A COMMENSAL ESCHERICHIA COLI STRAIN FROM HEALTHY DONOR AFTER INCUBATION WITH IGA IN VITRO

M. Siniagina¹, I. Baichurina¹, M. Markelova¹, I. Semin², A. Kruglov^{3,2}, D. Matyushkina⁴, V. Musarova⁴, S. Abdulkhakov¹, T.V. Grigoryeva¹

¹Kazan Federal University, Institute of Fundamental Medicine and Biology, Kazan, Russian Federation, ²Moscow State University, Belozersky Institute of Physico - Chemical Biology, Moscow, Russian Federation, ³German Rheumatism Research Center, a Leibniz Institute, Berlin, Germany, ⁴Scientific Research Institute of Systems Biology and Medicine of the on Consumer's Rights Protection and Human Well-Being Surveillance, Moscow, Russian Federation

Contact E-Mail Address: marias25@mail.ru

Introduction: Crohn's disease (CD) is characterized by an increase in the relative abundance of Escherichia coli and a disturbance of the mucosal immune system, accompanied by an increase in the level of IgA in the intestinal lumen. IgA antibodies are secreted by the mucosa to block bacteria from penetrating the epithelium.

Aims & Methods: The aim of the study was to evaluate the effect of IgA on a commensal strain of E. coli 1_39_1 isolated from the feces of a healthy donor and closely related to probiotic E. coli Nissle1917 [1].

Commensal E. coli isolate 1_39_1 from a healthy individual was incubated with IgA (600 µg) as well as 2% BSA and PBS (negative controls) for 2 hours at room temperature (in triplicate).

Total RNA from samples was isolated with standard phenol-chloroform extraction method and then treated with DNase I (NEB). rRNA was depleted with NEBNext rRNA Depletion kit for bacteria (NEB). mRNA library was made using NEBNext Ultra II RNA library Prep kit (NEB).

Next-generation sequencing was performed on the NextSeq 500 Illumina platform. Sequence reads were mapped on reference genome E. coli strain 1_39_1 (GCA_008041535.1) using Bowtie2, counted with featureCounts. Differently expression of genes was made by Deseq2 in R.

Results: In this study treatment of the clinical E. coli strain from healthy individual with IgA leads to differential expression of 218 genes. Of particular interest was the significantly increased expression of genes encoding serum survival lipoprotein Iss (iss), proteins involved in adhesion (type 1 fimbrial protein), invasion and vesicle formation (bamB, nlpA), motility-associated proteins (fliC/fljB, flgK, motA) and O6-antigen synthesis (wzx, wzy). IgA treatment stimulates bacterial cell division by increasing the expression of genes ftsQ, zapC, zipA and decreasing the expression of division inhibitor sulA.

At the same time, the expression of pks-island genes encoding the colibactin production system (clbJ, clbI, clbE, clbC) decreased. The functional role of colibactin is controversial, but it is necessary for probiotic E. coli to realize its anti-inflammatory effects.

Conclusion: Testing a commensal strain of E. coli from a healthy donor for IgA treatment revealed an increase in the expression of virulent factors such as adhesion, invasion, motility and immune stimulation that help bacteria survive and colonize the intestine.

Thus, in addition to imbalance in bacterial community, CD is accompanied by a change in the interaction of commensal bacteria with human immune system leading to an increase in bacterial virulence.

References:

1. Siniagina MN, et al. Diversity and adaptations of *Escherichia coli* strains: exploring the intestinal community in Crohn's disease patients and healthy individuals. *Microorganisms*. 2021 Jun;9(6):1299.

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P0232

INTERACTION BETWEEN CHITINASE 3-LIKE 1 (CHI3L1) AND BACTERIAL PROTEIN CHIA: A DECISIVE STEP FOR CROHN'S DISEASE-ASSOCIATED ADHERENT AND INVASIVE *E. COLI* TO ENTER WITHIN HUMAN MACROPHAGES

M. Fargeas¹, C. Douadi¹, F. Faure², A. Buisson², N. Barnich¹

¹Université Clermont Auvergne, M2iSH, Clermont-Ferrand, France,

²CHU Estaing Clermont-Ferrand, IBD Unit, Clermont-ferrand, France

Contact E-Mail Address: margot.fargeas@uca.fr

Introduction: Crohn's Disease (CD)-associated adherent-invasive *E. coli* (AIEC) are, by definition, able to adhere to and invade intestinal epithelial cells (IECs), and to survive and replicate within macrophages inducing inflammatory response. Besides, macrophages from CD patients are specifically defective to control AIEC replication.

It has been recently shown that anti-TNF agents limit AIEC replication within macrophages by modulating Chitinase 3-Like 1 (CHI3L1) expression. AIEC bacteria adhere to IECs through the interaction between the AIEC protein ChiA and CHI3L1. Whether CHI3L1-ChiA interaction could play a role in promoting AIEC entry into macrophages is unknown.

Aims & Methods: We aimed to assess whether the CHI3L1-ChiA interaction is implicated to promote AIEC entry and survival within macrophages and to decipher the involved mechanisms.

The physical interaction between these two proteins have been assessed by Western blot. Human cultured macrophages (THP-1) and human macrophages-derived monocytes (hMDM) were infected with the reference AIEC LF82 strain (LF82 AIEC WT), the corresponding *chiA*-negative mutant (LF82- Δ *chiA*) and its transcomplemented for *chiA* (LF82- Δ *chiA*:: Δ *chiA*), and with a commensal strain of *Escherichia coli*(K12C600). Other AIEC strains, isolated from CD patients were also used.

Fluorescent protein (green and red) genes have been added in bacteria's genomes in order to visualise them during co-infection observed by cell-live or confocal imagery. Anti-CHI3L1 antibodies and recombinant CHI3L1 have been used to block ChiA-CHI3L1 interaction.

Results: After incubation with AIEC, recombinant CHI3L1 protein binds AIEC LF82 bacteria with a 2.5-fold higher intensity than the *chiA*-invalidated mutant ($p < 0.05$) confirming ChiA-CHI3L1 interaction. LF82- Δ *chiA* bacteria uptake (at 1h post-infection) within human macrophages was reduced of 40 % and 45 % in THP-1 and hMDM, respectively, compared to wild type LF82 ($p < 0.05$). In contrast, we did not show any impact on AIEC survival at 10h and 24h post-infection.

Live imaging recording macrophages infection with a mixture (1:1 ratio) of LF82 AIEC WT (labelled in red) and the LF82- Δ *chiA* mutant (labelled in green), showed that LF82- Δ *chiA* mutant had a two-fold reduced entry into hMDM ($p < 0.05$) than LF82 AIEC WT.

Incubation with recombinant CHI3L1 to inhibit ChiA-CHI3L1 interaction, led to a two-fold decrease of AIEC uptake within macrophages at 1h post-infection ($p < 0.05$). Blockage of ChiA-CHI3L1 interaction using anti-CHI3L1

antibodies significantly decreased the survival ability within macrophages of several AIEC bacteria strains isolated from CD patients including LF82 ($p < 0.05$), demonstrating that this mechanism may be common to different AIEC strains.

Conclusion: ChiA-CHI3L1 interaction plays a key role in the CD-associated AIEC ability to enter within macrophages. Blocking this interaction may be promising to target AIEC in patients with CD.

Disclosure: Nothing to disclose.

P0233

DEEP LEARNING-BASED IMAGE ANALYSIS REVEALS SIGNIFICANT DIFFERENCES IN NUMBER AND DISTRIBUTION OF CD3 AND $\gamma\delta$ T CELLS BETWEEN CROHN'S COLITIS AND ULCERATIVE COLITIS

E.S. Røyset^{1,2,3}, H.P.S. Pettersen^{1,3,2}, W. Xu⁴, A. Larbi⁴, A.K. Sandvik^{1,5,6}, S. Steigen^{7,8}, I. Catalan-Serra⁹, I. Bakke^{1,2}

¹Norwegian University of Science and Technology, Department of Clinical and Molecular Medicine, Trondheim, Norway, ²St. Olav's Hospital, Trondheim University Hospital, Clinic of Laboratory Medicine, Trondheim, Norway, ³St. Olav's Hospital, Trondheim University Hospital, Department of Pathology, Trondheim, Norway, ⁴Singapore Immunology Network (SiGN), Agency for Science Technology and Research, Singapore, Singapore, ⁵St. Olav's Hospital, Trondheim University Hospital, Department of Gastroenterology and Hepatology, Clinic of Medicine, Trondheim, Norway, ⁶Norwegian University of Science and Technology, Centre of Molecular Inflammation Research, Trondheim, Norway, ⁷University Hospital of North Norway (UNN), Department of Pathology, Tromsø, Norway, ⁸UiT The Arctic University of Norway, Tromsø, Norway, Department of Medical Biology, Tromsø, Norway, ⁹Levanger Hospital, Norwegian University of Science and Technology. Centre for Molecular Inflammation, Gastroenterology, Levanger, Norway

Contact E-Mail Address: elin.s.royset@ntnu.no

Introduction: Colon mucosa of Ulcerative colitis (UC) and Crohn's disease (CD) display variations in the number and distribution of immune cells that are difficult to assess by eye. Digital pathology enables deep learning-based analysis on whole slide images (WSI) to extract complex quantitative data. This may uncover differences in inflammatory patterns and help identify histological features with prognostic or predictive value. T cell disturbances in IBD mucosa create a pro-inflammatory environment. The epithelial area has a large population of tissue resident $\gamma\delta$ T cells that play key roles in gut immunity, but their role in IBD is not clear ¹.

Aims & Methods: In this study, we use deep learning-based segmentation and cell detection on 57 WSIs from 37 CD patients, 83 WSIs from 58 UC patients, and 41 WSIs from 33 healthy controls, to quantify CD3 and $\gamma\delta$ T cells in the epithelial, subepithelial and lamina propria compartments of proximal and distal colon mucosa, defined by Nancy histological index.²

We assessed the impact of oral corticosteroids, age, and gender on mucosal numbers of CD3 and $\gamma\delta$ T cells, and used flow cytometry to assess correlation between relative amounts of $\gamma\delta$ T cells in blood and colon mucosa.

Results: We found significantly lower numbers of intraepithelial $\gamma\delta$ T cells in inactive CD compared to inactive UC (Fold change (FC): 0.5, 95% CI 0.3-0.8, $p = 0.007$). HC had more intraepithelial $\gamma\delta$ T cells than inactive CD, but less than inactive UC, although the differences were not significant. However, oral corticosteroids were found to impact the intraepithelial numbers of $\gamma\delta$ T cells. Adjusting for this, the difference between inactive UC and HC became significant (FC 1.7, 95% CI 1.0-2.8, $p = 0.049$).

Further, histological disease activity was not associated with change in $\gamma\delta$ T cells in the epithelium in CD, in contrast to a significant loss of $\gamma\delta$ T cells from the epithelium in active UC (FC 0.3, 95% CI 0.2–0.5, $p < 0.001$). Interestingly, the total number of intraepithelial CD3 cells was not significantly affected by disease activity in CD or UC, which implies a role for other T cell subsets in the active UC epithelium. Another interesting finding was the generally higher numbers of CD3 cells in colon mucosa in CD compared to UC and HC.

By delineating a narrow subepithelial zone we found significantly higher numbers of CD3 cells in inactive CD than in inactive UC (FC 1.4, 95% CI 1.0–1.9, $p = 0.024$) and HC (FC 1.6, 95% CI 1.2–2.2, $p = 0.01$). The numbers of CD3 cells were also higher in lamina propria (FC 1.6, 95% CI 1.1–2.1, $p = 0.016$) and in the epithelium (FC 1.4, 95% CI 1.0–1.9, $p = 0.06$) in inactive CD than in HC. The numbers of $\gamma\delta$ T cells beneath the epithelium or in lamina propria did not differ significantly between CD, UC, and HC, and was not affected by disease activity. Proximal colon had significantly higher numbers of CD3 and $\gamma\delta$ T cells than distal colon. We found no effect of age or gender, and no significant correlation between the relative abundance of $\gamma\delta$ T cells in blood and mucosa.

Conclusion: The study uncovers significant differences in number and distribution of CD3 and $\gamma\delta$ T cells in particularly the epithelial microenvironment between inactive and active CD, UC, and HC. We hypothesize that fewer intraepithelial $\gamma\delta$ T cells in CD may represent a deficiency state of mucosal innate immunity³ leading to impaired acute responses and higher strain on other immune cells deeper down in the gut wall.

The study demonstrates the utility of deep learning techniques in tissue segmentation and cell quantification to describe the complex features of chronic inflammation more precisely in IBD.

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P0234

CLAUDIN-2 OVEREXPRESSION IN STEM CELL ZONE CORRELATES WITH INCREASED INTESTINAL PERMEABILITY AND EPITHELIAL CELL PROLIFERATION DURING SHORT RECOVERY PERIOD IN ACUTE MURINE DSS MODEL OF INFLAMMATORY BOWEL DISEASE

M. Antolić¹, K. Špiranes Spes¹, A. Markota¹, A. Volaj-Bijelić¹, V. Milutinović¹, A. Ognjenović¹, A. Paravić Radičević², I. Glojnarčić¹, M. Bosnar³, R. Suzuki³, A.J. Brown³, S. Čužić¹, V. Eraković Haber⁴
¹Selvita Ltd., *In vivo* Pharmacology and Toxicology Department, Zagreb, Croatia, ²Selvita Ltd., *In vitro* Pharmacology and Toxicology Department, Zagreb, Croatia, ³Sosei Heptares, Translational Sciences, Cambridge, United Kingdom, ⁴Selvita Ltd., Translational Sciences, Zagreb, Croatia

Contact E-Mail Address: snjezana.cuzic@selvita.com

Introduction: Claudins are transmembrane proteins of tight junctions (TJs). Alterations in the expression of many claudins along the gastrointestinal tract may lead to loss of the epithelial barrier function and contribute to the pathogenesis of inflammatory bowel diseases (IBD). In addition, tight junction proteins can contribute to the control of cell proliferation required for intestinal tissue repair. A better understanding of the role of claudins in cell proliferation during intestinal inflammation is needed.

Aims & Methods: The aim of this study was to investigate the connection between stem cell zone proliferation and epithelial tight junction protein claudin-2 expression on intestinal tissue repair in a mouse model of dextran sodium sulphate (DSS) induced acute colitis with the recovery phase. The expression of claudin-2 and Ki-67 as a marker of cell proliferation was evaluated on colon tissue sections by immunohistochemistry and correlated with colitis-associated parameters such as colon shortening, endoscopy score and intestinal permeability.

Results: DSS (1,5%) challenge given for 6 days followed by 6 days of recovery phase elicited increased colitis associated parameters such as disease activity index score (DAI), colon shortening and intestinal permeability in challenged group, which were all decreased in cyclosporine A treated animals. Colonoscopy examination showed the presence of oedema, mucosal thickening and vascular pattern changes in colon, while histopathology analysis revealed chronic inflammation and mucosal damage with beginning the of re-epithelization in the disease control group.

Significantly upregulated expression of claudin-2 and Ki-67 marker was detected in the disease control group in comparison with the water control and cyclosporine A treated group. A strong correlation between claudin-2 protein expression and cell proliferation marker Ki-67 in the colon can be seen in all groups, as well as the correlation between claudin-2 and clinical read-out of intestinal permeability (Spearman's Rank-Order Correlation, $p < 0.001$).

Conclusion: Our findings reveal significant upregulation of colonocyte proliferation and claudin-2 expression at the tight junctions along the basolateral membrane in the stem cell niche during DSS induced colitis model suggesting a greater role of tight junction proteins in the development of new epithelial cells in crypt base (Díaz-Coránguez, 2019). Results of present study further highlighted the role of claudin 2 in intestinal epithelial renewal.

In summary, results of our study indicate a role of claudin 2 expressing epithelial cells situated within stem cell niche in crypt proliferation and their contribution to increased permeability of mucosal barrier.

The strong correlation between colonic claudin-2 overexpression and increased intestinal permeability makes claudin-2 protein a good histopathological marker and therapeutic target for the leaky intestinal barrier in IBD.

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P0235

IDENTIFICATION OF A DISTINCT MICROBIOTA SIGNATURE IN CROHN'S DISEASE-ASSOCIATED AND CRYPTOGLANDULAR PERIANAL FISTULAS

L.F. Ouboter^{1,2}, Q.R. Ducarmon³, E. van Lingen¹, R.D. Zwiitink³, L. Hawinkels¹, M.F. Pascutti², A.E. Van Der Meulen - De Jong¹, M. Barnhoorn¹

¹Leiden University Medical Center, Gastroenterology and Hepatology, Leiden, Netherlands, ²Leiden University Medical Center, Immunology, Leiden, Netherlands, ³Leiden University Medical Center, Medical Microbiology, Leiden, Netherlands

Contact E-Mail Address: m.c.barnhoorn@lumc.nl

Introduction: Crohn's disease (CD) is thought to result, in part, from a dys-regulated mucosal immune response towards the commensal gut microbiota. Perianal fistulas are a severe complication of CD, but also occur in patients without CD (cryptoglandular fistulas). The gut microbiota of CD patients with active inflammation is known to be different from healthy controls.

However, the existence of a fistula-specific microbiota in CD-associated perianal fistulizing disease has not been unraveled yet. In this pilot study, we aimed to identify the microbiota in the feces and fistula tract in both patients with CD-associated and cryptoglandular fistulas.

Aims & Methods: We analyzed fecal (n=16) and fistula swab (n=16) samples from 24 patients with perianal fistulas (CD: n=14; cryptoglandular: n=10) using 16S rRNA sequencing. From eight patients we obtained both fecal and fistula swab samples. No patients, apart from one CD patient, used antibiotics. Twelve out of fourteen CD patients used biologics, including infliximab, adalimumab, and/or vedolizumab, during sample collection. Microbiota analyses and visualizations were performed in R (v4.0.4).

Differential abundance analysis was performed at genus level using DE-Seq2 with the Wald test. P-values were adjusted using Benjamini-Hochberg correction and adjusted p-values < 0.05 were considered significant. In addition, RNA in situ hybridization (RNAscope®) was applied on formalin-fixed, paraffin-embedded specimens for the detection of bacterial RNA using a 16S RNA probe for eubacteria.

Results: Analyses of the fecal and fistula microbiota revealed a different microbial composition between the two locations, including more skin bacteria (e.g. *Lawsonella*, *Cutibacterium*, *Staphylococcus*), bacteria belonging to the Peptostreptococcus family, and especially a high relative abundance of the phylum Fusobacteriota in the fistula tracts. Fusobacteriota was especially abundant in CD-associated fistula tracts.

Comparison of CD and cryptoglandular fistula microbiota showed a significantly higher level of oral disease-associated bacteria (*Sneathia* - belonging to phylum Fusobacteriota, and *Eikenella*) in CD fistulas compared to cryptoglandular fistulas, next to enrichment of *Sutterella*. In cryptoglandular fistulas high levels of some so-called 'colitis protective bacteria' (*Coprostanoligenes*, *Holdemanella*, *Parasutterella*, *Christensenellaceae*, *Subdoligranulum*) were found compared to CD fistulas. Besides this, we were able to detect bacteria infiltrating the tissue around the fistula tract in CD fistulas.

Conclusion: In this study we revealed the existence of microbiota specific for CD-associated perianal fistulas with increased relative abundance of oral disease-associated bacteria and *Sutterella*, the latter known for its degradation of IgA¹. Observed differences in the fistula microbiota between CD and non-CD patients could lead to identification of new biomarkers to distinguish both diseases.

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P0236

SERUM PROTEOME PROFILES IN CROHN'S DISEASE PATIENTS WITH DIFFERENT PHENOTYPES TOWARDS BIOMARKER IDENTIFICATION

L.A. Lucaciu¹, M. Ilies², S. Pasca^{2,3}, I.-E. Pralea², A. Uifalean⁴, R. Nicoara⁴, R. Seicean⁵, C.A. Iuga^{2,4}, A. Seicean^{6,1}

¹Iuliu Hatieganu University of Medicine and Pharmacy, Gastroenterology and Hepatology, Cluj-Napoca, Romania, ²MedFuture Research Center for Advanced Medicine, Iuliu Hatieganu University of Medicine and Pharmacy, Proteomics and Metabolomics, Cluj-Napoca, Romania, ³Iuliu Hatieganu University of Medicine and Pharmacy, Haematology, Cluj-Napoca, Romania, ⁴Iuliu Hatieganu University of Medicine and Pharmacy, Pharmaceutical Analysis, Cluj-Napoca, Romania, ⁵Clinical Emergency County Hospital Cluj-Napoca, First Surgical Clinic, Iuliu Hatieganu University of Medicine and Pharmacy, General Surgery, Cluj-Napoca, Romania, ⁶Regional Institute of Gastroenterology and Hepatology, Prof. Dr. O. Fodor, Gastroenterology and Hepatology, Cluj-Napoca, Romania

Contact E-Mail Address: laura_lucaciu@yahoo.com

Introduction: Crohn's disease (CD) is a chronic inflammation of the gastrointestinal tract leading to progressive, often irreversible bowel damage, such as strictures, fistulae and/or functional impairment. The complexity and heterogenous presentation highlight the need for individualized therapeutic approach.

Many studies have identified CD biomarkers using proteomic tools; however, clinical and disease signature markers indicative of the molecular progression of the disease are yet to be developed.

Aims & Methods: We aimed to analyse the serum proteome of CD patients with different phenotypes by employing mass-spectrometry (MS) techniques, in order to identify novel candidate biomarkers for disease progression.

We prospectively included in this study 30 CD patients and 15 healthy controls (HC). CD patients who had confirmed strictures or penetrating disease at the time of inclusion in this study (n=15), and a group of patients with persistent inflammation but no strictures or fistulae (n=15) were selected. Baseline demographic data, disease characteristics and phenotype, as well as the type and duration of IBD treatment were recorded. Serum samples were collected and subjected to depletion of highly abundant proteins and to label-free nano-LC coupled with Q-TOF mass spectrometry analysis (nano-LC HDMS).

For the analysis of two groups we used Welch's t-test or Mann-Whitney-Wilcoxon rank sum test; for correlation analysis we used Spearman's rho test. Significant proteins were chosen when p<0.05, fold change >1.5, and rho >0.8. The mean decrease in Gini from a random forest model with 2000 trees was used to determine the importance of selected proteins and clinical biomarkers in differentiating between CD and healthy individuals and between CD phenotypes, where B1= inflammatory and B2/B3 = stricturing/penetrating (B1 and B2/B3). Bioinformatic tool Metascape was used towards identification of pathways and protein interactions of proteins with changed abundance.

Results: The serum proteome was characterized and over 300 non-redundant proteins were identified in each sample group with good coefficient of variation (CV<15%) and peptide coverage. A total of 21 proteins, including haptoglobin, plexin, serum amyloid 1 distinguished between CD and HC groups. A statistically significant panel of 28 proteins was identified between the B1 versus B2/B3 phenotypes.

Twenty-four proteins were significantly abundant in the B1 phenotype group compared to the B2/B3 group, including: Interleukin-18 (IL-18), Cilia- and flagella-associated protein 36 (CFAP36), Plexin-A2 (PLXNA2), Protein S100-Z, Immunoglobulin heavy variable 1-58 (IGHV1-58), Plasma

serine protease inhibitor (SERPINA5). In the B2/B3 group, there was a significant elevation of 4 proteins in comparison to the inflammatory group: WD repeat-containing protein 31, Leucine-rich alpha-2-glycoprotein (LRG), Serum amyloid A-1 protein (SAA1), Plexin-A1 (PLXNA1).

Conclusion: Proteomic analysis by MS is able to differentiate among inflammatory and complex CD. Some of the proteins that differentiate stricturing/penetrating phenotype were found to be implicated in acute inflammatory response (SAA1, LRG) Th1 and natural killer cell immune responses (IL-18), innate and adaptative immune responses (haptoglobin, IGHV1-58), coagulation, cellular proliferation, adhesion and migration (PLXN A1/A2, SERPINA5). Unique biomarker panels based on protein sets were identified and could provide significant insight into CD progression.

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P0237

SALIVARY EXOSOMES AGGRAVATE COLITIS BY REGULATING THE GUT IMMUNITY

C. Yang¹, J. Chen¹, Y. Xu¹, P. You¹, T. Peng¹, N. Chen¹

¹Peking University People's Hospital, Beijing, China

Contact E-Mail Address: yangcongyi@yeah.net

Introduction: Inflammatory bowel disease (IBD) is a chronic intestinal immune-dysfunctional disease involving the ileum, rectum, colon and even the entire digestive tract. More and more reports recognized the close correlation between the oral cavity and IBD incidence. Human saliva, as a readily available body fluid, may be a powerful indicator for evaluation of both local and systemic diseases. Numerous studies have shown that exosomes are important for information exchange, especially in the communication between distant organs.

However, the role of salivary exosomes in the colitis remains unknown. This study aimed at exploring the effect and mechanism of salivary exosomes on colitis.

Aims & Methods: Salivary exosomes were obtained from IBD patients using ultracentrifugation. In vivo, we used C57BL/6 mice to illustrate exosomes can travel from the oral cavity to the colorectum. Human myeloid leukemia mononuclear (THP-1) cells and Caco-2 cells were stimulated with lipopolysaccharides (LPS), which simulated an inflammation environment in vitro.

Results: Co-culture of THP-1 cells and Caco-2 cells with salivary exosomes from IBD patients were shown to raise inflammation in macrophages, which leads to increased release of inflammatory factors including TNF- α , IL-6, IL-1 β and promotes the polarization of M1 phenotype of macrophages.

Conclusion: In conclusion, the membrane structure of exosomes can resist the action of gastric acid and safely transport their contents to the intestine, where they can be taken up by macrophages to play a role. Salivary exosomes from IBD patients were found to promote intestinal inflammation via activating macrophages. Abnormal elevation of inflammatory factors was positively correlated with disease activity in IBD patients.

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P0238

THE INTERACTION BETWEEN SEROTONIN REUPTAKE TRANSPORTER AND BRAIN-DERIVED NEUROTROPHIC FACTOR IN INFLAMMATORY BOWEL DISEASE PATIENTS

M. Sochal¹, A. Gabryelska¹, A. Binienda², M. Ditmer¹, P. Białasiewicz¹, J. Fichna², R. Talar-Wojnarowska³, E. Matecka-Wojcieszko³

¹Medical University of Lodz, Department of Sleep Medicine and Metabolic Disorders, Lodz, Poland, ²Medical University of Lodz, Department of Biochemistry, Lodz, Poland, ³Medical University of Lodz, Department of Digestive Tract Diseases, Lodz, Poland

Contact E-Mail Address: marta.insmk@gmail.com

Introduction: The interplay between neuromodulators and serotonergic signaling might have an important role in the pathophysiology of inflammatory bowel diseases (IBD).

Interactions between mentioned signaling pathway and neurotrophins, such as brain-derived neurotrophic factor (BDNF) have been widely studied in the central nervous system (CNS), however, there is little data regarding this subject outside of this area.

Serotonergic transmission is heavily dependent on the serotonin reuptake transporter (SERT). It regulates the amount of serotonin in synapses by retrieving released serotonin back to the vesicles, thus changing the intensity of signal transmission. The direct interplay between BDNF and SERT in the CNS is quite evident, but interactions within the gastrointestinal tract remain elusive.

Aims & Methods: The aim of the study was to compare the expression of SERT mRNA and BDNF mRNA in IBD and healthy controls as well as assess their interactions and influence on the disease course.

The study group consisted of 68 patients with IBD (27 UC - ulcerative colitis, 41 CD - Crohn's disease) and 27 healthy controls (HC). Disease activity was assessed using the Harvey-Bradshaw index or partial Mayo score for CD and UC respectively. Venous blood samples were collected. RNA isolation from peripheral blood mononuclear cells was performed using the Trizol method. Synthesis of cDNA was conducted with a reverse transcription kit. The level of expression of chosen genes was determined by qRT-PCR. Amplification of the studied genes was compared to the reference gene β -actin. Relative expression was calculated using $\Delta\Delta C_t$ method. The study has been financed by National Science Centre, Poland-2018/31/N/NZ5/03715.

Results: IBD group showed an increased expression of SERT mRNA ($p=0.023$) and BDNF mRNA ($p=0.015$) compared to HC. SERT mRNA expression positively correlated with BDNF mRNA ($r=0.24$, $p=0.044$). In IBD patients, women have higher SERT mRNA expression than men ($p=0.019$), but not BDNF. There was no difference in genes expressions between the UC and CD group or between subjects with exacerbation and remission. The expression of SERT mRNA and BDNF mRNA was not affected by chronic diseases such as rheumatoid arthritis, asthma, diabetes, or surgical history ($p<0.05$).

Conclusion: Both SERT and BDNF may be important factors contributing to the pathophysiology of IBD, independently of the subjects' clinical status, IBD type, and other concomitant chronic conditions. Our results show that further research on the subject of interactions between SERT and BDNF in IBD might contribute to the state of knowledge on this condition and potentially improve current clinical practice.

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P0239

INTESTINAL CD8+ T CELL EXHAUSTION IS LINKED TO DISEASE ACTIVITY IN ULCERATIVE COLITIS

M. Grigorian¹, L.S. Mayer¹, H. Salie¹, A.M. Globig¹, B. Hockenjos¹, L. Krimmel¹, R. Thimme¹, B. Bengsch¹, P. Hasselblatt¹

¹University Hospital Freiburg, Dept. Of Medicine II, Freiburg, Germany

Contact E-Mail Address: Maximilian.Grigorian@uniklinik-freiburg.de

Introduction: The immune pathogenesis of ulcerative colitis (UC) is linked to imbalanced CD4+ T-cell responses. In contrast, the contribution of CD8+ T cells to disease pathogenesis, their spatial localization within the intestine as well as their functions in UC are not well characterized. CD8+ T cells may become dysfunctional and acquire an exhausted phenotype during chronic viral infection or cancer. Recently, exhausted T cell (Tex) signatures have been proposed as a potential prognostic marker in autoimmune diseases.

Aims & Methods: We therefore set out to perform a comprehensive analysis of CD8+ T cells with regard to their spatial distribution as well as functions in UC patients. Immune phenotyping in formalin-fixed and paraffin-embedded sigma biopsies from patients with ulcerative colitis (n = 21) was performed using Imaging Mass Cytometry (IMC) and subsequent Phenograph cluster analysis. In addition, lymphocytes were isolated from sigmoid biopsies of UC patients in remission (n = 9) and active disease (n = 20) and analyzed *ex vivo* by flow cytometry. Results were correlated with disease activity (Mayo score) and mucosal inflammation (assessed endoscopically and histologically [Nancy score]).

Results: IMC analysis and subsequent whole tissue cluster analysis revealed two clusters of CD8+ T cells localized within epithelia and the submucosa, respectively. Further analysis defined 13 distinct CD8+ T cell clusters in which markers of activation as well as T cell exhaustion (Tex) were predominantly induced during active disease.

Unbiased spatial analysis as well as a cell-based neighborhood approach revealed that intraepithelial CD8+ T cells had an activated phenotype during flaring disease, but their abundance was rather limited as compared to subepithelial CD8+ T cells. CD8+ T cells expressing markers reminiscent of Tex also expressed effector cell markers. They were mainly localized in the submucosa and their spatial location correlated with the presence of CD20+ B cells. *Ex vivo* FACS analysis of intestinal CD8+ T cells confirmed that expression of exhaustion markers was significantly increased during active disease as compared to remission.

These cells also displayed dysfunctional cytokine profile patterns, as assessed by an established functional exhaustion score. This phenotype also closely correlated with clinical, endoscopic and histological markers of UC disease activity.

Conclusion: Our findings define clusters of CD8+ T cells correlating with disease activity in UC and displaying a specific spatial localization within the intestine. Interestingly, inflammation in the intestines of UC patients is associated with the induction of CD8+ T-cell responses that phenotypically and functionally resemble Tex.

Our data support a model in which pathogenic activated effector CD8+ T cells expand in active disease and develop exhaustion features that limit their immunopathogenicity. The functional relevance, prognostic value and therapeutic relevance of these exhausted CD8+ T cell signatures in UC need to be analyzed in future studies.

Disclosure: Nothing to disclose.

P0240

FOOD ADDITIVE NANOPARTICLES IS ASSOCIATED WITH SPECIFIC PRO-INFLAMMATORY BACTERIAL CHANGES IN CROHN'S DISEASE. THE ENIGMA STUDY

J. Zhang^{1,2,3}, Q. Sun^{1,2,3}, J.J. Teh⁴, S. Kang⁴, J. Hu^{3,5}, W. Lin^{1,2,3}, G. Trakman^{6,7}, A. Hamilton⁶, A. Wilson O'Brien⁶, J.Y.L. Ching^{1,2}, J.J.Y. Sung⁸, J. Yu^{1,2}, M. Morrison⁴, M.A. Kamm^{6,7}, S.C. Ng^{1,2,3,9}

¹The Chinese University of Hong Kong, Department of Medicine & Therapeutics, Hong Kong, Hong Kong, China (SAR), ²The Chinese University of Hong Kong, State Key Laboratory of Digestive Disease, Li Ka Shing Institute of Health Sciences, Hong Kong, Hong Kong, China (SAR), ³Microbiota I-Center (MagIC), Hong Kong, Hong Kong, China (SAR), ⁴The University of Queensland Diamantina Institute, Faculty of Medicine, Brisbane, Australia, ⁵The Chinese University of Hong Kong, Institute of Digestive Disease, Hong Kong, Hong Kong, China (SAR), ⁶St Vincent's Hospital, Department of Gastroenterology, Melbourne, Australia, ⁷The University of Melbourne, Department of Medicine, Melbourne, Australia, ⁸Nanyang Technological University, Lee Kong Chian School of Medicine, Singapore, Singapore, ⁹The Chinese University of Hong Kong, Centre for Gut Microbiota Research, Faculty of Medicine, Hong Kong, Hong Kong, China (SAR)

Contact E-Mail Address: zhangjingwang12@gmail.com

Introduction: Emerging evidence suggests that food additives lead to intestinal inflammation via modulating gut microbiota in animal models. In this study, we aim to determine food additives consumption and their interactions with gut microbiota in patients with Crohn's disease (CD).

Aims & Methods: Previous and current consumption of nine main food additives intake (polysorbate-80, carboxymethylcellulose, carrageenan, aspartame, sucralose, saccharin, titanium dioxide, aluminosilicate, and sulfites) was quantified in 156 subjects including 92 Crohn's disease patients (CD), 21 first-degree relatives of CD (FDR), 21 non-related healthy household members of CD patients (HHM) and 22 healthy controls (HC), using a validated 26-item food additive questionnaire.

Fecal shotgun metagenomic sequencing was performed to analyze bacterial profiles. The stool dissimilarity score for each subject was defined as the median Bray-Curtis dissimilarity to the reference NC group. The bacterial species which differentially abundant among different groups were determined by MaAsLin2 with age, gender and smoking status adjusted.

Results: No significant differences of food additive consumption were observed among the CD, FDR, HHM, and HC groups. Nevertheless, nanoparticles are still the predominant factor in separating the bacteria community in CD and HC. Besides, nanoparticles are independent element among all types of food additives.

The Principal Coordinates Analysis (PCoA) showed that the CD and HC groups separated completely, with the FDR and HHM intermediate between these two groups. In line with it, a large proportion of the FDR and HHM subjects were also found to possess dissimilarity scores of a similar magnitude to the CD group. The consumption of the food additive nanoparticles (Aluminosilicate (AlSiO) and Titanium dioxide (TiO2)) was positively correlated with the stool dissimilarity scores in CD subjects ($P < 0.05$).

Using only the CD datasets from CD-HHM pairs in comparison to HC, a total of 33 CD-depleted species and 25 CD-enriched species were identified. Of these, 3 of the CD-depleted species and 10 of the CD-enriched species showed concordant changes in the HHM. *Fusobacterium ulcerans*, which was not detectable in the HC group, was positively correlated with both AlSiO and TiO2 intakes in the CD and HHM groups ($R^2 = 0.27$, $P < 0.01$ and $R^2 = 0.43$, $P < 0.001$, respectively).

Additionally, among all pathways which *F. ulcerans* read counts assigned to, both ALSiO and TiO2 positively correlated with L-histidine degradation pathway ($R=0.28$, $P<0.001$; $R=0.34$, $P<0.001$) and negatively correlated with starch degradation pathway ($R=-0.18$, $P<0.05$; $R=-0.24$, $P<0.01$).

Conclusion: Long-term exposure to food additive nanoparticles is associated with gut microbiome derangements in CD and HHM via modulating the relative abundances of specific members of the stool microbiota. These food additive-associated microbial changes may play a critical role in the pathogenesis of Crohn's disease.

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Disclosure: Siew Chien Ng and Francis Ka Leung Chan are the scientific co-founders and sit on the board of Directors of GenieBiome Ltd. Siew Chien Nghas served as an advisory board member for Pfizer, Ferring, Janssen, and Abbvie and a speaker for Ferring, Tillotts, Menarini, Janssen, Abbvie, and Takeda. She has received research grants from Olympus, Ferring, Janssen and Abbvie. Francis Ka Leung Chan has served as an advisor and lecture speaker for Eisai Co. Ltd., AstraZeneca, Pfizer Inc., Takeda Pharmaceutical Co., and Takeda (China) Holdings Co. Ltd.

P0241

EMERGING ROLE OF IL-33/ST2 AND GUT MICROBIOTA AXIS IN THE INFLAMMATORY PROCESS OF ULCERATIVE COLITIS PATIENTS WITH ILEAL POUCH-ANAL ANASTOMOSIS

L.R. Lopetuso¹, L.M. Vetrone¹, V. Petito¹, D. Pugliese¹, L. Parisio¹, L. Laterza¹, M. Neri², F. Scaldaferrì¹, A. Gasbarrini¹, A. Papa¹
¹CEMAD – IBD Unit, Fondazione Policlinico Universitario “A. Gemelli” IRCCS - Università Cattolica di Roma, Surgical and Medical Sciences Department, Roma, Italy, ²Department of Medicine and Aging Sciences, Italy, Chieti, Italy

Contact E-Mail Address: lopetusoloris@libero.it

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 IL-33/ST2 axis controls the mucosal healing process during intestinal inflammation. Restorative proctocolectomy with ileal pouch-anal anastomosis is a surgical procedure in patients with ulcerative colitis (UC) refractory to medical therapies. Pouchitis, the most common complication, is the inflammation of the pouch with a controversial etiology.

Aims & Methods: We aimed to explore the potential combined involvement of the IL-33/ST2 axis and gut microbiota in the inflammatory process of pouchitis.

23 ulcerative colitis patients with ileal pouch-anal anastomosis were enrolled. After clinical, endoscopic and histological assessment (based respectively on Pouchitis Disease Activity Index and Pouchitis Histological Score) 13 showed pouchitis and 10 a normal pouch. Mucosal samples were collected from the afferent ileal loop and from the pouch and processed for cytokines assessment, IHC and histological evaluation, and gut microbiota analyses (16S ribosomal RNA gene amplicon pyrosequencing). Multivariate analyses were run to generate transcriptional interaction networks and identify biomarkers for patients with inflamed pouches.

Results: Between the two categories of patients, at Multiplex analysis, IL-1Ra, IL-6, IL-8, IL-17, IP-10, MCP-1, MIP-1a, MIP-1b resulted increased in samples obtained from the inflamed pouch vs. those obtained from the normal pouch. In patients with pouchitis, IL-7 resulted reduced in the inflamed pouch vs. samples obtained from the afferent ileal loop. In patients with the normal pouch, no differences were recorded between the pouch and the afferent ileal loop. In patients with pouchitis, at ELISA, IL-33 and ST2 protein levels were significantly reduced in the pouch vs. the afferent

ileal loop and resulted overall decreased vs. samples obtained from patients with normal pouch indicating a potential IL-33/ST2-mediated defective healing process. At western blot, full-length, bioactive IL33, ST2L and sST2 were expressed in all experimental groups; the cleaved, less active form of IL33 was increased in only patients with pouchitis. IHC confirmed these observations. IL-33 and ST2 staining were less intense within the inflamed and ulcerated mucosa of pouchitis patients compared to the normal pouch, and in close proximity to areas of re-epithelialization.

Microbiota analysis showed an overall decreased biodiversity in patients with pouchitis vs. patients with normal pouch (both at pouch and afferent ileal loop level). Lower levels of Verrucomicrobia and increased abundance of Actinobacteria were recorded in inflamed pouch vs normal pouch. In patients with pouchitis, the afferent ileal loop and the pouch showed significantly decreased levels of Akkermansia muciniphila and augmented abundance of Collinsella vs. samples obtained from patients with normal pouch. In patients with pouchitis, multivariate analyses evidenced a significant inverse correlation between Collinsella e Collinsella aereofaciens abundance and ST2 levels.

Conclusion: In patients with pouchitis vs patients with normal pouch, divergent inflammatory molecular pathways and microbial populations distinctly characterize the pouch and the afferent ileal loop.

Overall, our results suggest a potential role for IL-33/ST2 and gut microbiota axis in driving the gut mucosal wound healing in patients with ileal pouch-anal anastomosis. Further studies are underway to determine mechanisms of action that support these findings.

Disclosure: Nothing to disclose.

P0242

GENOMIC DIVERSITY OF FAECALIBACTERIUM PRAUSNITZII STRAINS FROM MICROBIOTA OF PATIENTS WITH INFLAMMATORY BOWEL DISEASES AND HEALTHY VOLUNTEERS

M. Markelova¹, M. Siniagina¹, N. Danilova¹, A. Odintsova², S. Abdulkhakov^{1,3}, R. Abdulkhakov³, T.V. Grigoryeva¹
¹Kazan Federal University, Institute of Fundamental Medicine and Biology, Kazan, Russian Federation, ²Republican Clinical Hospital of Tatarstan Republic, Kazan, Russian Federation, ³Kazan State Medical University, Kazan, Russian Federation

Contact E-Mail Address: mimarkelova@gmail.com

Introduction: The microbiome of patients with inflammatory bowel disease (IBD) is characterized by specific dysbiosis, including a decrease in the relative abundance of *Faecalibacterium prausnitzii* species, one of the prevailing representatives of the human intestinal bacterial community. Currently, *F. prausnitzii* is proposed to be used as a new generation probiotic in various diseases. However, there are only limited data on the genetic diversity of the bacteria in patients with IBD and healthy individuals.

Aims & Methods: The aim of the study was to reveal the genetic diversity of the *F. prausnitzii* from microbiota of IBD patients.

Total DNA was isolated from fecal samples of 72 IBD patients (35 with Crohn's disease (CD) and 37 with ulcerative colitis (UC)) and 42 healthy volunteers, followed by shotgun sequencing on the Illumina NextSeq 500 platform [1].

Strain-level profiling of metagenomic samples was performed with Pan-PhlAn 3 using *F. prausnitzii* reference genomes database. Clusters based on the presence of *F. prausnitzii* genes were identified using k-means method.

Results: *F. prausnitzii* genomes were found in the microbiota of 40 healthy individuals, 28 CD patients and 26 UC patients. By the presence of genes in each strain, we revealed two clusters, which characterize the genetic

diversity of *F. prausnitzii*. It was found that the frequency of occurrence of the strains from CD and UC patients in the first cluster is significantly higher (82.1% and 80.8% of all patients' strains, respectively) than from control group – 50% ($p < 0.05$ assessed by Exact Fisher test with BH adjustment). The second cluster is predominantly represented by the strains from healthy controls (50% of all controls' strains, 17.9% of the CD patients' and 19.2% of the UC patients' strains).

The genomes of *F. prausnitzii* from the first cluster (IBD cluster) differ significantly by a reduced frequency of occurrence of 1739 genes and an increased frequency of occurrence of 375 genes ($p < 0.05$ assessed by Exact Fisher test). It was found that the gene for γ -glutamyl- γ -aminobutyrate hydrolase involved in the synthesis of 4-aminobutyrate is significantly less frequently detected in the strains from the IBD cluster. 4-aminobutyrate is a substrate for the production of butyrate, which has anti-inflammatory properties and serves as the main energy source for colonocytes.

In addition, it was found that the genes involved in the synthesis of the bacterial cell wall also have a reduced frequency of occurrence in the IBD cluster, while the genes participating in peptidoglycan breakdown have an increased frequency of occurrence.

Thus, these alterations may lead to cell wall disintegration and to its barrier dysfunction. It was also found that the frequency of occurrence of genes coding iron binding proteins was significantly reduced in *F. prausnitzii* from the IBD cluster, which may lead to a decrease in the competition ability of the strains in the intestinal microbiota.

Conclusion: The strain-level metagenomic profiling revealed that *F. prausnitzii* from CD and UC patients are likely to produce less amounts of butyrate, have an impaired cell wall and less competitive ability than strains from healthy volunteers. Thus, the *F. prausnitzii* from healthy donors could potentially be used as a next-generation probiotics to alleviate symptoms of IBD.

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P0243

A PROSPECTIVE INTERVENTIONAL STUDY TO EVALUATE THE EFFECT OF HYPOXIA ON HEALTHY VOLUNTEERS AND PATIENTS WITH INFLAMMATORY BOWEL DISEASE: THE ALTITUDE IBD STUDY

S. Vavricka¹, J. Zeitz², M. Madanchi¹, P.A. Ruiz-Castro¹, L. Biedermann¹, Y. Morsy¹, M. Scharl¹, M. Gassmann³, T. Lutz³, A. Kunz⁴, D. Bron⁴, G. Rogler¹, T. Greuter¹

¹Universitätsspital Zürich, Gastroenterologie und Hepatologie, Zurich, Switzerland, ²Hirslanden Clinic, GastroZentrum Hirslanden, Zurich, Switzerland, ³University of Zurich, Institute of Veterinary Physiology, Vetsuisse Faculty, Zurich, Switzerland, ⁴Swiss Aeromedical Center, Dubendorf, Switzerland

Contact E-Mail Address: th_greuter@bluewin.ch

Introduction: It is unknown how high altitude exposure causes inflammatory bowel disease (IBD) flares. We assessed disease activity in healthy controls, IBD patients after 3h exposure in a hypobaric pressure chamber (imitating an altitude of 4000m above sea level).

Aims & Methods: In a prospective study, 11 Crohn's disease (CD, 6 males, 35.6y±13.7), 9 ulcerative colitis (UC, 3 males, 31.4y±10.8) patients and 10 healthy controls (7 males, 27.7y±4.9) underwent rectosigmoidoscopy in

our outpatient clinic (490m, baseline T1) and after 3h exposure in a hypobaric pressure chamber (follow-up day 1 T2 and day 7 T3). Symptoms were assessed using the Harvey Bradshaw Index and the partial Mayo Score before and after hypobaric pressure chamber exposure (baseline T1, day 1 T2, day 7 T3 and day 30 T4).

Disease activity was further assessed using CRP levels and fecal calprotectin. Intestinal mucosa-associated microbial composition was analyzed using high-throughput sequencing.

Results: The 3h exposure in a hypobaric pressure chamber was well tolerated in all subjects. Mean oxygen saturation decreased from 97.5%±1.3 to 80.9%±4.1, and increased back to normal levels (98.8%±1.2%) after the hypobaric intervention ($p < 0.0001$). Clinical and endoscopic disease activity were not significantly changed before vs. after intervention.

However, mild flare was seen in 2 UC patients and another UC patient was lost to follow-up due to a disease flare. New endoscopic lesions were detected in one healthy subject and one UC patient. Fecal calprotectin levels significantly increased in CD patients during the follow-up period ($p = 0.031$), but not in UC and healthy controls.

No changes in CRP levels were observed. Percentage of calprotectin-based disease remission (fecal calprotectin <100ug/g) decreased in all groups after hypobaric pressure chamber exposure, and increased thereafter with a significant decrease in the control group (100% at baseline vs. 50% at day 1, $p = 0.029$) and all patients combined (73.3% at baseline vs. 36.7% at day 7, $p = 0.013$). No differences in alpha and beta diversity of stool microbiota composition before vs. after hypobaric pressure chamber exposure were observed.

Conclusion: In this prospective study involving IBD patients and healthy controls, a 3h exposure in a hypobaric pressure chamber (corresponding to an altitude of 4000m) did not result in higher disease activity.

However, mild flares and development of endoscopic lesions were seen in a subset of patients. Calprotectin-based remission rates significantly decreased between baseline and day 7 suggesting a subclinical effect of short-term hypoxia, not explained by changes in the microbiome. (Clinicaltrials.gov number, [NCT02849821](https://clinicaltrials.gov/ct2/show/study?term=NCT02849821))

Disclosure: Nothing to disclose.

P0244

PARTICULATE MATTER FROM NATURAL PRECURSOR INCREASES SUSCEPTIBILITY TO INFLAMMATORY BOWEL DISEASE

M. Korbush¹, K. Paliienko², T. Dovbynychuk¹, T. Borisova², G. Tolstanova¹

¹Taras Shevchenko National University of Kyiv, Kyiv, Ukraine,

²Palladin Institute of Biochemistry National Academy of Sciences of Ukraine, Neurochemistry, Kyiv, Ukraine

Contact E-Mail Address: korbush1313mari@gmail.com

Introduction: The epidemiological data pointed out that exposure to ambient air pollution may increase the risk of irritable bowel syndrome and ulcerative colitis both in children and adults (Opstelten et al. 2016; Elten et al. 2020). Air pollutants affect the intestines through mucociliary clearance of particulate matter (PM) from the lungs, by food or water intake (Beamish et al. 2011).

Aims & Methods: In the present study, we tested the hypothesis that water-suspended smoke preparations (SPs) derived from the combustion of poplar wood might affect the integrity of the intestinal mucosa, induce an inflammatory response, and increase the susceptibility to chemically-induced colonic inflammation after the introduction of SP intravenously or through a gastric tube. Smoke from poplar wood was collected under laboratory conditions during the entire flaming and mixed combustion phase, as well as the smoldering phase. Male Wistar rats (180-200 g) were

injected with SP in two ways: 1) into the tail vein at a dose of 500 µg/100 g (n = 28); 2) by gavage at a dose of 180 µg/100 g (n=20). In 1 hour after SP injection, the experimental colitis was induced by a single rectal injection of 0.1 ml 6% iodoacetamide (7 cm from the anus) or vehicle 1% methylcellulose. Rats were euthanized in 2 h after colitis induction.

We examined colonic vascular permeability by Evans blue extravasation (mg/g wet colon), MPO level, total glycoprotein level at surface mucus by PAS-staining, intestinal permeability by the translocation of bacteria into the blood of the portal vein.

Results: Intravenous administration of the SP did not increase the negative effect of iodoacetamide-induced colitis on changes in the state of the endothelial barrier, myeloperoxidase activity, and the total glycoprotein level at surface colonic mucus in the rat colon. But, intravenous administration of SP led to the appearance of blood in the, which may be due to the damage to the fenestrated capillaries of the glomerulus.

However, intravenous administration of the drug did not increase the negative effect of iodoacetamide-induced colitis on changes in the state of the endothelial barrier, myeloperoxidase activity, and the amount of superficial mucus in the colon. At the same time, oral administration of SP increased the translocation of bacteria into the blood of the portal vein which represents the increased gut permeability of rats.

These changes were accompanied by the Oral administration of SP to simulated colitis rats likely reduced the amount level of total glycoprotein at surfaceperforal colonic mucus compared to the placebo group with colitis. However, oral administration of SP did not have a significant effect on colonic vascular permeability and the activity of myeloperoxidase vs. the placebo group with colitis.

Conclusion: The airborne particulate matter PM, obtained from the combustion of natural precursors such as poplar wood, can cause primary pro-inflammatory changes in the intestines in a very short time after penetration into the organism both through the blood and mucociliary clearance by food ingestion. Moreover, they can contribute to the violation of the integrity of the intestinal barrier in the conditions of simulated experimental colitis.

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Disclosure: Nothing to disclose.

P0245

MYCOBACTERIUM AVIUM PARATUBERCULOSIS INCIDENCE IN PATIENTS WITH CROHN'S DISEASE AND CONTROLS: A SINGLE CENTRE STUDY

T. Nugent¹, N. O'Sullivan¹, E. Low¹, E. Herlihy¹, K. Hazel¹, I. Grant², C. O'Morain¹

¹Beacon Hospital, Department of Gastroenterology, Dublin, Ireland, ²Queens University, Institute for Global Food Security, School of Biological Sciences, Belfast, United Kingdom

Contact E-Mail Address: nugentti@tcd.ie

Introduction: Mycobacterium avium subspecies paratuberculosis (MAP) has been postulated to play a role in the pathogenesis of Crohn's Disease (CD)(1). Present in food such as pasteurised dairy and potable water, MAP was first identified in 1895 as the cause of a chronic enteritis in cattle known as Johne's disease, which shares a number of clinical and histopathological similarities to CD (2)(3).

MAP was first cultured from patients with CD in the 1980s and subsequent trials have demonstrated an association between MAP and CD, although this relationship is not fully understood (1)(4-7).

Aims & Methods: This study aimed to measure and compare serum samples of patients with CD and healthy controls for the presence of MAP.

CD patients and asymptomatic healthy controls were recruited at a single centre (Beacon Hospital). Whole blood samples were drawn, processed and then transported to a specialist facility for testing within a 24 hour period (Queens University Belfast). Each sample was blind tested for the presence of MAP using both an adapted culture method and a phage assay previously used to test human serum for the presence of MAP (7)(8).

Results: 45 participants, 22 CD patients and 23 controls were enrolled. Participant characteristics and results are described in Table 1.

Pozzato culture method was positive in 81.8% of CD patients and 95.7% of controls. Phage assay results were positive in 77.2% of CD patients and 78.3% of controls. Mean phage plaque numbers were 166.7 for CD patients compared with 198.9 for controls. Estimated MAP/ml for CD was 381.0 and 516.7 for controls.

	Crohn's Disease (CD)		Control	Crohn's Disease			Control	Crohn's Disease			Control	
Age (range)	49 (27-79)	34 (24-74)		Treatment ¹				- mean plaque no.			166.7	198.9
Gender			- No treatment	3		-		- Est. mean MAP/ml ²			381.0	516.7
- Male	13	12	- Amino-salicylates	1		-						
- Female	9	11	- Immuno-suppressant	2		-						
Harvey Bradshaw Index			- Biological agent	17		-						
- Remission (<5)	13	-	'More than one category possible									
- Mild Dis. (5-7)	8	-	Results	CD (+)	CD (-)	Control (+)	Control (-)					
- Moderate Dis. (8-16)	1	-	- Phage plaque assay	17 (77.2%)	5 (22.7%)	18 (78.3%)	5 (21.7%)					
- Severe Dis. (>16)	0	-	- Pozzato Culture	18 (81.8%)	4 (18.2%)	22 (95.7%)	1 (4.3%)					

Table 1.

Conclusion: This study showed significantly elevated levels of MAP in blood samples taken from both CD patients and asymptomatic healthy controls. This may be as a result of persistent MAP infection in human populations or secondary to consistent and regular exposure to viable MAP in dietary intake. The increased MAP levels shown in this study, relative

to previous human studies, may be explained by a reduced transit time and thus quicker time to sample testing. Lower levels of MAP detection in CD patients relative to controls is also noted, one explanation for which is the potential effect of CD therapies on MAP, restricting its replication or encouraging dormancy. Viable MAP is consistently present in the blood of both Crohn's patients and controls however further research is required to determine what role, if any, this zoonotic bacterium plays in disease pathogenesis.

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Disclosure: Nothing to disclose.

P1043

LOW FREQUENCIES OF CIRCULATING INHIBITORY TIGIT⁺CD38⁺ EFFECTOR T CELLS IDENTIFY AN IMMUNOLOGICALLY DISTINCT SUBGROUP OF PEDIATRIC PATIENTS WITH SEVERE CROHN'S DISEASE

M. Heredia¹, L.M.M. Costes¹, I. Tindemans¹, M. Aardoom², R. Klomberg², P. Kemos³, M.E. Joosse¹, D.H. Hulleman-van Haaften¹, B. Tuk¹, F. Ruemmele⁴, N. Croft³, J.C. Escher², L. de Ridder², J.N. Samsom¹

¹Erasmus University Medical Center-Sophia Children's Hospital, Laboratory of Pediatrics, Division Gastroenterology and Nutrition, Rotterdam, Netherlands, ²Erasmus University Medical Center-Sophia Children's Hospital, Pediatric Gastroenterology, Rotterdam, Netherlands, ³Blizard Institute, Queen Mary University of London, Centre for Immunobiology, London, United Kingdom, ⁴Universite Sorbonne, Paris-Cite Hospital, Paris, France

Contact E-Mail Address: m.heredia@erasmusmc.nl

Introduction: Inflammatory bowel disease (IBD), including Crohn's disease (CD) and ulcerative colitis (UC), is a T-cell driven intestinal inflammation. Current T-cell suppressive therapeutic regimens are moderately successful due to a large clinical heterogeneity amongst patients. Detailed understanding of aberrant inflammatory and inhibitory T-cell responses in individual patients is lacking.

Previously, we have shown that, in healthy individuals, 40% of peripheral blood CD38⁺(CD62L^{neg}CD4⁺) effector T cells, which are enriched for intestinal antigen specificity, express the inhibitory molecule T-cell immunoglobulin and ITIM domain (TIGIT). TIGIT⁺CD38⁺ effector T cells have

a regulatory function, produce IL-10 and express multiple co-inhibitory receptors. Conversely, TIGIT^{neg}CD38⁺ effector T cells are enriched in inflammatory IFN- γ producing cells. In a small cohort of pediatric-onset IBD patients, low frequencies of TIGIT⁺CD38⁺ effector T cells were associated with a reduced duration of clinical remission.

We hypothesize that a subgroup of IBD patients has reduced frequencies of circulating inhibitory TIGIT⁺CD38⁺ effector T cells, reflecting a distinct pathogenesis associated with a more severe disease course.

Aims & Methods: In the Rotterdam PIBD-SETQuality cohort were included newly diagnosed pediatric IBD patients (CD: n=37; UC: n=16), IBD-negative controls (n=12) and age-matched healthy controls (n=22). We monitored TIGIT⁺ and TIGIT^{neg}CD38⁺ effector T cells in peripheral blood by flow cytometry and collected plasma to measure plasma protein concentration at diagnosis and during immunosuppressive therapy.

Results: At diagnosis, 50% of CD patients had strongly reduced frequencies of inhibitory TIGIT⁺CD38⁺ effector T cells (TIGIT^{low} patients) compared to UC patients and age-matched healthy controls. TIGIT^{low} CD patients needed earlier anti-TNF treatment with 60% of patients receiving anti-TNF within 1 year versus 36% for CD patients with normal frequencies of TIGIT⁺CD38⁺ effector T cells (TIGIT^{norm} patients).

Moreover, 53% of TIGIT^{low} patients experienced a disease relapse by 1 year versus 25% of TIGIT^{norm} patients, suggesting a more severe disease course. Reduced frequencies of TIGIT⁺CD38⁺ effector T cells associated with active inflammation as frequencies were restored to the level of TIGIT⁺ cell frequencies in HC after 3 months of induction therapy.

Phenotypic characterization of TIGIT^{neg}CD38⁺ effector T cells in CD patients at diagnosis showed an inflammatory profile enriched in Ki67, reflecting recent proliferation, and high expression of chemokine receptors associated with inflammatory non-classical T helper-1 IFN- γ ^{high}IL-17^{low} producing (Th1*) cells. In agreement, high frequencies of TIGIT^{neg}CD38⁺ effector T cells correlated with high plasma IFN- γ concentrations.

Conclusion: These results demonstrate that reduced frequencies of circulating inhibitory TIGIT⁺CD38⁺ effector T cells discriminate a subgroup of pediatric CD patients with high frequencies of inflammatory Th1* cells and high plasma IFN- γ concentrations.

TIGIT^{low} CD patients have a more severe disease course and a higher chance of receiving anti-TNF within 1 year, altogether suggesting a distinct disease pathogenesis.

Disclosure: Nothing to disclose.

P0246

PREVALENCE AND RISK FACTOR OF PERIODONTITIS IN PATIENTS WITH INFLAMMATORY BOWEL DISEASE: A CASE-CONTROL, PROSPECTIVE STUDY

G. Baima¹, M. Muwalla¹, G. Testa², M. Vernero³, M. Aimetti¹, D.G. Ribaldone²

¹University of Turin, Department of Surgical Sciences, Turin, Italy,

²University of Turin, Department of Medical Sciences, Turin, Italy,

³IRCCS Policlinico San Matteo, Università degli Studi di Pavia, Clinica Medica 1, Pavia, Italy

Contact E-Mail Address: davrib_1998@yahoo.com

Introduction: A plausible bidirectional association between periodontitis and IBD is receiving growing scientific interest. However, most of the available literature presented arbitrary case definitions for periodontitis, inaccurate assessment of the outcomes, uneven samples of IBD and non-IBD patients, and the risk of residual confounders in the analyses.

The aim of this study was to evaluate the association between periodontitis and inflammatory bowel disease (IBD) respect to an age and gender-matched control group of healthy controls.

Aims & Methods: Patients affected by IBD and healthy controls were consecutively recruited and compared for the diagnosis of periodontitis assessed according to CDC/AAP periodontitis case definitions via a full-mouth periodontal examination, including plaque index (FMPS), probing depth, clinical attachment level and bleeding on probing. The association of risk variables with both IBD and periodontitis was tested through univariate analysis and multivariate logistic models.

Results: One hundred eighty patients with IBD (117 Crohn's disease, CD and 63 ulcerative colitis, UC) and 180 healthy controls were compared. Significantly more patients with IBD had periodontitis and severe periodontitis (85.6% and 36.7%, respectively) than controls (65.6% and 25.6%, respectively). Differences remained significant when UC (85.0% in cases and 38.3% in controls) and CD (85.4% in case and 35.0% in controls) were considered separately, and they were higher in the 35-50 and 51-65 age groups. Individuals with IBD presented a chance ~3 and ~4.5 higher of having moderate (OR = 3.21; 95% CI 1.80-5.72; $p < 0.001$) and severe periodontitis (OR = 4.48; 95% CI 2.30-8.73; $p < 0.001$), respectively.

Significant variables associated with periodontitis in the whole sample (360 individuals) were: older age, presence of IBD, and higher FMPS. When focusing on the IBD sample, gender (male), IBD-associated surgery, IBD duration, and localization (pancolitis) were factors significantly associated with the co-occurrence of periodontitis.

Conclusion: Within the investigated sample, CD and UC patients had a significantly higher prevalence of periodontitis than controls without IBD. The risk association with disease-associated characteristics suggests a bi-directional relationship.

Disclosure: I disclose this.

P0247

RISK FACTORS AND LONG-TERM OUTCOMES ASSOCIATED WITH IMMUNOSUPPRESSION IN PATIENTS WITH ULCERATIVE PROCTITIS: RESULTS FROM THE ENEIDA REGISTRY

R. Ferreira-Iglesias^{1,2}, S. Porto Silva^{1,2}, S. Marin³, M.J. Casanova⁴, M. Mañosa Ciria⁵, C. González-Muñoz⁶, R. de Francisco⁷, B. Caballol Oliva⁸, L. Arias⁹, M. Piqueras Cano¹⁰, Y. Zabana¹¹, M. Rivero¹², X. Calvet Calvo¹³, F. Mesonero Gismero¹⁴, P. Varela Trastoy¹⁵, R. Busta Nista¹⁶, R. Gómez Perosanz¹⁷, P. Vega¹⁸, M. González-Vivó¹⁹, M. Iborra²⁰, L. Jiménez Márquez²¹, L. Madero^{22,23}, I. Rodríguez-Lago²⁴, M. Rodríguez González²⁵, M.I. Vera Mendoza²⁶, A. Ponferrada Diaz²⁷, M. Vela²⁸, L. Torrealba Medina²⁹, M. Vandomselar³⁰, E. Iglesias-Flores³, J.P. Gisbert⁴, M. Calafat Sard⁵, E. García-Planella⁶, I. Pérez-Martínez⁷, E. Ricart⁸, B. Sicilia Aladrén⁹, R. Mena¹⁰, M. Esteve Comas¹¹, C. Rivas¹², E. Brunet¹³, A. López San Román¹⁴, M.Á. De Jorge Turrión¹⁵, B. Velayos Jiménez¹⁶, M. Quiñones Calvo¹⁷, C. Regueiro Expósito¹⁸, L. Márquez Mosquera¹⁹, P. Nos Mateu²⁰, L. Nieto^{1,2}, E. Domènech⁵, M. Barreiro de Acosta^{1,2}, ENEIDA Project of GETECCU

¹Hospital Universitario de Santiago de Compostela, Gastroenterology, Santiago de Compostela, Spain, ²IDICHUS, Santiago de Compostela, Spain, ³UCO/IMIBIC/Hospital Universitario Reina Sofía, Gastroenterology, Cordoba, Spain, ⁴Hospital Universitario de La Princesa, Instituto de Investigación Sanitaria Princesa and CIBEREHD, Gastroenterology, Madrid, Spain, ⁵Hospital Universitari Germans Trias i Pujol. Centro de Investigación Biomédica en Red de Enfermedades Hepáticas y Digestivas (CIBERehd), Gastroenterology, Badalona, Spain, ⁶Hospital Santa Creu i Sant Pau, Gastroenterology, Barcelona, Spain, ⁷Hospital Universitario Central de Asturias, Gastroenterology, Oviedo, Spain, ⁸Hospital Clinic. Centro de

Investigación Biomédica en Red de Enfermedades Hepáticas y Digestivas (CIBERehd). IDIBAPS, Gastroenterology, Barcelona, Spain, ⁹Hospital Universitario de Burgos, Gastroenterology, Burgos, Spain, ¹⁰Hospital Consorci Terrassa. Centro de Investigación Biomédica en Red de Enfermedades Hepáticas y Digestivas (CIBERehd), Terrassa, Spain, ¹¹Hospital Universitari Mútua Terrassa. Centro de Investigación Biomédica en Red de Enfermedades Hepáticas y Digestivas (CIBERehd), Gastroenterology, Terrassa, Spain, ¹²Hospital Universitario Marqués de Valdecilla, Gastroenterology, Santander, Spain, ¹³Hospital de Sabadell, Institut Universitari Parc Tauli, UAB, Gastroenterology, Barcelona, Spain, ¹⁴Hospital Ramon y Cajal, Gastroenterology, Madrid, Spain, ¹⁵Hospital Universitario de Cabueñes, Gastroenterology, Gijón, Spain, ¹⁶Hospital Clínico Universitario de Valladolid, Valladolid, Spain, ¹⁷Hospital Universitario Fundación Alcorcón, Gastroenterology, Madrid, Spain, ¹⁸Hospital Clinico Universitario de Ourense, Gastroenterology, Ourense, Spain, ¹⁹Hospital del Mar, Gastroenterology, Barcelona, Spain, ²⁰La Fe University and Politecnico Hospital. Centro de Investigación Biomédica en Red de Enfermedades Hepáticas y Digestivas (CIBERehd), Gastroenterology, Valencia, Spain, ²¹Hospital Universitario de Fuenlabrada, Gastroenterology, Fuenlabrada, Spain, ²²Hospital General Universitario de Alicante, Alicante, Spain, ²³ISABIAL(Instituto de Investigación Sanitaria y Biomédica de Alicante)y CIBEREHD, Alicante, Spain, ²⁴Hospital de Galdakao, Gastroenterology, Galdakao, Spain, ²⁵Hospital de Ciudad Real, Gastroenterology, Ciudad Real, Spain, ²⁶Hospital Universitario Puerta de Hierro, Gastroenterology, Madrid, Spain, ²⁷Hospital Infanta Leonor, Madrid, Spain, ²⁸Hospital Virgen de la Luz de Cuenca, Gastroenterology, Cuenca, Spain, ²⁹Trueta, Girona, Spain, ³⁰Hospital de Torrejon, Torrejon de Ardoz, Spain

Contact E-Mail Address: manubarreiro@hotmail.com

Introduction: Ulcerative proctitis may have a mild and less aggressive course, although evidence is scarce because these patients are excluded from participation in randomized controlled clinical trials.

Aims & Methods: The aim is to identify clinical characteristics and complications associated with ulcerative proctitis refractory to conventional therapy. Patients included in the prospectively maintained ENEIDA registry from GETECCU (IBD Spanish Group) with ulcerative proctitis were included. Socio-demographic data and complications associated with immunosuppression (hospitalizations, surgeries, tumors) were evaluated.

We defined ulcerative proctitis based on ECCO guidelines and immunosuppression as the use of immunomodulators and/or biologics. Logistic regression was used to identify the independent factors associated with immunosuppressive therapy. The differences between the probability of persistence of biological therapy were analysed with Kaplan Meier.

Results: From a total of 34.716 patients with ulcerative colitis (ENEIDA registry, November 2021), 6281 (18%) patients with ulcerative proctitis were identified. Mean age was 53±15 years and mean duration of illness was 12±9 years.

Surgery was necessary only in 1.7% of patients, 31 (0.5%) panproctocolectomy or subtotal colectomy. 134 (2%) patients were hospitalized, 316 (5%) needed surgeries, 13 (0.2%) developed colorectal tumor and 316 (5%) other different tumors. 636 (10%) patients were refractory to 5-ASA and corticosteroids, necessitating immunosuppression: 487 thiopurines (7.4%), 49 with methotrexate (0.8%), 191 with infliximab (9%), 125 with adalimumab (2%), 50 with golimumab (0.8%), 57 with vedolizumab (0.9%), 6 with ustekinumab (0.1%) and 3 with tofacitinib. 316 (5%) patients needed one biologic therapy, 95 (1.5%) needed 2 biologics and 40 (0.6%) at least three different biologics. Polyarthritis [OR=3.58, CI 1.87-6.71; $p < 0.001$] and

thrombosis [OR=5.57, IC 0.98-28.75; p=0.039] were associated with higher risk of immunosuppression; no smoking [OR=0.58, IC 0.35-0.98; p=0.039] was associated with low risk. Immunosuppression was related to higher risk of hospitalization (mean 0.36 ±0.86 vs 0.06 ±0.30; p<0.001).

Conclusion: 10% of patients with ulcerative proctitis need immunosuppression therapy. Non-smokers have a lower immunosuppression requirement, however, polyarthritis or a history of thrombosis confers higher risk. Immunosuppression is associated with higher risk of hospitalization.

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P0248

ECONOMIC IMPACT OF INFLAMMATORY BOWEL DISEASE IN CATALONIA. A POPULATION-BASED ANALYSIS

E. Brunet^{1,2}, L. Melcarne¹, L.P. Llovet Soto¹, E. Vela^{3,4}, M. Cléries^{3,4}, C. Pontes^{5,6}, P. García-Iglesias^{1,2}, A. Puy Guillén¹, A. Villoria Ferrer^{1,2}, X. Calvet Calvo^{1,2}

¹Parc Tauli, Gastroenterology, Sabadell, Spain, ²CIBERehd, Instituto de Salud Carlos III, Madrid, Spain, ³Generalitat de Catalunya, Information and Knowledge Unit, Barcelona, Spain, ⁴IDIBELL, Digitalization for the Sustainability of the Healthcare System (DS3), Barcelona, Spain, ⁵Generalitat de Catalunya, Healthcare Area, Barcelona, Spain, ⁶Universitat Autònoma de Barcelona, Department of Pharmacology, Therapeutics and Toxicology, Bellaterra, Spain

Contact E-Mail Address: eduardbrunet91@gmail.com

Introduction: Recent studies have brought to light the important economic impact in healthcare costs and resources utilization of IBD. The annual cost of IBD-patients in US is over 3-fold higher costs than their matched non-IBD patients (1).

Aims & Methods: The aim of this study is to evaluate the current healthcare expenditures of IBD in Catalonia.

All patients with IBD included in the Catalan Health Surveillance System (CHSS) including data on more than 7 million individuals in 2020.

Data on prevalence, incidence, comorbidities, stratification of risk, use of healthcare resources and economic impact were also extracted from the CHSS according to ICD-10-CM codes. Health expenditure was calculated according to the standard costs of each service provided by the Department of Health (Generalitat de Catalunya) (2).

The utilization of healthcare services and associated expenditure of IBD were compared with the population of patients not identified as IBD adjusted by age, sex, and income level (hereinafter referred to as "non-IBD").

Results: The prevalence and incidence of IBD in 2020 per 100,000 inhabitants was 405.61 and 27.2 respectively. Total number of IBD patients in 2020 was 37,381. Prevalence of comorbidities (neoplasia, arthritis, chronic obstructive pulmonary disease, asthma, cardiac disease, ictus and mental disease) was higher in IBD patients' when compared to non-IBD population. The risk of hospitalization in IBD was twice those of the non-IBD. The global healthcare expenditures of patient with IBD was 164,085,799€. The average annual expenditure for an IBD patient was 4,212.3€ versus 1,257.6€ for non-IBD population; being more than 3.4-fold higher (table 1).

Sanitary resource	IBD population			Non-IBD population			Relation
	Total annual cost (€)	cost per patient (€)	% cost	Total annual cost (€)	cost per patient (€)	% cost	
Primary Healthcare	9,750,778	230.3	5.9%	6,375,231	163.7	13%	x1.5
Pharmacy	100,888,316	2,589.9	61.5%	18,122,860	466.1	37.1%	x5.6
Hospitalization	24,157,004	620.1	14.7%	12,030,129	308.8	24.6%	x2
Emergency room	6,092,252	156.4	3.7%	3,778,156	97	7.7%	x1.6
Outpatient clinic	16,014,048	411.1	9.8%	4,314,309	110.8	8.8%	x3.7
Socio-sanitary	2,351,141	60.4	1.4%	1,458,510	37.4	3.0%	x1.6
Others	4,832,260	93	3%	2,065,575	73.9	5.9%	x2.3
Total	164,085,799	4,212.3	100%	48,987,769	1,257.6	100%	x3.4

Table 1. Comparison of the cost of the population with IBD and the matched population for each health resources

Conclusion: Patients with IBD presented a higher risk of comorbidities (1.5-2 fold) and healthcare resources utilization. Healthcare expenditure per patient were approximately 3.4 times higher than the non-IBD population.

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P0249

SEROLOGIC RESPONSE WITH ANTIMICROBIAL ANTIBODIES DURING THE PRECLINICAL PHASE OF INFLAMMATORY BOWEL DISEASE

I. Rodríguez-Lago¹, J.L. Cabriada¹, M. Barreiro-de Acosta²

¹Hospital Universitario de Galdakao, Gastroenterology, Galdakao, Spain, ²Hospital Clínico Universitario de Santiago de Compostela, Gastroenterology, Santiago de Compostela, Spain

Contact E-Mail Address: iago.r.lago@gmail.com

Introduction: Previous data have shown that the inflammatory process underlying ulcerative colitis (UC) and Crohn's disease (CD) can start years before the diagnosis. Serum proteomic and serologic markers have been identified during this period, providing the opportunity for early detection of the initial immune disturbances.

Aims & Methods: Our aim was to determine if patients with an incidental diagnosis of UC or CD can demonstrate a serologic response based on antimicrobial antibodies in the years preceding the symptomatic onset of the disease. We performed a single-center prospective study including all asymptomatic subjects with a diagnosis of UC or CD during the colorectal

cancer screening program between October 2013 and February 2022 were included. The diagnosis of IBD was established by a combination of clinical data, including the presence of endoscopic findings suggestive of UC or CD and after histologic confirmation. ASCA IgA, ASCA IgG (EliA ASCA IgA/IgG, ThermoFisher) and ANCA (EUROPattern, PerkinElmer; EliA IgG, ThermoFisher) antibodies were determined. Positive results were considered above 10 U/mL for ASCA, 3.5 for ANCA-MPO and 2.00 for ANCA-PR3. Descriptive statistics were used.

Results: A total of 26 patients were included, 19 with UC (21% left-sided, 32% extensive; 53% former smokers), and 7 with CD (57% ileal, 29% colonic; 14% active smokers), with a median age of 51 years (IQR, 51-57). Two patients showed at least one positive test (7.7%). One patient (5%) with extensive UC showed positive ANCA results, and he developed symptoms 2 months after diagnosis. One patient (14%) with stricturing ileocolonic disease CD at diagnosis showed positivity to ASCA IgA/IgG, and he has remained asymptomatic after a median of 42 months. After a median follow-up of the whole cohort of 53.5 months (IQR, 26-67), 12 patients (46%) developed symptomatic disease.

Conclusion: A lower than expected proportion of patients with an incidental diagnosis of IBD demonstrate a serological response based on antimicrobial antibodies, suggesting that this situation corresponds to the initial phases of IBD when systemic immune disturbances might not be detectable yet.

Disclosure: Nothing to disclose.

P0250

THE BI-DIRECTIONAL RISK OF INFLAMMATORY BOWEL DISEASE AND ANXIETY OR DEPRESSION: A SYSTEMATIC REVIEW AND META-ANALYSIS

T. Bisgaard¹, K. Allin^{1,2}, R. Elmahdi¹, T. Jess^{1,2}

¹Aalborg University, Center for Molecular Prediction of Inflammatory Bowel Disease, PREDICT, Department of Clinical Medicine, Copenhagen, Denmark, ²Aalborg University, Department of Gastroenterology and Hepatology, Aalborg, Denmark

Contact E-Mail Address: taniabisgaard@gmail.com

Introduction: There is increasing awareness of the gut-brain axis and the interplay between psychiatric and gastrointestinal diseases. An association between inflammatory bowel disease (IBD), and anxiety and depression has been suggested, but the magnitude and directionality of risk remains uncertain.

Aims & Methods: This systematic review and meta-analysis of unselected population-based cohort studies examines the risk of depression or anxiety in IBD patients and the risk of IBD in patients with depression or anxiety. The objective is to quantify the bi-directional risk of anxiety or depression following a diagnosis of IBD, and the risk of IBD in individuals with depression or anxiety using population representative data.

We performed a systematic literature search using MEDLINE and Embase for studies published from 1991 through 2021. We undertook Random Effect Model meta-analysis for relative rate estimates of eligible studies to calculate a pooled hazard ratio (HR) for the risk of anxiety and depression in IBD and undertook subgroup meta-analysis to calculate risk by IBD subtype (Crohn's disease (CD), ulcerative colitis (UC)), sex and for pediatric-onset IBD.

Results: Out of 6,391 screened articles, 8 studies fulfilled all inclusion criteria. Five studies examining anxiety and depression among >100,000 individuals with IBD were included in meta-analyses, which showed an increased risk of both anxiety (HR 1.52, 95% CI 1.29-1.79) and depression (HR 1.62, 95% CI 1.41-1.86) following an IBD diagnosis. The risk of anxiety was increased following both CD (HR 1.73, 95% CI 1.43-2.09) and UC (HR 1.39 (95% CI 1.21-1.61).

The risk of depression was also elevated both following CD (HR 1.69, 95% CI 1.52-1.89), and UC (HR 1.52, 95% CI 1.31-1.77). Pediatric-onset CD patients had a particularly elevated risk of anxiety (HR 2.21, 95% CI 1.98-2.47). There were no significant differences in risk between males and females. Two studies investigating more than 400,000 individuals with depression showed a 2-fold increased risk of IBD following depression. The overall quality of included studies was good, and risk of publication bias was low.

Conclusion: This meta-analysis of population-based studies shows a 1.6-fold increased risk of depression and a 1.5-fold increased risk of anxiety following IBD, with pediatric-onset IBD patients having a particularly elevated risk of anxiety. Population-representative evidence for IBD risk after depression or anxiety diagnosis is sparse but points to a 2-fold increased risk of IBD following depression. This bidirectional association is clinically relevant and could indicate shared or mutually dependent disease mechanisms.

Disclosure: Nothing to disclose.

P0251

RISK OF POLYPS AND COLORECTAL CANCER IN PATIENTS WITH MICROSCOPIC COLITIS: CASE-CONTROL STUDY WITH LONG-TERM FOLLOW-UP

I. Fajardo¹, Y. Zabana^{1,2}, A. Salas³, M. Aceituno^{1,2}, L. Ruiz^{1,2}, M. Esteve^{1,2}, F. Fernández-Bañares^{1,2}

¹Hospital Universitari Mútua Terrassa, Department of Gastroenterology, Terrassa, Spain, ²Centro de Investigación Biomédica en Red de Enfermedades Hepáticas y Digestivas (CIBERehd), Madrid, Spain, ³Hospital Universitari Mútua Terrassa, Department of Pathology, Terrassa, Spain

Contact E-Mail Address: ingridfajan@gmail.com

Introduction: A previous study (Fernandez-Bañares et al, UEGJ 2016;4s: A434) showed that in microscopic colitis (MC) there is a low frequency of polyps and colorectal cancer (CRC) compared to the general population at medium risk, without observing differences with a group of chronic diarrhoea and normal colonic histology.

Aims & Methods: The aim of the present study is to assess whether this low incidence of adenomas in patients with MC and chronic diarrhoea persists in the long term. Patients with follow-up colonoscopies for control of colonic polyps or for diarrhoea recurrence after index colonoscopy were included in two groups: patients in the MC group (32/100 patients, Group A) and in the chronic diarrhoea group (68/200 patients, Group B). Colonic polyps were recorded, collecting adenomas, advanced adenomas (AA; high-grade dysplasia -HGD-, villous component and size > 1cm) and CRC. A conditional logistic regression analysis was performed (COXREG: 1 case-2 controls, matched by age and sex).

Results: With a median follow-up of 9 years (IQR =7-12 years), 2 CRC were diagnosed in Group B (2/200). A total of 44 colonoscopies were performed in Group A and 105 in Group B, with no significant differences between groups (p=0.35). Recurrent diarrhoea was present in 25% of Group A and 38% of Group B (p=0.19). In these endoscopies, the total frequency of adenomas was: Group A 28% and Group B 56% (p=0.009). The frequency of AA was: Group A 12.5% and Group B 14.7% (p=1). The frequency of HGD/CRC was 0% in Group A and 5.8% in Group B (p=0.30). For adenomas, the COXREG OR was 0.2 (CI=0.05-0.75; p=0.017) and for AA (with CRC included) 0.8 (CI 0.26-2.9; p=0.8).

Conclusion: After long-term follow-up, patients with MC have a decreased frequency of adenomas and a trend to have less HGD/CRC compared with patients with chronic diarrhoea and normal colonic histology. These differences, therefore, are probably due to the MC itself and not to a protec-

tive effect of diarrhoea, as had been previously suggested. These results support the recommendation of not doing specific screening for CRC prevention in patients with MC.

Disclosure: Nothing to disclose.

P0252

EVOLUTION OF DISEASE PHENOTYPE, TIME TO BIOLOGICAL THERAPY AND MEDIUM-, LONG-TERM SURGERY RATES IN CROHN'S DISEASE PATIENTS IN WESTERN HUNGARY – A POPULATION-BASED STUDY BETWEEN 2007–2018, DATA FROM THE VESZPREM COUNTY COHORT

L. Gonczi¹, L. Lakatos², P.A. Golovics³, Z. Kürti¹, T. Pandur⁴,

G. Dávid², Z. Erdelyi², I. Szita², P.L. Lakatos⁵

¹Semmelweis University, Department of Internal Medicine and Oncology, Budapest, Hungary, ²Ferenc Csolnoky County Hospital, Department of Gastroenterology, Veszprem, Hungary, ³Hungarian Defence Forces Medical Centre, Department of Gastroenterology, Budapest, Hungary, ⁴Grof Eszterhazy Hospital, Department of Gastroenterology, Papa, Hungary, ⁵McGill University Health Center, Division of Gastroenterology, Montreal, Canada

Contact E-Mail Address: lorantgonczi@gmail.com

Introduction: The number of prospective population-based studies evaluating the natural disease course and surgical outcomes of Crohn's disease (CD) are still limited from Eastern Europe. The present study is a continuation of the Veszprem IBD population-based cohort with a follow-up of the incidence and disease course of IBD since 1977.

Aims & Methods: Our aim was to evaluate disease course by examining progression in disease phenotype, time to biological therapy and surgery rates in a prospective population-based database from Veszprem Province, including incident CD patients diagnosed between January 1, 2007 and December 31, 2018.

Data of 421 incident CD patients were analyzed (male/female: 237/184; median age at diagnosis: 29 years(y) [IQR: 21–42]). Both in-hospital and outpatient records were collected and comprehensively reviewed at diagnosis and during clinical follow-up. The mean length of follow-up was 8.53y (SD: 3.3). Disease phenotype was evaluated based on the Montreal classification. Probability of medium-, long-term change in disease course and surgical outcomes were analyzed using Kaplan–Meier survival analysis.

Results: Disease location was ileal (L1), colonic (L2) in and ileo-colonic (L3) in 29.7%/ 24.5%/ 45.8% of patients at diagnosis. At the end of follow-up (8.53y), disease location was 27.1%/ 22.8%/ 50.1% (L1/L2/L3). The proportion of patients with upper gastrointestinal manifestation remained stable (7.6% and 8.1%), while perianal disease increased from 13.5% to 19% by the end of follow-up. Disease behavior at diagnosis was luminal (B1) in 62.5% of the patients. The probability of disease behavior progression from luminal into stenosing or penetrating phenotype was 11.9% (SE:1.7) at 3 years, 13.2% (SE:1.7) at 5 years and 17.6% (SE:1.7) at 10 years. The Probability of receiving biological therapy after diagnosis was 20.9% (SE:2.0) at 5 years and 28.8% (SE:2.0) at 10 years in this cohort.

Overall resective surgery rate was 29.5% in the total population, while perianal surgery rate was 31.3% in patients with perianal disease at the end of follow-up. The probability of resective surgery was 20.7% (SE:2.0) at 1 year, 26.1% (SE:2.2) at 5 years and 30.7% (SE:2.4) at 10 years. For the probability of first perianal surgery among patients with perianal disease.

Conclusion: The probability of progression in disease behavior was lower compared to data from previous decades and similar to results from recent pan-European population-based data. (Burisch 2018, JCC). One-year surgery rates after diagnosis were considerably higher compared to previous data from our cohort or compared to Western and Northern Euro-

pean centers. (Lakatos 2011, IBD). Medium-term (5y) surgery rates were similar (~20%) compared to recent Hungarian and European data, while long-term (10y) rates decreased compared to data from previous decades. (Lakatos 2011, IBD; Lakatos 2012, AJG).

Disclosure: Nothing to disclose.

P0253

INCIDENCE, PREVALENCE, DISEASE PHENOTYPE AND MAXIMAL THERAPEUTIC STEP IN ULCERATIVE COLITIS PATIENTS IN WESTERN HUNGARY – A POPULATION-BASED STUDY BETWEEN 2007–2018, DATA FROM THE VESZPREM COUNTY COHORT

L. Lakatos¹, Z. Kürti², L. Gonczi², P.A. Golovics³, T. Pandur⁴,

G. Dávid¹, Z. Erdelyi¹, I. Szita¹, P.L. Lakatos⁵

¹Ferenc Csolnoky County Hospital, Department of Gastroenterology, Veszprem, Hungary, ²Semmelweis University, Department of Internal Medicine and Oncology, Budapest, Hungary, ³Hungarian Defence Forces Medical Centre, Department of Gastroenterology, Budapest, Hungary, ⁴Grof Eszterhazy Hospital, Department of Gastroenterology, Papa, Hungary, ⁵McGill University Health Center, Division of Gastroenterology, Montreal, Canada

Contact E-Mail Address: lorantgonczi@gmail.com

Introduction: Recent trends indicate a change in the epidemiology of inflammatory bowel disease (IBD) with previously low incidence areas now reporting progressive rise. The number of epidemiological population-based studies are still limited from Eastern Europe.

The present study is a continuation of the Veszprem IBD population-based cohort with a follow-up of the incidence and disease course of IBD since 1977.

Aims & Methods: Our aim was to analyze the incidence and disease phenotype at diagnosis, and the maximal therapeutic step distributions during follow-up in a prospective population-based database from Veszprem Province, including incident ulcerative colitis (UC) patients diagnosed between January 1, 2007 and December 31, 2018.

Data of 467 incident UC patients were analyzed (male/female: 236/231; median age at diagnosis: 36 years(y) [IQR: 25–54]). Both in-hospital and outpatient records were collected and comprehensively reviewed at diagnosis and during clinical follow-up. The source of age- and gender-specific demographic data for statistical analysis was derived from the results of a national population census in 2011 (Hungarian Central Statistical Office). Disease extension was evaluated based on the Montreal classification.

Results: Adjusted mean incidence rate was 11.02 (CI95%: 10.1–12.1) /10⁵ person-years in this 12 year period [males: 11.53 (CI95%: 10.2–13.1) /10⁵; females: 10.54 (CI95%: 9.3–12.0) /10⁵]. Prevalence rate was 283.51 (CI95%: 265.7–300.7) /10⁵ persons in 2011 and 317.79 (CI95%: 298.8–335.8) in 2015. For detailed annual incidence rates and age-specific mean incidence rates. Peak onset age in UC was 20–29 years of age. Diagnostic delay from symptom onset was ≥1year in 19.1%, and ≥3 years in 4.1% of the patients. Disease extension was proctitis (E1) in 22.3%, left sided colitis (E2) in 43.9%, and extensive colitis (E3) in 33.8% of the patients at diagnosis. Patients with extensive colitis were younger (32.9y, SD:16.6) at diagnosis compared to patients with proctitis (40.1y, SD:15.9; p<0.001) or left sided colitis (44.0y; SD:19.1; p<0.001). Extraintestinal manifestations were as follows: hepatic 5.4% (PSC 2.1%), arthritis 10.7%, ocular 0.9%, skin 3.6%. Active smokers at diagnosis were 12.6%, while past-smokers 18.2%. Distribution of maximal therapeutic steps during the course of follow-up (8.34y, SD: 3.5) were 5-ASA in 46.9%, systemic corticosteroids in 16.3%, immunosuppressive therapy in 19.3%; anti-TNF biologic therapy in 12.2% and other biologic therapy in 4.3%.

Conclusion: The incidence of UC in this 12 year period was high, comparable to high-incidence areas in Western European countries, and comparable to previous data from the Veszprem cohort, while prevalence rates continue to rise compared to our previous data. (Lakatos 2011, IBD). Disease extension at diagnosis and distribution of highest treatment step was comparable to European population-based data. (Burisch 2019, JCC).

Disclosure: Nothing to disclose.

P0254

EVOLUTION OF DISEASE PHENOTYPE, TIME TO BIOLOGICAL THERAPY AND MEDIUM-, LONG-TERM COLECTOMY RATES IN ULCERATIVE COLITIS PATIENTS IN WESTERN HUNGARY – A POPULATION-BASED STUDY BETWEEN 2007–2018, DATA FROM THE VESZPREM COUNTY COHORT

Z. Kürti¹, L. Gonczi¹, L. Lakatos², P.A. Golovics³, T. Pandur⁴, G. Dávid³, Z. Erdelyi³, I. Szita³, P.L. Lakatos⁵

¹Semmelweis University, Department of Internal Medicine and Oncology, Budapest, Hungary, ²Ferenc Csolnoky County Hospital, Department of Gastroenterology, Veszprem, Hungary, ³Hungarian Defence Forces Medical Centre, Department of Gastroenterology, Budapest, Hungary, ⁴Grof Eszterhazy Hospital, Department of Gastroenterology, Papa, Hungary, ⁵McGill University Health Center, Division of Gastroenterology, Montreal, Canada

Contact E-Mail Address: lorantgonczi@gmail.com

Introduction: The number of prospective population-based studies evaluating the natural disease course and surgical outcomes of ulcerative colitis (UC) are still limited from Eastern Europe. The present study is a continuation of the Veszprem IBD population-based cohort with a follow-up of the incidence and disease course of IBD since 1977.

Aims & Methods: Our aim was to evaluate disease course by examining progression in disease phenotype, time to biological therapy and colectomy rates in a prospective population-based database from Veszprem Province, including incident UC patients diagnosed between January 1, 2007 and December 31, 2018.

Data of 467 incident UC patients were analyzed (male/female: 236/1231; median age at diagnosis: 36 years(y) [IQR: 25-54]). Both in-hospital and outpatient records were collected and comprehensively reviewed at diagnosis and during clinical follow-up. The mean length of follow-up was 8.34y (SD: 3.5). Disease phenotype was evaluated based on the Montreal classification. Probability of medium-, long-term change in disease course and surgical outcomes were analyzed using Kaplan–Meier survival analysis.

Results: Disease extension was proctitis (E1), left sided colitis (E2), and extensive colitis (E3) in 22.3%/ 43.9%/ 33.8% of patients at diagnosis. The probability of disease progression into more extensive phenotype was 6.9% (SE:1.2) at 3 years, 8.3% (SE:1.3) at 5 years and 11.3% (SE:1.6) at 10 years. The Probability of receiving biological therapy after diagnosis was 9.9% (SE:1.4) at 3 years, 13.9% (SE:1.6) at 5 years and 17.8% (SE:2.0) at 10 years in this cohort.

Overall colectomy rate was 4.1% in the total population at the end of follow-up. The probability of colectomy was 1.5% (SE:0.6) at 1 year, 3.6% (SE:0.9) at 5 years and 4.4% (SE:1.0) at 10 years in Kaplan–Meier analysis.

Conclusion: The probability of progression in disease extent was low overall, similar to results from recent pan-European population-based data. (Burisch 2019, JCC). Medium- and long-term colectomy rates were lower compared to Western European centers, but somewhat higher compared to our previous data from the Veszprem cohort (2002–2006). (Lakatos 2011, IBD).

Disclosure: Nothing to disclose.

P0255

RISK OF AND RISK FACTORS FOR COLORECTAL CANCER IN ULCERATIVE COLITIS – A POPULATION-BASED STUDY FROM WESTERN HUNGARY BETWEEN 1977–2018, DATA FROM THE VESZPREM COUNTY COHORT

P.A. Golovics¹, L. Gonczi², L. Lakatos³, T. Pandur⁴, G. Dávid³, Z. Erdelyi³, I. Szita³, P.L. Lakatos⁵

¹Hungarian Defence Forces Medical Centre, Department of Gastroenterology, Budapest, Hungary, ²Semmelweis University, Department of Internal Medicine and Oncology, Budapest, Hungary, ³Ferenc Csolnoky County Hospital, Department of Gastroenterology, Veszprem, Hungary, ⁴Grof Eszterhazy Hospital, Department of Gastroenterology, Papa, Hungary, ⁵McGill University Health Center, Division of Gastroenterology, Montreal, Canada

Contact E-Mail Address: golovics.petra@gmail.com

Introduction: Limited data are available on the incidence and predictors of colorectal cancer (CRC) in ulcerative colitis (UC) derived from population based studies, especially from the Eastern European region. The present study is a continuation of the Veszprem IBD population based cohort with a follow-up of the incidence and disease course for over 40 years.

Aims & Methods: Our aim was to analyze the incidence and risk factors of CRC in a prospective population-based database from Veszprem Province, including incident UC patients diagnosed between January 1, 1977 and December 31, 2018.

Data of 1,370 incident UC patients were analyzed (male/female: 702/668; median age at diagnosis: 37 years(y) [IQR: 26-51]), with a median of 17y (IQR 9-24) follow-up. Both in-hospital and outpatient records were collected and comprehensively reviewed at diagnosis and during clinical follow-up. Disease extension was evaluated based on the Montreal classification. The risk of CRC was estimated using standardized incidence ratios (SIR). Age- and sex-specific CRC rates of the background population were derived from the National Cancer Registry (NCR) and Hungarian Central Statistical Office (KSH).

Results: CRC was diagnosed in 41/1,370 patients (2.99%), equaling an incidence rate of 41/23,240 person-year-duration. Median age at diagnosis of CRC was 59y (IQR: 50-67.5). The overall standardized incidence ratio of CRC in UC patients was 2.02 (CI95%: 10.1-12.1), compared to the background population. Marked elevation in SIRs were showed with more extensive disease (SIR_{proctitis}: 0.19, CI95%: 0.03-1.37; SIR_{left-sided}: 2.09, CI95%: 1.36-3.21; SIR_{extensive}: 3.77, CI95%: 2.41-5.91). The number of CRCs diagnosed during the complete follow-up increased by disease duration (0-10y: 4/395, 1.01%; 11-20y: 16/498, 3.21%; 20+y: 21/477, 4.40%). The cumulative risk of developing CRC after a disease duration of 10 years was 0.9% (SE: 0.3), 3.5% (SE: 0.7) after 20 years, and 6.5% (SE: 1.1) after 30 years. Patients with extensive disease and chronic continuous disease activity had higher probability of developing CRC compared to left sided disease extension and remitting disease activity (pLogRank=0.015 and 0.003). Longer disease duration, extensive colitis, chronic continuous disease activity, primary sclerosing cholangitis (PSC), anaemia and dysplasia were identified as risk factors for developing CRC in univariate analysis. In a multivariate logistic regression model, longer disease duration (p=0.018), PSC (p=0.001), anaemia (p=0.036) and dysplasia (p=0.029) remained significant predictors of CRC.

Conclusion: The cumulative risk of CRC was somewhat lower compared to previous results from this cohort; and also lower compared to previously reported results from Western European and North American studies. Longer disease duration, extensive colitis, chronic continuous disease activity, dysplasia, and PSC were identified as important risk factors for developing CRC.

Disclosure: Nothing to disclose.

P0256

EVOLUTION OF DISEASE PHENOTYPE, TIME TO BIOLOGICAL THERAPY AND MEDIUM-, LONG-TERM SURGERY RATES IN IBD-U PATIENTS IN WESTERN HUNGARY – A POPULATION-BASED STUDY BETWEEN 1977–2018, DATA FROM THE VESZPREM COUNTY COHORT

L. Gonczi¹, L. Lakatos², P.A. Golovics³, T. Pandur⁴, G. Dávid², Z. Erdelyi², I. Szita², P.L. Lakatos⁵

¹Semmelweis University, Department of Internal Medicine and Oncology, Budapest, Hungary, ²Ferenc Csolnoky County Hospital, Department of Gastroenterology, Veszprem, Hungary, ³Hungarian Defence Forces Medical Centre, Department of Gastroenterology, Budapest, Hungary, ⁴Grof Eszterhazy Hospital, Department of Gastroenterology, Papa, Hungary, ⁵McGill University Health Center, Division of Gastroenterology, Montreal, Canada

Contact E-Mail Address: lorantgonczi@gmail.com

Introduction: The number of epidemiological population-based studies on unclassified inflammatory bowel disease (IBD-U) patients are very limited. The present study is a continuation of the Veszprem IBD population based cohort with a follow-up of the incidence and disease course of IBDU since 1977.

Aims & Methods: Our aim was to evaluate disease course by examining progression in disease phenotype, time to biological therapy and surgery rates in a prospective population-based database from Veszprem Province, including incident IBD-U patients diagnosed between January 1, 2007 and December 31, 2018.

Data of 119 incident IBD-U patients were analyzed (male/female: 55/64; median age at diagnosis: 34 years(y) [IQR: 24-47]). Both in-hospital and outpatient records were collected and comprehensively reviewed at diagnosis and during clinical follow-up. The mean length of follow-up was 18.0y, (SD: 8.9). Probability of medium-, long-term change in disease course and surgical outcomes were analyzed using Kaplan–Meier survival analysis.

Results: Disease extension at diagnosis was proctitis in 7.6%, one-sided colitis (left-sided colitis, or isolated right-sided colitis) in 36.1%, and extensive (pancolitis) in 56.3%. The probability of progression in colonic disease extent over the course of follow-up was 6.7% (SE:2.3) at 3 years, 10.3% (SE:2.8) at 5 years and 15.3% (SE:3.4) at 10 years. In originally IBD U patients, new disease activity in the terminal ileum developed in 6.7% (n=8) patients over the total follow-up. The cumulative probability of developing terminal ileitis was 2.6% (SE:1.5) at 5 years and 3.5% (SE:1.7) at 10 years. Perianal disease developed in 5% (n=6) of all patients during the total follow-up. The probability of biological therapy initiation was 8.7% (SE:2.6) at 5 years, 11.4% (SE:3.0) at 10 years after diagnosis. In a sub-analysis of patients diagnosed after the year 2000 (n=62), the probability of receiving biological therapy was 15.5% (SE:4.8) after 5 years, and 19.4% (SE:5.3) after 10 years of follow-up. The overall surgery rate was 16.8% at the end of follow-up. Segment resection was performed in 5.0% of the patients, and 11.8% underwent subtotal- or total colectomy. The cumulative probability of resective surgery was 7.6% (SE:2.4) at 1 year, 9.3% (SE:2.7) at 5 years, 13.5% (SE:3.3) at 10 years, and 18.5% (SE:3.9) at 20 years. Colorectal cancer was detected in n=5 cases (4.2%) during the total follow-up.

Conclusion: Initial disease phenotype was severe in most cases of IBD-U, and colonic progression is substantial over time. However development of terminal ileitis or perianal disease was relatively low in this cohort. Therapeutic strategy was aggressive with high proportions of biological therapy, similar to the therapeutic strategies of Crohn's disease. Surgery rates were high, comprising mainly colectomies, which is also suggestive of the severe disease course of IBD-U.

Disclosure: Nothing to disclose.

P0257

SUBCLINICAL INFLAMMATORY BOWEL DISEASE PRECEDES THE DIAGNOSIS AND LEADS TO AN INCREASE IN HEALTHCARE RESOURCES UTILIZATION: MULTICENTER CASE-CONTROL STUDY

I. Rodríguez-Lago¹, U. Aguirre², P. Ramírez de la Piscina³, A.I. Muñagorri⁴, E. Zapata⁵, R. Higuera⁶, I. Montalvo⁷, A. Iriarte⁸, M. Fernández-Calderón⁹, P. Arreba¹⁰, J. Carrascosa¹¹, J.L. Cabriada¹, M. Barreiro-de Acosta¹²

¹Hospital Universitario de Galdakao, Gastroenterology, Galdakao, Spain, ²Research Unit, Hospital Universitario de Galdakao; Research Network on Chronic Disease REDISSEC, Network for Research on Chronicity, Primary Care, and Health Promotion (RICAPPS), Galdakao, Spain, ³Hospital Universitario Araba, Gastroenterology, Vitoria, Spain, ⁴Hospital Universitario Donostia, Gastroenterology, Donostia, Spain, ⁵Hospital de Mendara, Gastroenterology, Mendara, Spain, ⁶Hospital de Urduliz, Gastroenterology, Urduliz, Spain, ⁷Onkologikoa, Gastroenterology, Donostia, Spain, ⁸Hospital de Bidasoa, Gastroenterology, Irún, Spain, ⁹Hospital de Mondragón, Gastroenterology, Mondragón, Spain, ¹⁰Hospital Universitario de Basurto, Gastroenterology, Bilbao, Spain, ¹¹Hospital de Zumárraga, Gastroenterology, Zumárraga, Spain, ¹²Hospital Clínico Universitario de Santiago, Gastroenterology, Santiago de Compostela, Spain

Contact E-Mail Address: iago.r.lago@gmail.com

Introduction: Ulcerative colitis (UC) and Crohn's disease (CD) are two chronic conditions of the gastrointestinal tract. Previous data have shown that the inflammatory process starts years before the initial symptoms and the diagnosis.

Our aim was to determine if patients with an incidental diagnosis of UC or CD have an increase in healthcare utilization in the years preceding the symptomatic onset of the disease.

Aims & Methods: We performed a multicenter retrospective case-control study. Asymptomatic patients with a diagnosis of UC or CD during the colorectal cancer screening program at 9 hospitals between October 2010-January 2021 were included. Cases were matched 1:3 with controls adjusted by sex, age and date, excluding subjects with any visit to Gastroenterology, and with a cohort of patients with a symptomatic debut of IBD.

The main outcomes were the number of outpatient or Emergency Room visits, hospital admissions, radiological examinations (ultrasound, CT, MRI), sick-leaves, and prescriptions of antibiotics or systemic steroids up to 5 years before the diagnosis. Descriptive statistics were used, followed by chi-square tests and a multivariable hurdle or negative binomial regression model, adjusted by gender, age at diagnosis, smoking habits and Charlson index, in order to perform a per year and grouped (3 and 5 years) analysis.

Results: A total of 124 cases were included (87 UC, 30 CD, 7 IBD unclassified; median 56 years (IQR, 53-62); 44% female) and compared with 372 controls. Baseline characteristics including comorbidities were comparable between both cohorts. Patients demonstrated an increase in the number of visits to Primary Care during the combined periods including 3 and 5 years before the diagnosis (aIRR 1.59, 95% confidence interval [CI] [1.37-1.86], p=0.001; aIRR 1.43, 95% CI [1.24-1.67], p=0.01; respectively). This difference was also observed in the comparison of visits to specialized care physicians (aOR 62.74, 95% CI [26.10-151.41], p<0.0001; aOR 66.90, 95% CI [28.16-158.97], p<0.001; 3 and 5 years before, respectively). Systemic steroids were more frequently prescribed to patients also (aOR 2.84, 95% CI [1.21-6.69], p=0.03; aOR 2.25, 95% CI [1.06-4.79], p=0.04; 3 and 5 years before, respectively). Patients with symptomatic IBD had an increased number of visits to specialist care, Emergency Room, CT/US ex-

aminations, and prescriptions of both antibiotics and systemic steroids during the whole study period, while they showed a lower number of visits to Primary Care, compared to those with preclinical disease.

Conclusion: Patients with IBD show an increased need for medical assistance in the years prior to the diagnosis, even during the presymptomatic phase of the disease. Tools focused on early identification of IBD may start on Primary Care facilities, but certain factors as steroids may alter the development of symptoms and the full spectrum of the disease.

Disclosure: Nothing to disclose.

P0258

PHENOTYPIC DIFFERENCES IN INFLAMMATORY BOWEL DISEASE BETWEEN WOMEN AND MEN: SEXEII STUDY OF ENEIDA

C.J. Gargallo Puyuelo¹, E. Ricart², E. Iglesias-Flores³, R. De Francisco⁴, J. Gisbert⁵, C. Taxonera Samsó⁶, M. Mañosa Ciria⁷, M. Aguas⁸, T. Arroyo Villarino⁹, M. Minguez Pérez¹⁰, J. Guardiola¹¹, A. Lopez Sanromán¹², M. Rivero¹³, J. Barrio Andres¹⁴, M.I. Vera Mendoza¹⁵, L. De Castro¹⁶, E. García-Planella¹⁷, X. Calvet Calvo¹⁸, M.D. Martín-Arranz¹⁹, S. García López²⁰, B. Sicilia Aladrén²¹, D. Carpio Lopez²², L. Márquez Mosquera²³, L. Madero²⁴, M. Esteve Comas²⁵, D. Monfort Miquel²⁶, P. Varela Trastoy²⁷, P. Vega²⁸, G. Alcain Martinez²⁹, A. Rodriguez Pescador³⁰, O. Garcia-Bosch³¹, J.L. Pérez-Calle³², O. Merino³³, M. Sierra³⁴, C. Tardillo³⁵, R. Lorente Poyatos³⁶, A. Macho Conesa³⁷, M.F. García Sepulcre³⁸, A. Algaba³⁹, J. Hinojosa⁴⁰, L. Bujanda Fernández de Piérola⁴¹, J. Riera Oliver⁴², Y. Ber Nieto⁴³, A. Ponferrada Diaz⁴⁴, V.J. Morales Alvarado⁴⁵, M.P. Martinez Montiel⁴⁶, L. Ramos Lopez⁴⁷, J. Llaó Guàrdia⁴⁸, E. Domenech Morral⁴⁹, F. Gomollon⁵⁰,

on behalf of the ENEIDA Registry of GETECCU

¹Hospital Lozano Blesa, Zaragoza, Spain, ²Hospital Clinic, Gastroenterology, Barcelona, Spain, ³Hospital Universitario Reina Sofía, Digestive, Cordoba, Spain, ⁴Hospital Universitario Central de Asturias, Oviedo, Spain, ⁵Hospital Universitario de La Princesa, Instituto de Investigación Sanitaria Princesa and CIBEREHD, Digestive Services, Madrid, Spain, ⁶Hospital Clinico, Madrid, Spain, ⁷Hospital Universitari Germans Trias i Pujol, Gastroenterology, Badalona, Spain, ⁸La Fe University and Politecnico Hospital, Gastroenterology Unit, Valencia, Spain, ⁹H.C.U. Lozano Blesa, Zaragoza, Spain, ¹⁰Hospital Clinic Universitari de Valencia, Valencia, Spain, ¹¹Hospital Universitario de Bellvitge, Gastroenterology, L'Hospital de Llobregat (Barcelona), Spain, ¹²Hospital Ramón y Cajal, Madrid, Spain, ¹³Marqués de Valdecilla University Hospital, Gastroenterology, Santander, Spain, ¹⁴Hospital Rio Hortega, Valladolid, Spain, ¹⁵Hospital Universitario Puerta de Hierro, Digestive, Madrid, Spain, ¹⁶University Hospital of Vigo, Gastroenterology, Vigo, Spain, ¹⁷Hospital del la Santa Creu i Sant Pau, Madrid, Spain, ¹⁸Hospital de Sabadell, Institut Universitari Parc Tauli, UAB, Unitat de Malalties Digestives, Barcelona, Spain, ¹⁹Hospital La Paz, Gastroenterology, Madrid, Spain, ²⁰Hospital Universitario Miguel Servet, Zaragoza, Spain, ²¹H Hospital Universitario de Burgos, Gastroenterology, Burgos, Spain, ²²Complejo Hospitalario Universitario de Pontevedra, Gastroenterology and Hepatology, Pontevedra, Spain, ²³Hospital del Mar, Gastroenterology, Barcelona, Spain, ²⁴Hospital Universitario de Alicante, Alicante, Spain, ²⁵Gastroenterology, Hospital Universitari Mutua Terrassa, Barcelona, Spain, ²⁶H. Consorci de Terrassa, Terrassa, Spain, ²⁷Hospital Universitario de Cabueñes, Gijón, Spain, ²⁸Complejo Hospitalario Universitario de Ourense, Gastroenterology

Department, Ourense, Spain, ²⁹Hospital Clínico de Malaga, Malaga, Spain, ³⁰Hospital Galdakao, Galdakao, Spain, ³¹Hospital de Sant Joan Despí Moisès Broggi, Digestive Diseases Department, Sant Joan Despí, Spain, ³²Hospital Universitario Fundación Alcorcon, Alcorcon, Spain, ³³Cruces, Bilbao, Spain, ³⁴Complejo Asistencial de Leon, Gastroenterology, Leon, Spain, ³⁵Hospital de Nuestra Señora de la Candelaria, Santa Cruz Tenerife, Spain, ³⁶Hops. General Ciudad Real, Ciudad Real, Spain, ³⁷Hospital Universitario de Valladolid, Valladolid, Spain, ³⁸Hospital Elche, Elche, Spain, ³⁹Hospital Fuenlabrada, Fuenlabrada, Madrid, Spain, ⁴⁰Hospital Universitario de Manises, Gastroenterology Service, Manises-Valencia, Spain, ⁴¹Instituto Biodonostia, San Sebastián, Spain, ⁴²Hospital Son Llatzer, Palma, Spain, ⁴³Hospital San Jorge, Huesca, Spain, ⁴⁴Hospital Infanta Leonor, Madrid, Spain, ⁴⁵Hospital General de Granollers, Gastroenterology/Endoscopy, Barcelona, Spain, ⁴⁶Hospital 12 de Octubre, Madrid, Spain, ⁴⁷Hospital Universitario de Canarias, Tenerife, Spain, ⁴⁸Althaia, Xarxa Assistencial Universitària de Manresa, Manresa, Spain, ⁴⁹Hospital Germans Trias i Pujol, Gastroenterology Unit, Badalona, Barcelona, Spain, ⁵⁰Hospital Clínico Universitario Lozano Blesa, Servicio de Aparato Digestivo, Zaragoza, Spain

Contact E-Mail Address: carlajerusalén@hotmail.com

Introduction: Little evidence exists on possible phenotypic differences in inflammatory bowel disease (IBD) between men and women. In published studies, gender is one more variable, whose possible effects may be masked by interference with other variables, or not appear due to a small sample size.

Aims & Methods: AIM: To assess whether there are differences in the clinical patterns of IBD between women and men.

METHODS: Multicenter observational study that included all patients diagnosed with Crohn's disease (CD) or ulcerative colitis (UC) from the ENEIDA registry (GETECCU).

Results: A total of 51,595 patients from 86 centers were included, 25,947 with CD (13,238 men, 12,709 women) and 25,648 with UC (13,596 men and 12,052 women). Women in our IBD cohort more often had a family history of IBD than men (14.5% vs 12.8%, $p < 0.001$)

Significant differences were observed in the age of onset of both CD and UC between men and women. The age at onset of CD was lower in men [mean age: 34.7(15) vs. 35.7(16) years, $p < 0.001$], while in UC it was lower in women [mean age: 41.2 (16) vs. 38.4(15) years, $p < 0.001$].

In CD, males more often had a penetrating behavior (20% vs 16%, $p < 0.001$), more frequently developing intra-abdominal fistulas (14.7% vs 11.7%, $p < 0.001$) and related complications such as intra-abdominal abscess (8.2% vs 6.4%, $p < 0.001$) and perforation (3.6% vs 3%, $p = 0.005$). Men also had a higher prevalence of perianal disease (27.4% vs. 23.1%, $p < 0.001$). Women more often had an inflammatory behaviour (65.8% vs 62.9%, $p < 0.001$).

In UC, women more often had involvement limited to the rectum (26.3% vs. 19.3%, $p < 0.001$), while extensive UC was more frequent in men (40.7% vs. 34.3%, $p < 0.001$). Toxic megacolon (1.07% vs. 0.71%, $p = 0.003$) and perforation (0.43 vs. 0.25%, $p = 0.018$) were also more prevalent in men.

Extraintestinal manifestations were more frequent in women. 27.3% of women with CD (3475) vs. 20.4% of men with CD (2703) had extraintestinal manifestations, $p < 0.001$. In UC, 16% of women (1937) vs. 12.4% of men (691) had extraintestinal manifestations, $p < 0.001$. See Table 1.

Surgical treatment was more frequent in men in both CD (40.9% vs. 38.5%, $p < 0.001$) and UC (9.2% vs 6.8%, $p < 0.0001$)

	Men with CD n=13238	Women with CD n=12709	p-value	Men with UC n=13596	Women with UC n=12052	p-value
Peripheral spondyloar- thropathy	999 (7.55%)	1582 (12.45%)	<0.001	603 (4.44%)	819 (6.80%)	<0.001
Ankylopoietic spondylitis	556 (4.20%)	373 (2.93%)	<0.001	226 (1.66%)	137 (1.14%)	<0.001
Sacroiliitis	413 (3.12%)	384 (3.02%)	0.672	173 (1.27%)	187 (1.55%)	0.065
Erythema nodosum	233 (1.76%)	805 (6.33%)	<0.001	77 (0.57%)	252 (2.09%)	<0.001
Pyoderma gangrenosum	81 (0.61%)	125 (0.98%)	0.001	66 (0.49%)	90 (0.75%)	0.009
Uveitis	137 (1.03%)	224 (1.76%)	<0.001	71 (0.52%)	100 (0.83%)	0.003
Episcleritis	84 (0.63%)	151 (1.19%)	<0.001	46 (0.34%)	58 (0.48%)	0.089
Venous Thrombosis	155 (1.17%)	111 (0.87%)	0.021	150 (1.10%)	82 (0.68%)	<0.001
Primary sclerosing cholangitis	63 (0.48%)	46 (0.36%)	0.186	175 (1.29%)	85 (0.71%)	<0.001

CD: Crohn's disease, UC: ulcerative colitis

Table 1. Extraintestinal manifestations

Conclusion: Men seem to develop a more complex inflammatory bowel disease than women. In CD, men more often have a penetrating pattern and in UC, they have more extensive disease. Complications and the need for surgery are also more frequent in men than in women in both CD and UC. However, extraintestinal manifestations are more prevalent in women than in men, with the exception of venous thrombosis and primary sclerosing cholangitis.

Disclosure: Nothing to disclose.

P0259 WITHDRAWN

P0260

DE NOVO INFLAMMATORY BOWEL DISEASE PICKED UP VIA NATIONAL BOWEL CANCER SCREENING PROGRAMME: 10 YEAR EXPERIENCE AT A LARGE ENGLISH SCREENING CENTRE

K. Georgas¹, S. Mahdibeiraghdar¹, K. Kaur¹, M. Gismond¹, C. Banks¹, D. Murugiah¹, J. Stebbing¹, M. Gallagher¹, C. Alexakis¹

¹Royal Surrey NHS Foundation Trust, Guildford, United Kingdom

Contact E-Mail Address: k.georgas@nhs.net

Introduction: In England, all adults from the age of 60 years are offered two yearly faecal occult blood testing, as part of the national bowel cancer screening (BCS) programme. Those with positive stool tests are offered colonoscopy. The finding of incidental cases of inflammatory bowel disease (IBD) amongst individuals undertaking BCS has previously been reported¹, but this cohort of patients has never been characterised in depth.

Aims & Methods: We aimed to describe and characterise all new cases of IBD picked up in patients undertaking BCS at a single large screening centre in South East England covering 1.6 million people, over a 10 year period. Using endoscopy reporting software, we retrospectively identified all BCS colonoscopy reports for the period January 2012 until December 2021.

All reports were reviewed for endoscopic evidence of mucosal inflammation. Patients with pre-existing IBD were excluded from analysis, as were those with radiation proctitis. For patients with reports describing new endoscopic colonic or terminal ileal (TI) inflammation, two independent

experts in IBD reviewed the colonoscopy reports, the endoscopic images and the corresponding histology to validate true cases of de novo IBD. In instances where the opinions of the two experts differed, a third IBD expert reviewed such cases, to conclude on the final diagnosis. For all confirmed cases of de novo IBD, data was collected including patient demographics, disease subtype (ulcerative colitis (UC), Crohn's disease (CD), indeterminate colitis (IC)), severity of mucosal inflammation, other endoscopic data, and IBD treatments/management offered at time of index BCS colonoscopy.

Results: 5200 screening colonoscopies were performed in 4059 patients over the study period. After excluding existing IBD patients, 103 patients had endoscopic evidence of new mucosal inflammation. Following the validation exercise by the three IBD experts, we identified 73 (1.4%) incident cases of IBD. Mean age at diagnosis was 66.3 years. 63.0% of cases were male. 97.3% of patients had confirmatory biopsies taken at procedure. 52.1% of cases included inspection of the terminal ileum.

Other non-IBD pathology was identified in 64.4% of patients (malignancy 3.0%, polyps 43.9%, diverticulosis 45.5%, other pathology 7.6%). IBD subtypes were as follows: UC 50.7% (proctitis E1 - 37.8%, left sided disease E2 - 35.1%, pancolitis E3 27.0%), CD 20.5% (TI disease only 13.3%, colonic disease 86.7%) and indeterminate colitis 28.8%. 80.1% of patients had mild mucosal disease.

No patients had evidence of severe mucosal inflammation. IBD specific treatment was started post colonoscopy in 16.4% of cases. This included 8 patients started on oral mesalazine, and 4 patients on topical mesalazine agents. In 17.8% of cases, the endoscopist either referred or suggested referral to specialist gastroenterology services at the time of colonoscopy.

Conclusion: Uncovering incident cases of IBD through national BCS is not uncommon. Fortunately, the disease severity appears to be mild in most cases. With numbers of older-onset IBD rising worldwide, colorectal cancer screening programmes potentially offer a juncture to identify, stage and initiate treatment in this cohort of patients.

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Disclosure: Nothing to disclose.

P0261

DISEASE ACTIVITY PATTERNS OF INFLAMMATORY BOWEL DISEASE - A DANISH NATIONWIDE COHORT STUDY 1995-2018

M.D. Wewer^{1,2,3}, E. Langholz^{4,5}, P. Munkholm^{6,5}, F. Bendtsen^{5,2}, J.B. Seidelin^{4,5}, J. Burisch^{3,5,2}

¹Medical Faculty, University of Copenhagen, Copenhagen, Denmark, ²Hvidovre Hospital, University of Copenhagen, Hvidovre, Denmark, ³Gastro Unit, Medical Division, Hvidovre, Denmark, ⁴Hvidovre Hospital, Copenhagen Center for Inflammatory Bowel Disease in Children, Adolescents and Adults, Hvidovre, Denmark, ⁵Herlev Hospital, University of Copenhagen, Department of Gastroenterology, Herlev, Denmark, ⁶University of Copenhagen, Department of Clinical Medicine, Copenhagen, Denmark, ⁶North Zealand Hospital, University of Copenhagen, Hillerød, Denmark, Department of Gastroenterology, Hillerød, Denmark

Contact E-Mail Address: madswewer@gmail.com

Introduction: Data on the disease activity patterns of patients with inflammatory bowel disease (IBD) in the biological era is scarce, and little is known about the influence on long-term outcomes.

Aims & Methods: We aimed to describe the median and long-term disease activity patterns of IBD patients. We included all incident patients diag-

nosed with IBD as well as all prevalent individuals alive and diagnosed with IBD in Denmark between 1995 and 2018 in a nationwide registry study. We used information regarding IBD-related hospitalizations, IBD-related surgeries excluding perianal surgery, redeemed prescriptions of IBD-treatments to identify episodes of active disease and to grade these as mild-moderate or severe flares during each year of follow-up.

Mild-moderate: a course of topical corticosteroids, oral budesonide, or topical 5-aminosalicylic acid.

Severe: hospitalization, surgery, oral corticosteroids or biological therapy. The disease activity patterns for 5 and 10-year periods were assessed. Patients with UC having had colectomy were considered to have no subsequent events. Patients with rheumatological or dermatological disease which shares treatment regimens were excluded.

Results: A total of 17,820 Crohn's disease (CD) and 32,516 ulcerative colitis (UC) were included in this study. In incident patients with CD, severe disease activity occurred in 80% (N=11,330/14,169) in the year of diagnosis while 5.4% (N=764/14,169) had mild-moderate disease. The following years, the proportion of CD patients in remission during a year increased steadily to 89% (N=1,522/1,713) after 20 years of disease. In incident patients with UC, severe disease activity occurred in 75% (N=20,507/27,396) in the year of diagnosis, 3.4% (N=945/27,396) underwent colectomy and 13% (N=3,521/27,396) had mild-moderate disease. The proportion of UC patients in remission each year increased to 72% (N=2,316/3,228) being in remission after 20 years. After 10- and 20 years, 9.5% and 14% of UC patients had in total undergone colectomy.

When assessing all prevalent patients in Denmark, during each year approximately 75% and 60% of the CD and UC patients, respectively, were in remission while 22% and 15% had an episode of severe disease. This pattern remained stable throughout the study period. 5- and 10-year disease activity patterns are found in Table 1.

In Cox models adjusted for sex, age at IBD diagnosis and primary sclerosing cholangitis (PSC), the quiescent disease pattern in CD patients had a significantly higher risk of intestinal cancer (HR: 2.38, 95%CI: 1.11-5.11). No other association between the 10-year disease activity patterns and intestinal cancer was found among CD or UC patients.

Disease activity pattern	Patients with Crohn's disease (5-year pattern: N=9,162, 10-year pattern: N=5,788)	Patients with ulcerative colitis (5-year pattern: N=18,662, 10-year pattern: N=11,663)	
No year with disease activity	8.3% (N=756/9,162)	3.7% (N=684/18,662)	
1-2 years with disease activity	60% (N=5,511/9,162)	55% (N=10,197/18,662)	
3-4 years with disease activity	26% (N=2,393/9,162)	32% (N=5,960/18,662)	
5 years with disease activity	5.5% (N=502/9,162)	9.8% (N=1,821/18,662)	
Chronic continuous	6.0% (N=346/5,788)	11% (N=1,252/11,663)	First 10 years with at least 8 years with activity
Chronic intermittent	16% (N=904/5,788)	16% (N=1,887/11,663)	First 10 years with activity pattern that does not meet any of the other criteria
Decreasing	45% (N=2,583/5,788)	45% (N=5,272/11,663)	First 5 years with 2 or more years with activity. Following 5 years 2 or less years with activity
Increasing	4.2% (N=242/5,788)	5.0% (N=578/11,663)	First 5 years with less than 2 years with activity. Following 5 years 2 or more years with activity
Quiescent	30% (N=1,713/5,788)	23% (N=2,674/11,663)	First 10 years with 1 or less years with activity

Table 1.

Conclusion: In this nationwide cohort study, we reported the distribution of patients within temporal disease activity patterns. The share of patients in remission each year after diagnosis was increasing.

However, the prevalent cohort revealed, that the proportion of patients in remission each calendar year was stable. No clear relation was found regarding the 10-year disease activity patterns and risk of intestinal cancers or mortality.

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P0262

THE BURDEN OF URINARY SYMPTOMS IN PATIENTS WITH INFLAMMATORY BOWEL DISEASES: A CROSS-SECTIONAL OBSERVATIONAL STUDY

[R. Pellegrino](#)¹, [L. Romano](#)², [L. Napolitano](#)², [A.G. Gravina](#)¹, [A. Miranda](#)¹, [K. Priadko](#)¹, [A. Facchiano](#)¹, [A. Cuomo](#)³, [C. Mucherino](#)⁴, [F. Crocetto](#)², [C. Sciorio](#)⁵, [L. Spirito](#)⁶, [D. Arcaniolo](#)⁶, [V. Mirone](#)², [M. Romano](#)¹

¹University of Campania "Luigi Vanvitelli", Department of Precision Medicine, Naples, Italy, ²University of Naples "Federico II", Department of Neurosciences, Reproductive Sciences and Odontostomatology, Naples, Italy, ³U.O.C. Gastroenterologia ed Endoscopia Digestiva, Nocera Inferiore, Italy, ⁴A.O.R.N. "Sant'Anna e San Sebastiano", Gastroenterology, Caserta, Italy, ⁵Ospedale Manzoni, Urology, Lecco, Italy, ⁶University of Campania "Luigi Vanvitelli", Department of Woman, Child and General and Specialized Surgery, Naples, Italy

Contact E-Mail Address: raffaele.pellegrino@unicampania.it

Introduction: Inflammatory Bowel Diseases (IBD) (i.e., Crohn's Disease (CD) and Ulcerative Colitis (UC) may have extraintestinal manifestations, including disorders of the urinary tract. The prevalence of urinary symptoms (US) in CD or UC patients is still unclear.

Aims & Methods: This study aims to assess the prevalence of US in patients with CD or UC; to evaluate the variables implicated in any difference in US prevalence between CD or UC; to assess any relationship between disease activity and the US.

Type of study: cross-sectional, observational. Patients: 301 IBD patients, 161 males, and 140 females, 99 with CD, and 202 with UC, median age 45 years. The US assessed through standardized questionnaires i.e., the Bristol Female Lower Urinary Tract Symptoms (BFLUTS) for women and the NIH-Chronic Prostatitis Symptom Index (NIH-CPSI) together with the International Prostate Symptom Score (IPSS) for men. CD disease activity

was determined through the Crohn's Disease Activity Index (CDAI) whereas UC disease activity through the Partial Mayo Score (PMS) and/or the Total Mayo Score (TMS).

Results: The median BFLUTS total score for IBD female patients was 6 (3–11). Patients with a higher age at diagnosis (A3, according to Montreal classification) had worse filling (BFLUTS-F) symptoms ($p=0.049$) and a worse quality of life (BFLUTS-QoL, $p=0.005$). The IPSS questionnaire showed that in male IBD patients, 67.1% had mild, 28.5% moderate, and 4.4% severe symptom levels.

Following the NIH-CPSI, the overall prevalence of chronic prostatitis-like symptoms was 26.8% (in detail, 21.3% in CD and 29.2% in UC, $p < 0.01$). There were no significant differences in US scores levels between CD and UC patients in terms of BFLUTS, NIH-CPSI, and IPSS ($p > 0.05$). UC patients with proctitis (E1 according to Montreal classification) presented worse levels of NIH-CPSI and IPSS ($p < 0.05$).

In male patients with UC (according to NIH-CPSI) an S Montreal parameter of remission (S0) was associated with a higher percentage of patients with mild US compared to patients with worse levels of US ($p < 0.05$). The NIH-CPSI total score showed a good correlation with PMS ($p=0.003$) and TMS ($p=0.014$).

Conclusion: CD and UC patients often complain of US as assessed through the administration of standardized questionnaires. Age is associated with worse filling symptoms and QoL in female IBD patients. The US in male IBD patients are prevalently mild, and are more frequent in those with proctitis. Male UC patients in remission experience mild US more frequently than severe US. UC patients had a higher prevalence of chronic prostatitis-like symptoms than those with CD. In male UC patients, US correlated with disease activity. Evaluation of US through the use of validated questionnaires should be considered in IBD patients for prompt diagnosis and early treatment.

Disclosure: Nothing to disclose.

P0263

HIDRADENITIS SUPPURATIVA AND INFLAMMATORY BOWEL DISEASE IN A CASE-CONTROL STUDY

B. Neri¹, M. Mossa¹, V. Appolloni¹, C. Pensa², S. Lambiase², E. Calabrese¹, S. Salvatori¹, I. Marafini¹, G. Monteleone¹, E. Campione², L. Biancone¹

¹Università degli Studi di Roma Tor Vergata, Medicina dei Sistemi, Rome, Italy, ²Università degli Studi di Roma Tor Vergata, Dermatology Unit, Rome, Italy

Contact E-Mail Address: benedettoneri@gmail.com

Introduction: Hidradenitis Suppurativa (HS) is a chronic inflammatory skin disease characterized by recurrent nodules and abscesses in intertriginous areas association with Inflammatory Bowel Disease (IBD) has been suggested in few heterogeneous studies.

Aims & Methods: In a retrospective, single-center, case-control study, we aimed to assess characteristics of HS in patients (pts) with or without concomitant IBD.

In a case-control study, each IBD pt with concomitant HS (Case) was matched with 4 pts with HS but no IBD (Controls) for: gender and age (± 5 yrs). In a multidisciplinary approach, all Cases and Controls were assessed by the same dedicated gastroenterologists and dermatologists at the University "Tor Vergata" of Rome, Italy.

Inclusion criteria for Cases: age ≥ 15 and ≤ 85 yrs; well-defined diagnosis of IBD; well-defined diagnosis of HS. Inclusion criteria for Controls: age ≥ 15 and ≤ 85 yrs; well-defined diagnosis of HS; no diagnosis of IBD. Exclusion criteria for Cases and Controls: low compliance; incomplete data. HS was classified according to the Hurley score.

Data were expressed as median [range]. Clinical characteristics IBD and HS were reported and comparisons between groups assessed by the Student-t Test and χ^2 test.

Results: The study population included 120 pts with HS: 24 with IBD and 96 matched pts with no IBD (4 M [16.6%] vs 16 [16.6%]; $p=1$). In IBD, pts were: 18 (75%) Crohn's disease (CD), 5 (20.8%) Ulcerative Colitis (UC), 1 (4.2%) Unclassified Colitis. The median IBD duration was 15 [3–37] yrs. Extra-intestinal manifestations were recorded in 10 (41.7%) IBD pts. CD ($n=18$) involved: ileum (6 [33.3%]), colon (3 [16.7%]), ileum-colon (5 [27.8%]), upper GI (4 [22.2%]). CD behavior was non stricturing-non penetrating in 7 (38.9%), structuring in 7 (38.9%), penetrating in 4 (22.2%) pts. In CD pts with HS, perianal disease was observed in 10 (55.6%) and surgery in 8 (44.4%) pts. UC extent included proctitis in 1 (20%), left-sided in 1 (20%) and pancolitis in 3 (60%) pts.

No difference was observed in terms of median age in Cases vs Controls (40 [20–59] vs 37 [15–63] yrs; $p=0.68$). However, HS duration was significantly shorter in Cases vs Controls (5.8 [1–32] vs 11 [1–40] yrs; $p=0.0003$), although most IBD pts referred a long history of lesions compatible with undiagnosed HS.

The frequency of HS localizations was comparable between Cases and Controls (pts): axillary (5 [20.8%] vs 23 [23.9%]; $p=0.95$); inguinal (8 [33.3%] vs 27 [28.1%]; $p=0.8$), concomitant inguinal and axillary (8 [33.3%] vs 39 [40.9%]; $p=0.67$). Uncommon HS localizations (trunk, gluteal areas) did not significantly differ between Cases and Controls (8 [33.3%] vs 52 [54.1%]; $p=0.11$). Median Hurley stage of HS was comparable between groups (2 [1–3] vs 2 [1–3]; $p=0.34$). Active/ex smokers were 13 (54.2%) in Cases vs 69 (71.9%) in Controls ($p=0.15$). A history of previous or current treatment with TNF-antagonists was significantly more frequent in Cases vs Controls (13 [54.2%] vs 22 [22.9%]; $p=0.005$).

Conclusion: Perianal disease may be observed in a high proportion of CD patients with HS. HS may be underestimated in patients with IBD.

References: 1. Van der Zee et al, BJD 2017; 2. Linhaers M et al, IBD 2020

Disclosure: Nothing to disclose.

P0264

A SYSTEMATIC REVIEW AND META-ANALYSIS OF SLEEP QUALITY IN INACTIVE INFLAMMATORY BOWEL DISEASE

A. Barnes¹, S. Madigan¹, R. Mountfield¹, J. Baker¹, P. Spizzo¹, P. Bampton², S. Mukherjee³

¹Flinders Medical Centre, Gastroenterology, Bedford Park, Australia, ²Flinders University, College of Medicine and Public Health, Bedford Park, Australia, ³Flinders Medical Centre, Respiratory and Sleep medicine, Bedford Park, Australia

Contact E-Mail Address: shaunamadigan@gmail.com

Introduction: Poor sleep in people with inflammatory bowel disease (IBD) has been demonstrated to be prevalent and has been associated with disease activity.

Aims & Methods: This meta-analysis aimed to assess the prevalence of poor sleep in inactive inflammatory bowel disease and in controls by considering cohort and cross-sectional studies. Electronic databases were searched for publications from inception to November 1st, 2021. Meta-analysis was performed according to the preferred reporting item for systematic reviews and meta-analyses (PRISMA) guidelines. Quality of studies was assessed using the modified Newcastle-Ottawa Scale or Newcastle-Ottawa Scale as appropriate. Poor sleep and IBD activity were defined according to self-reported subjective sleep measures. A random effects model was used to determine the standardised mean difference between poor sleep in inactive IBD and healthy controls. Publication bias was assessed by funnel plot and Egger's test.

Results: 519 studies were screened with 9 studies included in the meta-analysis incorporating a total of 729 people with IBD and 508 controls. Publication date ranged from 2006 to 2020. A random effects model showed a standardised mean difference with poor sleep being more frequent in those with inactive IBD than controls with moderate effect size (Hedge's g 0.41, CI (0.22-0.59) and no significant heterogeneity. Funnel plot was symmetric and Egger's negative ($p=0.37$).

Conclusion: Poor sleep is more common in individuals with inactive IBD than healthy controls. This finding suggests that IBD activity may not be the sole driver of the observed poor sleep in this population. Further studies should consider potential mechanisms to explain this result including the role of subclinical inflammation and psychosocial factors that may influence sleep quality in people with IBD.

Disclosure: Nothing to disclose.

P0265

RISK OF CERVICAL CANCER IN INCIDENT ULCERATIVE COLITIS: A NATIONWIDE POPULATION-BASED STUDY SPANNING 10 YEARS

H.-S. Kim¹, J.K. Lee¹

¹Yonsei Univ. Wonju College of Medicine, Internal Medicine, Wonju, Korea (Republic of)

Contact E-Mail Address: hyskim@yonsei.ac.kr

Introduction: The association between ulcerative colitis (UC) and increased risk of cervical cancer in women remains controversial.

Aims & Methods: We investigated the risk of cervical cancer in patients with UC using the nationwide population-based claims data in South Korea. We analyzed the claims data of the Korean National Health Insurance (NHI). UC was defined using both ICD-10 codes and UC-specific prescription.

We analyzed incident cases of UC diagnosed between 2006 and 2015. Age-matched women without UC (control group) were randomly selected from the general population in a ratio of 1:3. Hazard ratios (HRs), adjusted for different covariates, were calculated using multivariate Cox proportional hazard regression.

Results: In total, 12,632 and 36,797 women with UC and without UC, respectively, were enrolled. Cervical cancer developed in 0.21% (68 person-years) among UC patients, and 0.14% (172 person-years) among control group, respectively. The HR (95% CI) of cervical cancer in UC group, with reference to control group, was 1.56 (0.97-2.50). When stratified according to age, the HR was significantly high in elderly UC patients (≥ 60 years) at 3.65 (1.54-8.66), compared those in control group. In UC patients, old age (≥ 40 years), and low socioeconomic status were associated with increased risk of cervical cancer.

Conclusion: The elderly UC patients had a higher incidence of cervical cancer than age-matched controls in Korea. In UC patients, old age These findings suggest that newly diagnosed UC patients in old age should be screened for cervical cancer.

Disclosure: Nothing to disclose.

P0266

A SYSTEMATIC REVIEW ON CLINICAL OUTCOMES IN PAEDIATRIC INFLAMMATORY BOWEL DISEASE PATIENTS

J. Van Hecke¹, L. Wauters², G. Veereman³

¹Free University Brussels, Medicine and Pharmacy, Brussels, Belgium, ²University Hospitals Leuven, Gastroenterology and Hepatology, Leuven, Belgium, ³UZ Brussels, Dept. of Paediatric Gastroenterology, Brussels, Belgium

Contact E-Mail Address: vanheckejonathan01@gmail.com

Introduction: Research on paediatric inflammatory bowel disease (PIBD) has grown over the past few years. Several IBD cohorts and registries in the world led to reports on disease progression in paediatric patients.

Aims & Methods: We aim to report on response and remission rates in PIBD by reviewing prospective cohorts and registries and comparing outcomes. One reviewer (JVH) performed a systematic worldwide literature search in MEDLINE and EMBASE from inception until March 17, 2022.

In addition, all publications of the ImproveCareNow registry were reviewed. Inclusion criteria were: prospective cohort studies with patients <18 years at diagnosis and minimum follow-up of 1 year mentioning disease phenotype and disease activity.

Exclusion criteria were:

- Reporting disease activity only at diagnosis,
- Retrospective cohort studies,
- Full-text unavailable,
- Outcome limited to steroid-free remission.

The Preferred Reporting Items for Systematic Reviews and Meta-Analyses Protocols (PRISMA) checklist guidelines and Newcastle-Ottawa scale for prospective cohort studies were applied.

Results: The search yielded 395 records and 7 inclusions with sample sizes ranging from 33 to 390 patients (total population: 888). The median follow-up ranged from 1 to 5 years. Proportions between groups were compared using a chi-square test with significance level of 5%.

Disease location is consistent with cohorts for Crohn's disease (CD) ($p=.004$) but not for ulcerative colitis (UC) ($p=.69$). L4 was more frequent in the Belgian cohort ($\chi^2=4$).

Primary outcome: proportions of disease activity differed at M0 and M12 ($p<.00001$) with more inactive ($\chi^2=5.5$) and less moderate-to-severe disease ($\chi^2=23$).

Secondary outcome: proportions of disease activity, limited to BELCRO (Belgium), did not differ between 1, 2, 3 and 5 years ($p=.94$). After 5 years these proportions did differ significantly from baseline (M0) ($p<.0001$ for evolution).

Country	Belgium [1]	Switzerland [2]	Hungary [3]	Hungary [3]	Scotland [4]	Turkey [5]
Population, n	CD, 84	UC, 56 CD, 90 IBD-U, 7	UC, 124	CD, 266	UC, 4 CD, 26 IBD-U, 3	UC, 22 CD, 12 IBD-U, 2
M0, n (%)	A, 4 (5) B, 16 (19) C, 64 (76)	A, 80 (52,3) B, 39 (25,5) C, 18 (11,8)	A, 2 (1,7) B, 49 (40,8) C, 69 (57,5)	A, 20 (7,8) B, 112 (43,8) C, 124 (48,4)	A, 25 (76) B, 5 (15) C, 3 (9)	A, 23 (67,6) B, 8 (23,5) C, 3 (8,3)
M12, n (%)	A, 39 (46) B, 18 (34) C, 3 (4)	A, 46 (51,1) B, 25 (27,8) C, 3 (3,3)	A, NA B, NA C, 9 (7,8)	A, NA B, NA Severe, 5 (2,1)	A, 24 (83) B, 4 (14) C, 1 (3)	A, 25 (73,5) B, 8 (23,5) C, 1 (2,9)

A: inactive disease; B: mild disease; C: moderate-to-severe disease. IBD-U: IBD type unclassified; NA: not available.

Table 1: disease activity at start of the study (M0) and 1 year follow-up (M12).

Conclusion: Prospective reports on evolution of disease severity in PIBD are scarce. The European cohorts report a significant decrease in disease activity after 1 year with more inactive and less moderate-to-severe dis-

ease. Proportions of disease activity did not differ between 1 to 5 year follow-up in the Belgian cohort but did differ significantly from baseline (M0) after 5 years.

The authors declare no competing interests nor funding.

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Disclosure: Nothing to disclose.

P0267

PREVALENCE OF IRON DEFICIENCY AND ANAEMIA IN THE OUTPATIENT INFLAMMATORY BOWEL DISEASE POPULATION: A DUTCH NATIONAL CROSS-SECTIONAL STUDY

R. Loveikyte^{1,2}, M. Boer¹, C.N. van der Meulen¹, R.W.F. ter Steege³, G. Tack⁴, J. Kuyvenhoven⁵, B. Jharap⁶, M.K. Vu⁷, L. Vogelaar⁸, R.L. West⁹, S. van der Marel¹⁰, T.E.H. Römkens¹¹, Z. Mujagic¹², F. Hoentjen^{13,14}, A.A. van Bodegraven¹⁵, F.D.M. van Schaik¹⁶, A.C. de Vries¹⁷, G. Dijkstra², A.E. Van Der Meulen - De Jong¹, on behalf of the Dutch Initiative on Crohn and Colitis (ICC)
¹Leiden University Medical Center, Department of Gastroenterology and Hepatology, Leiden, Netherlands, ²University Medical Center Groningen, Department of Gastroenterology and Hepatology, Groningen, Netherlands, ³Martini Hospital, Department of Gastroenterology and Hepatology, Groningen, Netherlands, ⁴Medical Center Leeuwarden, Department of Gastroenterology and Hepatology, Leeuwarden, Netherlands, ⁵Spaarnse Gasthuis Hospital, Haarlem, Haarlem, Netherlands, ⁶Meander Medical Center, Department of Gastroenterology and Hepatology, Amersfoort, Netherlands, ⁷Alrijne Hospital, Department of Gastroenterology and Hepatology, Leiderdorp, Netherlands, ⁸Diakonessenhuis Hospital, Department of Gastroenterology and Hepatology, Utrecht, Netherlands, ⁹Franciscus Gasthuis & Vlietland Hospital, Department of Gastroenterology and Hepatology, Rotterdam, Netherlands, ¹⁰Haaglanden Medical Center, Department of Gastroenterology and Hepatology, Den Haag, Netherlands, ¹¹Jeroen Bosch Hospital, Department of Gastroenterology and Hepatology, Den Bosch, Netherlands, ¹²Maastricht University Medical Center+, Department of Gastroenterology and Hepatology, Maastricht, Netherlands, ¹³University of Alberta, Division of Gastroenterology, Edmonton, Canada, ¹⁴Radboud University Medical Center, Department of Gastroenterology and Hepatology, Nijmegen, Netherlands, ¹⁵Zuyderland Medical Center, Department of Geriatrics, Internal- and Intensive Care Medicine (COMIK), Sittard-Geleen, Netherlands, ¹⁶University Medical Center Utrecht, Department of Gastroenterology and Hepatology, Utrecht, Netherlands, ¹⁷Erasmus University Medical Center, Department of Gastroenterology and Hepatology, Rotterdam, Netherlands

Contact E-Mail Address: r.loveikyte@lumc.nl

Introduction: Iron deficiency (ID) and anaemia in Inflammatory Bowel Disease (IBD) are associated with reduced quality of life, worse disease outcomes, and an increase in healthcare costs. In the European guidelines, anaemia is listed as one of the treatment goals, but data on the prevalence of anaemia and ID are inconsistent. Therefore, we evaluated the prevalence of ID, anaemia, and potential risk factors in a large Dutch outpatient population.

Aims & Methods: Between January and November 2021, consecutive adult outpatients with IBD, who did not have significant comorbidities associated with anaemia, were included in this study across 16 general, teaching, and academic hospitals within the Netherlands.

Besides demographic and clinical data, relevant biochemical parameters such as haemoglobin (Hb), Mean Corpuscular Volume (MCV), iron indices, and inflammatory markers (e.g., C-reactive protein (CRP) and faecal calprotectin (FCP)) were extracted from medical records. Active IBD was defined by either CRP >5 mg/L and/or FCP >150 mg/kg. ID was defined by ferritin <100 µg/L in case of biochemical inflammation and <30 µg/L in inactive IBD; if ferritin values were unavailable, transferrin saturation <20% was defined as ID despite biochemical inflammation.

The Dutch national reference range was used to define anaemia: Hb <7.5 mmol/L or <8.5 mmol/L for females and males, respectively. The data were analysed by stratifying patients into the Crohn's Disease (CD) and Ulcerative Colitis (UC) groups, with the latter also including patients with IBD-unclassified (IBDU).

Results: In total, 2197 patients (1271 CD, 849 UC, and 77 IBDU) were included in the study. Iron parameters were available in 59.3% of cases. The overall prevalence of anaemia, iron-deficiency anaemia (IDA), and ID was: 18.0%, 12.2%, and 43.4%, respectively. The prevalence of all three conditions did not differ between the CD and UC groups ($P > 0.05$ for all). Severe anaemia (Hb <6.2 mmol/L) was only observed in 28 patients. ID(A) was more frequently observed in biochemically active IBD compared with quiescent IBD (ID: 70.8% versus 23.9%; $P < 0.001$).

Female gender, younger age, low MCV, and an increase in biochemical inflammation were associated with ID in multivariable analysis: Log₂FCP [OR 1.39; 95% CI: 1.29–1.50; $P < 0.001$] and Log₂platelets [OR 1.85; 95% CI: 1.16–2.95; $P < 0.01$]. In multivariable analysis, low ferritin and MCV, inflammation, older age, and male gender were associated with a higher prevalence of anaemia; however, disease location or behaviour was not associated with the prevalence of anaemia or ID.

Conclusion: One in five outpatients with IBD suffers from anaemia that – despite infrequently measured iron parameters – is primarily caused by ID. Biochemical inflammation is the major risk factor associated with ID and anaemia prevalence regardless of IBD type or disease location.

High prevalence of ID and anaemia, even after the publication of the European treatment guidelines, suggests the need for screening and treatment optimisation.

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P0268

THE IMPACT OF SMOKING ON ULCERATIVE COLITIS AND INTERACTION WITH FAMILY HISTORY: A KOREAN POPULATION-BASED COHORT STUDY

H.S. Ahn¹, H.J. Kim¹

¹Korea University Medical College, Department of Preventive Medicine, Seoul, Korea (Republic of)

Contact E-Mail Address: iebm.ku@gmail.com

Introduction: The impact of smoking on ulcerative colitis (UC) among Asian populations is controversial. Although a few studies on gene-smoking interactions in IBD pathogenesis have been performed, they yielded inconsistent results, and the direction of interactions between current/former smoking and genetic factors are not well-studied.

Aims & Methods: Our aim was to evaluate the association between smoking and UC and assess interactions between smoking and family history in UC development. We used the National Health Insurance database to acquire information on all insured individuals and their dependents. A total of 5.5 million individuals were identified from 2002-2019 with information on familial relationships and smoking history. To examine the association between UC and current/former smoking, Cox proportional hazard regression was used and familial risk was estimated by comparing the incidence of individuals with and without a family history.

The amount of interaction and its statistical significance as a departure from additivity between family history and smoking were assessed using the relative excess risk due to interaction (RERI).

Results: Current smoking was associated with a decreased risk of disease (HR 0.53, 95% CI 0.49-0.56), while former smoking was associated with an increased risk (HR 1.62, 95% CI 1.53-1.71), compared to non-smokers. Through our family relationship analysis, we identified the familial group that consisted of 25,332 individuals with UC-affected FDR and 5,499,071 individuals with unaffected FDR, which made up the non-familial group. Among the familial group, 288 individuals developed UC, with the familial risk being 7.51 (95% CI 6.68-8.45). We observed an interaction between the familial risk of UC and both current and former smoking, but in opposing directions. The protective effect of current smoking was more pronounced among those with a family history, as their combined effect was lower than the sum of their individual risks (HR 4.37 vs 7.55), while the harmful effect of former smoking was more prominent among this group and their combined effect was higher than the sum of their individual effects (HR 10.20 vs 8.57), indicating statistically significant interactions (RERI current: -3.18 95% CI -4.89 - -1.47; former: 1.63 95% CI 1.00-4.25). Both effects were more pronounced in heavy smokers compared to moderate smokers, suggesting a dose-dependent relationship.

		No Smoking and No Family History	Smoking	Family History	Both Smoking and Family History	RERI (95% CI)
Current Smoking	Total	1.00	0.56	7.99	4.37	3.18 (4.89 - 1.47)
	Moderate	1.00	0.60	7.99	4.41	3.19 (5.07 - 1.31)
	Heavy	1.00	0.47	7.99	4.22	3.24 (5.58 - 0.90)
Former Smoking	Total	1.00	1.57	8.00	10.20	1.63 (1.00 - 4.25)
	Moderate	1.00	1.42	7.99	9.06	0.65 (2.30 - 3.60)
	Heavy	1.00	2.07	7.98	14.02	4.96 (0.10 - 10.02)

Table 1: Combined Effect of Family History and Smoking on the Risk of Ulcerative Colitis among First-Degree Relatives

Conclusion: Our nationwide population-based study found that current smoking was associated with a decreased risk, while former smoking increased the risk of developing UC, suggest that the effect of smoking on IBD does not differ between Asian and Western populations. An interac-

tion was observed between the family history of UC and smoking, in which the effect of current/former smoking were both more pronounced among those with a family history. Our results indicate the importance of familial factors and smoking in the etiology of UC and point towards a significant interaction.

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Disclosure: Nothing to disclose.

P0269

THE EFFECTS OF INFLAMMATORY BOWEL DISEASE ON CAREGIVERS: ABSENTEEISM AND JOB PRESENTEEISM. A SEGHP MULTICENTER STUDY (SPANISH SOCIETY OF PEDIATRIC GASTROENTEROLOGY, HEPATOLOGY AND NUTRITION)

M. Velasco Rodríguez-Belvis¹, L.M. Palomino Pérez¹, G. Pujol Muncunill², R. Martín Masot³, E. Medina Benítez⁴, M. Molina Arias⁵, A. Lozano Ruf⁶, I. Hidalgo Montes⁵, M. Herrador López³, J. Blasco Alonso³, J. Barrio⁶, M. Montraveta⁷, G. Botija Arcos⁸, Ó. Segarra Cantón⁹, I. Loverdos¹⁰, L. Peña Quintana¹¹, N. Ramos Rueda¹¹, A.E. Fernández Lorenzo¹², A. Moreno Álvarez¹², A.M. Castro Millán¹³, S. Fernández Cebrián¹⁴, E. Crehuá Gaudiza¹⁵, M.J. Balboa Vega¹⁶, A. Millán Jiménez¹⁷, R. García Romero¹⁸, I. Ros Arnal¹⁸, N. Ruiz Castellano¹⁹, M.L. Masiques Mas²⁰, R. Torres Peral²¹, C. Sánchez Sánchez²², F.J. Chicano Marín²³, A.M. Vegas Álvarez²⁴, C. Jovani Casano²⁵, M.d.l.M. Busto Cuiñas²⁶, S. Vicente Santamaría²⁷, E. La Orden Izquierdo²⁸, V.M. Navas López³, J. Martín de Carpi²

¹Hospital Infantil Universitario Niño Jesús, Madrid, Spain, ²Hospital Sant Joan de Déu, Barcelona, Spain, ³Hospital Regional Universitario de Málaga, Málaga, Spain, ⁴Hospital Doce de Octubre, Madrid, Spain, ⁵Hospital Universitario La Paz, Madrid, Spain, ⁶Hospital Universitario Fuenlabrada, Madrid, Spain, ⁷Hospital Germans Trias i Pujol, Barcelona, Spain, ⁸Hospital Universitario Fundación Alcorcón, Madrid, Spain, ⁹Hospital Vall d'Hebron, Barcelona, Spain, ¹⁰Hospital Parc Taulí, Sabadell, Spain, ¹¹Complejo Hospitalaria Universitario Insular Materno-Infantil, Las Palmas, Spain, ¹²Hospital Materno-Infantil Teresa Herrera de A Coruña, A Coruña, Spain, ¹³Hospital Universitario de Canarias, Santa Cruz de Tenerife, Spain, ¹⁴Complejo Hospitalario de Ourense, Ourense, Spain, ¹⁵Hospital Clínico Universitario de Valencia, Valencia, Spain, ¹⁶Hospital Universitario Virgen Macarena, Sevilla, Spain, ¹⁷Hospital Universitario de Valme, Sevilla, Spain, ¹⁸Hospital Infantil Miguel Servet Zaragoza, Zaragoza, Spain, ¹⁹Complejo Hospitalario de Navarra, Pamplona, Spain, ²⁰Hospital General de Granollers, Barcelona, Spain, ²¹Hospital clínico. Complejo Asistencial Universitario de Salamanca, Salamanca, Spain, ²²Hospital General Universitario Gregorio Marañón, Madrid, Spain, ²³Hospital Universitario Los Arcos del Mar Menor, Murcia, Spain, ²⁴Hospital Universitario Río Hortega, Valladolid, Spain, ²⁵Hospital General de Castellón, Castelló de la Plana, Spain, ²⁶Complejo Hospitalario de Pontevedra, Pontevedra, Spain, ²⁷Hospital Universitario Ramón y Cajal, Madrid, Spain, ²⁸Hospital Universitario Infanta Elena, Valdemoro, Madrid, Spain

Contact E-Mail Address: martavrb@gmail.com

Introduction: Pediatric inflammatory bowel disease (pIBD) impacts the physical, psychological, and socioeconomic functioning of patients and caregivers. However, work productivity and activity impairment are often poorly evaluated in this population.

Aims & Methods: The aim was to assess the effects on work productivity in caregivers of patients with pIBD.

We performed a multicenter, observational, cross-sectional and descriptive study from February 2021 to February 2022. The Work Productivity and Activity Impairment Questionnaires for Crohn's disease and Ulcerative Colitis (WPAI-CD-Caregiver and WPAI-UC-Caregiver), with 6 items each, were translated and adapted for the Spanish population and subsequently completed by the participants.

These questionnaires explore 4 aspects: absenteeism (failure to attend work by an employee who was thought to attend, excluding vacation periods, strikes and sick leave), presenteeism (understood as a phenomenon

that revolves around the worker's anxiety about losing their job and is influenced by a high level of stress that forces the individual to report to work when they are not able to do so), loss of productivity labor and impairment of daily activity due to pIBD. Demographic and clinical data and results of the questionnaires were collected using the REDCap® platform and analyzed with SPSS®.

Results: A total of 207 patients from 28 hospitals were included, 117 were male (56.5%), 138 with Crohn's disease, 65 with ulcerative colitis and 4 with IBD unclassified. The mean age at the time of completing the questionnaire was 14.2±2.4 years and the time of evolution of the disease was 2.4 years (IQR 1.2-4.9). Amongst the 207 patients, 115 (55.5%) were in remission (PUCAI < 10 or WPCDAI < 12.5).

Data from 310 parents (186 mothers and 124 fathers) were obtained. Up to 75.8% of the fathers and 67.2% of the mothers had a remunerated job at the time of completing the questionnaire. 62.8% of parents experienced absenteeism from work in the previous week with a median of 12.7% of lost hours (IQR 5-10); 69.1% recognized deterioration or impairment of productivity during the working day, with a decrease in productivity that week of 40% (IQR 20-60%).

The percentage of affectation/global deterioration of the working life of the parent secondary to the illness of the child was 38% (IQR 20-67). The deterioration of the parent's ability to carry out daily tasks was 54.3%.

Conclusion: pIBD negatively impacts the work and daily sphere of their parents. Having 50% more forms from mothers may be related to the fact that they are the main caregivers of the patients.

However, the employment rate of our sample corresponds to that of the population aged 20-64 published by the INE (The Spanish National Statistics Institute).

Disclosure: Nothing to disclose.

P0270

EXPOSURE TO SYSTEMIC ANTIBIOTICS INCREASES THE RISK OF INFLAMMATORY BOWEL DISEASE IN A DOSE-DEPENDENT MANNER: A POPULATION-BASED CASE-CONTROL STUDY IN KOREA

S.J. Oh¹, C.K. Lee¹, H.J. Kim¹

¹Kyung Hee University College of Medicine, Center for Crohn's and Colitis, Department of Gastroenterology, Seoul, Korea (Republic of)

Contact E-Mail Address: linus204@naver.com

Introduction: Environmental factors that alter the gut microbiome are thought to be involved in the epidemiological evolution of inflammatory bowel disease (IBD) globally. This study aimed to assess whether the increased use of antibiotics was associated with the development of IBD in Korea where the incidence and prevalence of IBD has been rapidly increasing in recent years.

Aims & Methods: A population-based case-control study was conducted using the National Health Insurance Service database from 2004 to 2018. Each case diagnosed with IBD was matched to five controls based on age, sex, and residence. Conditional logistic regression was used to estimate associations between antibiotic exposure and subsequent development of IBD. Systemic (oral, intravenous or intramuscular) antibiotic exposure 2-5 years prior to diagnosis was stratified by frequency and duration of prescription, and the class of antibiotic. We also separately analyzed the risk of childhood-onset (age <16) IBD according to antibiotic exposure in the first year of life.

Results: We identified 68,633 cases of IBD (ulcerative colitis [UC], 52,756; Crohn's disease [CD], 7,898) and 343,165 controls. Ever use of antibiotics was significantly associated with an increased risk of IBD (adjusted odds ratio [AOR], 1.35; 95% CI, 1.30-1.40). The risk of IBD and its subtypes increased with the cumulative frequency and duration of antibiotics.

Among the classes of antibiotics, metronidazole, and sulfonamides were associated with a higher risk, and metronidazole particularly increased the risk of CD by more than twice (OR, 2.37; 95% CI, 2.18–2.59). Antibiotic exposure in the first year of life was significantly associated with an increased risk of childhood-onset IBD (OR, 1.50; 95% CI, 1.24–1.81).

Any antibiotic use	Case	Control	Crude OR	Adjusted OR
IBD				
Never	7,900	47,921	ref	ref
Ever	60,733	295,244	1.25 (1.22 - 1.28)	1.35 (1.30 - 1.40)
UC				
Never	6,038	37,597	ref	ref
Ever	46,718	226,183	1.29 (1.25 - 1.32)	1.35 (1.29 - 1.40)
CD				
Never	1,777	9,905	ref	ref
Ever	13,426	66,110	1.32 (1.20 - 1.45)	1.41 (1.28 - 1.55)

Table.

Conclusion: Exposure to systemic antibiotics significantly increases the future development of IBD in a dose-dependent manner, suggesting that the perturbation of gut microbiome by antibiotics use may be one of several key environmental factors to influence development of IBD in newly industrialized countries.

Disclosure: This work was supported by the Big Data Research Group of the Korean Society of Gastroenterology and data analysis was supported by Data Science Team, Hanmi Pharm. Co., Ltd.

P0271

MORTALITY IN ELDERLY-ONSET INFLAMMATORY BOWEL DISEASES – A POPULATION-BASED STUDY FROM THE EPIDEMIOLOGICAL DATABASE OF THE ISRAELI IBD RESEARCH NUCLEUS (EPI-IIRN)

D. Ben Hur^{1,2}, G. Issaschar³, R. Moshe³, R. Lujan⁴, Z. Haklai⁵, Y. Loewenberg Weisband⁶, R. Kariv^{7,8}, N. Ledderman⁹, E. Matz¹⁰, I. Dotan¹¹, D. Turner⁴, G.D. Pinto³, M. Waterman^{1,12}
¹Rambam Health Care Campus, Department of Gastroenterology, Haifa, Israel, ²Rambam Health Care Campus, Department of Internal Medicine H, Haifa, Israel, ³Azrieli College of Engineering, Department of Industrial Engineering and Management, Jerusalem, Israel, ⁴Shaare Zedek Medical Center, The Hebrew University of Jerusalem, The Juliet Keidan Institute of Pediatric Gastroenterology and Nutrition, Jerusalem, Israel, ⁵Ministry of Health, Jerusalem, Israel, ⁶Clalit Research Institute, Innovation Division, Clalit Health Services, Tel Aviv, Israel, ⁷Maccabi Health Services, Tel Aviv, Israel, ⁸The Sackler Faculty of Medicine, Tel Aviv University, Tel Aviv, Israel, ⁹Meuhedet Health Services, Tel Aviv, Israel, ¹⁰Leumit Health Services, Tel Aviv, Israel, ¹¹Rabin Medical Center, Division of Gastroenterology, Petah Tikva, Israel, ¹²B. Rappaport Faculty of Medicine, The Technion - Israel Institute of Technology, Haifa, Israel

Contact E-Mail Address: d_ben-hur@rambam.health.gov.il

Introduction: Data on mortality in patients with elderly-onset inflammatory bowel disease (IBD) is conflicting. Our objective is to explore the overall mortality rates and causes in patients with elderly-onset IBD compared to elderly non-IBD patients.

Aims & Methods: As part of the validated epidemiological cohort of the Israeli IBD Research Nucleus (epi-IIRN), we included all elderly-onset IBD

patients (age at diagnosis>65 years) from the four Israeli health funds diagnosed from 1.1.2005 until 30.06.2020, covering 98% of the population. Each IBD case was matched to 3 non-IBD individuals by year of birth, sex, geographic district, and health fund. Time to mortality was compared using the Kaplan-Meier survival analysis, stratified by IBD subtype and sex. Cox proportional hazards models were sought to explore mortality risk adjusted by comorbidities (ischemic heart disease, heart failure, chronic obstructive pulmonary disease, cumulative number of other chronic diseases) as possible confounders. Main causes of death as reported to the Israeli Mortality Register were compared using the chi-square test.

Results: A total of 2,162 elderly-onset IBD patients were identified (46% males; median (IQR) age at inclusion 71 [68, 76]) and compared to 6,486 matched non-IBD controls. During median (IQR) follow up of 74 (40, 118) months, 632 of patients with IBD (29.2%, mortality rates 292.32/1000 PY, 95% CI 273.53-311.85/1000 PY) and 1,889 of controls (29.1%, mortality rate 291.24/1000 PY, 95% CI=280.31-302.42/1000 PY) died.

Time to mortality was similar in IBD and controls (p=0.79) as well as in IBD subgroups (CD (p=0.62) and UC (p=0.45)). Survival analysis remained similar when stratified by sex (females (p=0.96) and males (p=0.64)). Using the co-morbidity adjusted Cox model, the overall hazard of mortality (HR) was 1.07 (95% CI=0.98-1.17) for all IBD (HR=1.13 (95% CI=0.98-1.3) for CD and HR=1.03 (95% CI=0.91-1.15) for UC). No significant differences in the proportions of the different causes of death were observed (table).

	Elderly onset IBD n=2162	Matched non-IBD controls n=6486	P value
Malignancy	139 (6.4%)	390 (6%)	0.52
Heart disease	84 (3.9%)	274 (4.2%)	0.53
Septicemia	30 (1.4%)	80 (1.2%)	0.66
Cerebrovascular disease	23 (1.1%)	91 (1.4%)	0.28
Diabetes mellitus	19 (0.9%)	80 (1.2%)	0.22
Nephritis and nephrosis/nephrotic syndrome	14 (0.6%)	51 (0.8%)	0.62
Pneumonia and influenza	10 (0.5%)	50 (0.8%)	0.18
Dementia (non-Alzheimer)	11 (0.5%)	49 (0.8%)	0.3

Table. Most frequent defined causes of death among elderly-onset IBD patients and matched non-IBD controls.

Conclusion: Elderly-onset IBD was not associated with increased mortality risk compared with matched non-IBD elderly individuals. Causes of death were similar to individuals without IBD, with malignancy and heart diseases as the leading causes.

Disclosure: Nothing to disclose.

P0272

FACTORS ASSOCIATED WITH TREATMENT PERSISTENCE OF ANTI-TNF AGENTS AS FIRST LINE BIOLOGIC TREATMENT IN GREEK PATIENTS WITH INFLAMMATORY BOWEL DISEASES

E. Orfanoudaki¹, E. Theodoraki¹, K. Foteinogiannopoulou¹, I. Drygiannakis¹, G. Chlorakis¹, M. Tsafaridou¹, I. Koutroubakis¹
¹University Hospital of Heraklion, Medical School, University of Crete, Gastroenterology, Heraklion, Greece

Contact E-Mail Address: elina_or@yahoo.gr

Introduction: A remarkable proportion of inflammatory bowel disease (IBD) patients on long term anti-TNF therapy eventually discontinue their treatment due to either loss of response or adverse events.

Aims & Methods: We aimed to record the treatment persistence of anti-TNF agents as first line biologic therapy in IBD patients and possible factors associated with it. Consecutive IBD patients with no prior exposure to biologics who were initiated with either infliximab (IFX), adalimumab (ADA) or golimumab (GOL) between 2002-2022 having at least 36 months of follow up were studied retrospectively.

Demographic and clinical patient characteristics were recorded based on an updated prospective, longitudinal IBD registry. Treatment persistence was assessed using Kaplan Meier analysis for a 36month period and Mann Whitney test was used to identify predictors of drug persistence.

Results: Out of 268 naïve IBD patients commenced on anti-TNF during the study period, 220 who met the inclusion criteria were included [Males 126 (57%), median age (IQR) 47(35.5-58) years, Crohn's disease (CD) 158 (72%), median time of follow up after anti-TNF initiation (IQR) 51 (20-89) months, under IFX 130 (59%), under ADA 74 (34%), under GOL 16 (7%), concomitant immunomodulators 106 (48%)].

Thirty six months after anti-TNF treatment initiation, the persistence rates for IFX, ADA, GOL were 67%, 66% and 38% respectively. Concomitant immunomodulator use significantly prolonged drug survival (58 vs 46 months; p=0.045), as well as treatment intensification (66 vs 43 months; p=0.0002) and IFX use vs ADA (58 vs 45 months; p=0.034). No other factors including gender, disease type, BMI, disease duration at anti-TNF initiation were found to be associated with anti-TNF persistence.

Conclusion: Longer drug survival was observed for IFX and ADA (67% and 66%) compared with GOL (38%). Concomitant immunomodulator use, treatment intensification and IFX use play an important role in treatment persistence.

Disclosure: No conflicts of interest.

P0273

EPIDEMIOLOGY AND CHANGES IN PHARMACOLOGIC TREATMENT OF PEDIATRIC INFLAMMATORY BOWEL DISEASE OVER 10 YEARS IN CATALONIA

I. Loverdos¹, E. Vela², E. Brunet³, J. Martín de Carpi⁴, D. García Tirado¹, X. Calvet Calvo³

¹Parc Taulí Hospital Universitari. Institut d'Investigació i Innovació Parc Taulí (I3PT). Universitat Autònoma de Barcelona, Pediatric Gastroenterology, Sabadell, Spain, ²Unitat d'Informació i Coneixement, Servei Català de la Salut, Generalitat de Catalunya, Barcelona, Spain, ³Parc Taulí Hospital Universitari. Institut d'Investigació i Innovació Parc Taulí (I3PT). Universitat Autònoma de Barcelona, Digestive Diseases, Sabadell, Spain, ⁴Department of Pediatric Gastroenterology, Hepatology and Nutrition, Hospital Sant Joan de Déu, Barcelona, Spain

Contact E-Mail Address: ines.loverdos@gmail.com

Introduction: There is no data on the epidemiology of pediatric inflammatory bowel disease (PIBD) in Catalonia neither on the trends of pharmacologic treatment over time. The present study aims to evaluate the incidence, prevalence, associated morbidity and pharmacological treatment of PIBD between 2011-2020 in Catalonia.

Aims & Methods: Population-based retrospective cohort study. Children with diagnosis of PIBD (less than 18 years old) included in the Catalan Health Surveillance System database were identified using the ICD-9-CM and ICD-10-CM codes. Data on prevalence, incidence, associated morbidity and pharmacological treatment were extracted from the same database and analyzed for the study period.

Results: The pediatric population during the study period ranged from 1,369,079 in 2011 to 1,408,685 in 2020. The prevalence of PIBD rose from 27 per 100,000 inhabitants (aged <18 years old) in 2011 to 66.2 in 2020 but seems to plateau over the last 2 years of the study period. This trend was observed for ulcerative colitis (UC) (11.1 to 28.1 per 100,000 inhabitants) and Crohn's disease (CD) (15.9 to 38 per 100,000 inhabitants).

The incidence of PIBD was steadily increasing during the study period, especially for CD, and ranged from 6.8 per 100,000 inhabitants in 2011 (93 cases: 50 CD and 43 UC) to a maximum of 13.8 per 100,000 inhabitants in 2018 (193 cases: 114 CD and 79 UC). In 2019-2020 the incident cases decreased for CD and UC.

	2011	2012	2013	2014	2015	2016	2017	2018	2019	2020
IBD cases	371	426	514	593	653	696	780	882	933	932
CD prevalent cases	218	254	323	348	377	402	456	513	546	536
UC prevalent cases	153	172	191	245	276	294	324	369	387	396
IBD incident cases	93	103	151	144	146	135	171	193	155	122
CD incident cases	50	71	99	68	87	77	101	114	91	65
UC incident cases	43	32	52	76	59	58	70	79	64	57
Pediatric Population	1.369.079	1.385.127	1.389.929	1.389.796	1.390.956	1.393.928	1.399.850	1.402.825	1.404.978	1.408.685

Table.

The rate of IBD related hospital admissions decreased over the study period from 244.3 per 1,000 people/year in 2011 to 112.8 per 1,000 (despite of this trend there was a peak of admissions of 257.9 per 1,100 in 2016); while the number of outpatient clinic visits increased over the study period, from 1825 visits in 2011 to 4901 in 2020.

The percentage of patients with UC treated with systemic steroids decreased from 39.9% in 2011 to 17.9% in 2020 while the use of immunosuppressant treatment remained stable (38.6 to 30.1%). The use of biological treatment rose every year from 9.2% in 2011 to 19.9 % in 2020.

Regarding CD patients, the percentage of patients treated with systemic steroids and immune modulators decreased from 34.9% and 53% in 2011 to 12.7% and 30.2% respectively in 2020. The use of biological treatment remained stable over the study period (around 30-35%).

Conclusion: The prevalence of PIBD increased over the study period but seems to remain stable over the last 2 years, as the incident cases decreased in 2019-2020. It's important to elucidate if these change of trends in PIBD has been influenced by the SARSCOV2 pandemic or reflects a stabilization of PIBD as described in other countries. The admission rates of PIDB patients, use of systemic steroids and immunosuppressant treatment decreased (specially in UC), while the use of biologics rose.

Disclosure: Nothing to disclose.

P0274

POOR SLEEP IN IBD IS ASSOCIATED WITH ACTIVE DISEASE, ANXIETY AND DEPRESSION, AND OUTCOMES SUCH AS INCREASED FATIGUE, INCREASED DISABILITY, AND POOR QUALITY OF LIFE

A. Barnes¹, S. Madigan¹, P. Spizzo¹, R. Mountfield¹

¹Flinders Medical Centre, Gastroenterology, Bedford Park, Australia

Contact E-Mail Address: shaunamadigan@gmail.com

Introduction: Sleep has become of increasing interest in inflammatory bowel disease (IBD) as a patient reported outcome, and as a possible exacerbating factor or extra-intestinal manifestation.

Aims & Methods: This study aimed to document the associations with poor sleep in IBD, and its relationship with other important patient report outcomes such as Disability and Quality of Life. As part of the IBD-SLEEP study a questionnaire was distributed to tertiary hospital IBD mailing lists and advertised through social media and Crohn's Colitis Australia.

The questionnaire included validated instruments assessing IBD activity (HBI and SCCAI), sleep quality (Pittsburgh Sleep Quality Index (PSQI)), physical activity (international physical activity questionnaire), depression (PHQ9), anxiety (GAD7), fatigue (FACIT-F), disability (IBD-DI reduced form), and quality of life (EQ-5D-5L). Disease and treatment characteristics were also sought including medications, complications, and other comorbidities.

Results: There was 544 participants who completed the entire questionnaire. Mean age was 42 years (SD 13), 61% had Crohn's disease, and median disease duration was 10 years (IQR 3-17). Poor sleep quality as assessed by PSQI > 5 was associated with (odds ratio (OR), 95% CI, p value) patient reported active IBD (HBI > 5, SCCAI > 5, OR 3.26 (2.06-5.14) p<0.001), clinically significant depression (PHQ9 > 15, OR 4.28 (2.22-8.24) p < 0.0001), and clinically significant anxiety (GAD7 > 10, OR 4.44 (2.52-7.81) p < 0.001), but not physical activity in the form of total sitting time, vigorous activity, and total activity (METs). People with IBD who had poor sleep quality were more disabled (IBD-DI reduced form, p < 0.0001), had worse quality of life (EQVAS, p < 0.0001), and reported higher levels of fatigue (FACIT-F, p < 0.0001).

Conclusion: IBD patient reported sleep quality was associated with patient reported active disease as well as Anxiety and Depression. Poor sleep quality was associated with worse patient reported outcomes such as fatigue, disability, and quality of life. Consideration should be given in IBD clinic to assessing and addressing sleep quality.

Disclosure: Nothing to disclose.

P0275

NEW-ONSET INFLAMMATORY BOWEL DISEASE DURING TREATMENT WITH THE ANTI-INTERLEUKIN-17A MONOCLONAL ANTIBODY SECUKINUMAB. A CASE SERIES PRESENTATION

G. Gerasimatos¹, M.-T. Koutroumpi¹, G. Andrianakou¹, E. Karamintziou¹, E. Ionas¹, E. Strathgagos¹, G. Michalopoulos¹, A. Braimakis¹, E. Kotzagiannidou¹, L. Theodoropoulos¹, I. Karoumpalis¹, A. Konstantinidis¹, V. Ntelis¹

¹GHA G. Gennimatas, Department of Gastroenterology, Athens, Greece

Contact E-Mail Address: gerasimatos.ger@gmail.com

Introduction: IL-17 is a cytokine with strong proinflammatory action. Research studies has revealed high expression of IL-17 in the inflamed mucosa of patients with active Crohn disease(CD) or Ulcerative colitis(UC) in contrast with people with normal mucosa. In particular, patients with active CD have higher levels of IL-17 than those with UC. Anti-interleukin-17a monoclonal antibody is currently used against psoriasis, psoriatis arthritis and ankylosing spondylitis. Anti-IL-17a monoclonal antibody's role in IBD is still unclear although new findings suggest new-onset or flare of bowel disease. The aim of this study is to present 4 cases of new-onset patients treated in our hospital.

Aims & Methods: A retrospective study was performed by evaluation of 4 patients' clinical history under secukinumab for rheumatologic disease who developed IBD.

Results: Characteristics of patients and their IBD are summarized in Table 1.

Basal characteristics of patients and their IBD	Patient 1	Patient 2	Patient 3	Patient 4
Age(years)	42	30	51	41
Smoking history	Yes	Yes	Yes	Yes
Familiarity of IBD	No	No	No	No
Time of secukinumab treatment(months)	14	1	2	7
Indication of treatment	AS	AS	AS	AS
Location of IBD	B1,L3	B1p,L3,4	B1p,L3	B1,L3
Severity of IBD	Severe	Severe	Moderate	Moderate
IBD therapy	Adalimumab	Adalimumab	Infliximab	Corticosteroids/ASA
Response to treatment(RMN)	Yes	Yes	Yes	Yes

Table 1.

Conclusion: All patients were men with new-onset CD without family history of IBD. Three of them had smoking history and presented with IBD symptoms after one to 14 months under treatment with secukinumab. The 4th patient presented with symptoms of IBD after 14 months but he was under combination treatment with methotrexate for the first 11 months of secukinumab treatment and developed IBD 2 months after stopping methotrexate. The severity of IBD was moderate to severe with total (100%) response to treatment.

Despite the low incidence of IBD in patients treated with secukinumab, it seems that deteriorates their quality of life. According to our findings, an exhaustive search for patients with subclinical bowel disease is suggested. Patients who appear with GI symptoms after treatment with secukinumab should be referred for gastroenterological evaluation.

Disclosure: Nothing to disclose.

P0276

IMPACT OF INFLAMMATORY BOWEL DISEASE ON THE QUALITY OF LIFE OF PATIENT'S HOUSEHOLD MEMBERS

M. López-Vico¹, A.D. Sánchez-Capilla¹, E. Redondo-Cerezo¹
¹"Virgen de las Nieves" University Hospital, Gastroenterology, Granada, Spain

Contact E-Mail Address: leunamlv@gmail.com

Introduction: Inflammatory bowel disease is a chronic disease of unknown etiology characterized mainly by digestive symptoms with an increasing incidence and prevalence and with a rise in the direct and indirect costs. It is well established its impact on the quality of life of patients and their main caregivers.

Nonetheless, no study has yet considered the consequences of IBD on cohabitants with no direct involvement in patient's care. Due to the chronic and relapsing nature of IBD, our aims were to analyze quality of life in cohabitants of people with IBD and identify potential related factors.

Aims & Methods: We conducted a cross-sectional study that included patients with IBD and their house-hold members. Participants were recruited from a period of two months from patients attending the IBD unit of our hospital. Inclusion criteria were a definite diagnosis of IBD at any stage and household members living in the same house for a period of 1 year or more. Exclusion criteria were an age <18, refusal to participate or subjects unable to fulfill the questionnaires. Patients and household members that met all the inclusion criteria and none of the exclusion criteria and agreed to participate were included in the study.

Demographic data was obtained for patients and household members, including age, sex occupation, educational level, marital status, and the relationship with the patient in the case of household members.

IBD activity was assessed by using the Partial Mayo Score and the Harvey-Bradshaw score. Information was collected about prior surgeries, extraintestinal manifestations, past and current treatments, number of hospitalizations, number of relapses, and laboratory data such as CRP and calprotectin and others.

Quality of life was assessed in the case of the patients with the Inflammatory Bowel Disease Questionnaire (IBDQ-32) and for the household members we used the Household Members Quality of Life-Inflammatory Bowel Disease (HHMQoL-IBD) questionnaire.

Results: Fifty-six patients and 82 household members were included. Both groups had similar sociodemographic characteristics. We included 22 patients with UC, 32 patients with CD and 2 patients with indeterminate colitis.

The univariate analysis of the quality of life of cohabitants showed a significant association of HHMQoL-IBD and IBDQ-32 score in their relatives ($p<0.0001$), last CRP ($p=0.043$), number of disease flares in the last year ($p=0.04$), extraintestinal diseases ($p=0.01$) and particularly articular disease ($p=0.04$).

Cohabitants of patients with CD had significantly lower HHMQoL-IBD than UC ones (53 ± 18 vs. 62 ± 23 ; $p=0.049$).

Among cohabitants of patients with UC, patient's CRP in the last control was related to HHMQoL-IBD score ($p=0.043$) and the cohabitants's score was related with IBDQ-32 in patients ($p=0.019$). Among cohabitants of patients with CD, patient's CRP in the last control was related to HHMQoL-IBD score ($p=0.04$).

In a linear multiple regression analysis, IBDQ-32 score ($p<0.0001$) in patients and the presence of extraintestinal disease ($p=0.048$) were independent predictors of cohabitant's quality of life, and particularly articular disease.

Conclusion: Quality of life in household members of patients with IBD is related to patient's quality of life and extraintestinal conditions related to the disease.

Our study shows how important is to analyze and act in the patient's whole environment, taking into consideration not only clinical variables, which are the main ones, but also the relational conditions and impact of the disease.

Disclosure: Nothing to disclose.

P0277

EFFECTIVENESS OF SARS-COV2 BOOSTER VACCINATION IN PATIENTS WITH INFLAMMATORY BOWEL DISEASE (IBD): PRELIMINARY REPORT FROM A SINGLE REFERRAL CENTER IN SOUTHERN ITALY

D. Brinch^{1,2}, S. Muscarella¹, C. Cunsolo¹, M. Saladino¹, L.M. Amato¹, P. Melatti¹, L. Carrozza¹, F.M. Di Giorgio¹, P.L. Almasio³, M. Cappello¹

¹University of Palermo, PROMISE, Gastroenterology and Hepatology Section, Palermo, Italy, ²University of Palermo, Palermo, Italy, ³University of Palermo, PROMISE, Palermo, Italy

Contact E-Mail Address: danielebrinch@gmail.com

Introduction: Observational studies and metanalyses have reported comparable risk to contract the SARS-CoV-2 infection between the general population and patients with IBD. However, a matter of concern remains the effectiveness of Sars-Cov2 vaccine in patients with immune mediated disease and concomitant biological and/or immunosuppressive treatments.

Aims & Methods: Our aim was to evaluate the rate of new infections, symptomatic or asymptomatic, after full mRNA SARS-CoV2 vaccination, including a third dose, in a homogeneous cohort of patients with IBD followed up in a tertiary referral center from southern Italy. The relationships with disease characteristics and concomitant therapies were also assessed. Data were collected between 03/2021 and 03/2022.

Most patients received the third dose of SARS-CoV2 vaccine between 11/2021 and 01/2022. IBD type, disease features (location, behaviour, extra intestinal manifestations), biologic therapy, immunosuppressive treatment, previous surgery, smoking habit, comorbidities and vaccination protocol were analysed.

Results: Our cohort is composed of 108 patients with IBD, 52 CD and 56 UC, mean age 53,67 years, 58 pts were on biological therapy. 25/108 patients developed COVID-19 infection (23 %), 7/25 patients (28%) didn't receive the third dose because contracted the infection before the booster dose. There was a significant difference in the rate of infection between those who received the third dose and those who did not ($p<0,001$).

The COVID-19 population was younger ($48,6 \pm 16,5$) than the non COVID-19 population ($55,2 \pm 15,9$, $p=0,07$) and female sex was more frequent (56% vs 36%, $p=0,1$). 19/25 (76 %) had symptomatic infection (flu-like symptoms) but none of them experienced pneumonia or severe disease.

Symptomatic infection was more frequent in patients who didn't complete the vaccination protocol (68,42% VS 83,33%), though the difference was not significant. Biological therapy was not associated with the development of infection either symptomatic or asymptomatic. Smoking habit, comorbidity, type of IBD, were not significantly related to COVID-19.

Conclusion: Our results confirm the effectiveness of mRNA SARS-CoV2 vaccination in patients with IBD independently from concomitant immunosuppressive therapy since only 23% of them developed the infection, most with mild symptoms. The protective effect was statistically significant in those who received the booster dose. The need of additional doses in IBD patients on biologics will be a matter of debate.

Disclosure: Nothing to disclose.

P0278

NAFLD AND LIVER FIBROSIS IN PATIENTS WITH INFLAMMATORY BOWEL DISEASE: A CASE-CONTROL STUDY

S.J. Martínez-Domínguez^{1,2,3}, S. García Mateo^{1,2,3}, B. Gallego Llera², C.J. Gargallo-Puyuelo^{1,2,3}, P. Callau⁴, C. Mendi⁵, M.T. Arroyo Villarino^{1,2,3}, V. Laredo De La Torre^{2,3,1}, E. Alfambra Cabrejas², F. Gomollon^{1,2,3,6}
¹Hospital Clínico Universitario Lozano Blesa, Zaragoza, Spain, ²Aragón Health Research Institute (IIS Aragón), Zaragoza, Spain, ³University of Zaragoza, Zaragoza, Spain, ⁴Centro de Atención Primaria "Delicias Sur", Zaragoza, Spain, ⁵Centro de Atención Primaria "Universitas", Zaragoza, Spain, ⁶CIBER ehd, Madrid, Spain

Contact E-Mail Address: samuelmartinez94@hotmail.com

Introduction: The prevalence of Non-Alcoholic Fatty Liver Disease (NAFLD) is increasing rapidly around the world, becoming one of the main comorbidities in patients with Inflammatory Bowel Disease (IBD).

Aims & Methods: Consecutive outpatients ≥ 18 years with IBD were recruited in a reference center and patients ≥ 18 years without IBD were recruited in 2 Primary Care centers from the same health area. The presence of NAFLD and liver fibrosis was assessed by ultrasound and Transient Elastography (TE) considering NAFLD in case of ultrasound steatosis and/or CAP > 245 dB/m and risk of advanced liver fibrosis if TE was ≥ 8 kPa. Patients with risky alcohol consumption or chronic liver disease were excluded. A comparative analysis of cases and controls (univariate and multivariate) and risk factors associated with NAFLD and liver fibrosis was performed. A p value < 0.05 was considered statistically significant. The study was approved by local ethic committee.

Results: 702 patients with IBD and 189 controls without IBD were included (sample characteristics in Table 1).

Characteristics	CONTROLS n= 189	CASES n= 702	p value	OR (95% CI) Multivariate	p value Multivariate
Sex					
Female	92 (48.7)	349 (49.7)	0.800		
Male	97 (51.3)	353 (50.3)			
Age*	50 (40.6-61)	49 (39-59)	0.371		
CKD					
No	149 (78.8)	623 (90.4)	<0.001	2.484 (1.507-4.098)	<0.001
Si	40 (21.2)	66 (9.6)			
Diabetes/ prediabetes					
No	100 (52.9)	453 (64.5)	0.003	1.758 (1.151-2.685)	0.009
Si	89 (47.1)	249 (35.5)			
Cardiovascular disease					
No	188 (99.5)	675 (96.2)	0.017	0.153 (0.020-1.195)	0.073
Si	1 (0.5)	27 (3.8)			
BMI*	26.6 (23.3-29.8)	25.2 (22.6-28)	0.006	0.953 (0.870-1.044)	0.304
Waist-hip ratio					
Normal	101 (53.4)	347 (49.6)	0.345		
High	88 (46.6)	353 (50.4)			
Active lifestyle					
Si	78 (41.3)	188 (26.8)	<0.001	0.608 (0.392-0.943)	0.026
No	111 (58.7)	513 (73.2)			
IBD type					
EC	-	46.1%			
CU		53.9%			

BMI: Body Mass Index, CD: Crohn's Disease, CKD: Chronic Kidney Disease, IBD: Inflammatory Bowel Disease, UC: Ulcerative Colitis. N (%). * Median and interquartile range

Table 1. Characteristics of the sample

No statistically significant differences were found between the prevalence of NAFLD or liver fibrosis in cases and controls (44.2% vs 44.9%, $p=0.856$; 9.1% vs 2.7%, $p=0.061$, respectively).

In the multivariate analysis in patients with IBD, NAFLD was significantly associated with older age (OR (95% CI) 1.04 (1.02-1.06), $p < 0.001$), overweight/obesity (OR (95% CI) 0.26 (0.17-0.39), $p < 0.001$), increased waist-hip ratio (OR (CI 95%) 0.32 (0.21-0.48), $p < 0.001$) and absence of active lifestyle (OR (CI 95%) 2.41 (1.44-4.05, $p < 0.001$) whereas liver fibrosis was associated with hypertension (OR (CI 95%) 0.07 (0.10-0.45), $p = 0.006$). No association was found between NAFLD and/or liver fibrosis and type of IBD, location, extension, pattern or treatment of the disease.

Conclusion: NAFLD is highly prevalent both in the general population and in patients with IBD, and in both cases it is associated with the same risk factors.

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P0279

EFFECTIVENESS OF SMOKING CESSATION INTERVENTIONS IN PATIENTS WITH CROHN'S DISEASE: A SYSTEMATIC REVIEW

S. Nasr¹, I. Nsiri², F. Nabl²

¹Faculté de Médecine de Tunis and Mohamed Taher Maamouri Hospital, Gastroenterology Department, Nabeul, Tunisia, ²Monastir University, Monastir, Tunisia

Contact E-Mail Address: sahar.nasr2508@gmail.com

Introduction: Smoking cessation (SC) in Crohn's disease (CD) is extensively studied and widely accepted to be the most important modifiable factor to improve outcomes in these patients CD (14). Several studies have shown that SC can reverse the negative disease course with quitters having comparable outcomes and prognosis to non-smokers.

In spite of these findings, the percentage of smokers among patients with CD remains high. These observations highlight the critical need for effective and appropriate SC interventions in patients with Crohn's disease.

Aims & Methods: Therefore, we aimed in this review to provide a summary of the evidence base regarding the effectiveness of smoking cessation interventions in patients with Crohn's disease. This systematic review was designed and conducted in accordance with PRISMA guidelines.

The following databases were systematically searched from inception to February 2022 for relevant articles published either in English or French: PubMed, Embase, Google Scholar and Cochrane Library. Eligible studies were randomized control trials, non-randomized controlled trials, quasi-experimental studies, and cohort studies. We included interventions that primarily aimed to help Crohn disease patients, who are actively smoking or who present smoking relapses, to quit. All studies included were systematically reviewed by two different authors.

Results: Overall, five articles met the research criteria and were included. The designs of the interventions were highly heterogeneous. Studies sample size ranged from 17 to 474 patients. Nicotine dependence was assessed in two studies with The Heaviness Smoking Index and the Fagerström Test. The motivation to quit was assessed with the Richmond test or the motivation to quit score. Motivational interviewing and behavioral counseling were used in four studies. At the outcome level, The SC rates ranged from 14.8% to 42% and was $\leq 25\%$ in four studies.

Surprisingly, the highest rate was observed in a study where all patients included initially refused referral to a SC unit and where the intervention was limited to motivational interviewing. The three studies with control groups did not report statistically higher SC rates in the intervention groups. No predictors of success of SC interventions were identified in this review.

Conclusion: The findings of this review suggest that additional efforts are needed to design smoking cessation interventions in patients with CD.

Disclosure: Nothing to disclose.

P0280

EVALUATION OF STRESS, ANXIETY, DEPRESSION LEVELS AND INTESTINAL GENE EXPRESSION IN NEWLY DIAGNOSED IBD PATIENTS

S. Dragasevic¹, B. Stankovic², S. Djuranovic¹, A. Sokic Milutinovic¹, T. Milovanovic¹, N. Kotur², S. Lukic¹, S. Rajic³, M. Stulic¹, M. Stojkovic Lalosevic¹, S. Pavlovic², D. Popovic¹

¹University Clinical Center Serbia, School of Medicine, University of Belgrade, Clinic for Gastroenterology and Hepatology, Belgrade, Serbia, ²Institute of Molecular Genetics and Genetic Engineering, University of Belgrade, Belgrade, Serbia, ³University Clinical Center Serbia, Clinic for Gastroenterology and Hepatology, Belgrade, Serbia

Contact E-Mail Address: dragasevicsanja@gmail.com

Introduction: Stress is a significant environmental factor that contributes to the pathogenesis of inflammatory bowel disease (IBD), including Crohn's disease (CD) and ulcerative colitis (UC). The onset of IBD is associated with the changes in the patient's mental status, occurrence of depression and anxiety.

Aims & Methods: The aim of the study was to determinate the level of stress, depression and anxiety for newly diagnosed IBD patients and its association with the mucosal expression of *IL17A*, *IL17F*, and *IL23* genes compared with the control group. Study involved 50 active CD (median age = 35.0, male % = 66.0), 54 active UC patients (median age = 43.5, male % = 44.4) and 100 non-IBD control subjects (median age = 50.0, male % = 43.0). All subject were tested on Perceived Stress Scale (PSS), Patient Health Questionnaire (PHQ-9), and Hospital Anxiety and Depression Scale (HADS).

Endoscopic biopsies were taken from inflamed IBD mucosa and analyzed for the expression of *IL17A*, *IL17F*, and *IL23* genes. For IBD group, laboratory and endoscopic examination were also conducted at the same time-point. *IL17A*, *IL17F* and *IL23* gene expression was analysed using real-time PCR Taq-Man method.

Results: PSS score was significantly higher in CD and UC compared to control group (median 18.5, 22.0 and 6.5, respectively, $p < 0.0001$). In CD and UC groups, increased frequency of mild (PHQ-9 = 5-9), moderate (10-14) and moderately severe (15-19) depression has been detected (CD: 56%, 40%, 4%; UC: 57.4%, 35.2%, 7.4%, respectively), compared to control group where most of the subjects were not (PHQ-9 = 0-4) or have been mildly depressed (5-9) (82%, 18%, respectively).

Frequency of abnormal HADS score (11-21) was significantly higher in CD (58%) and UC (53.7%) than in the control group (15%) ($p < 0.0001$). PSS score correlated with the expression of *IL17F* mRNA level in inflamed ileal CD mucosa ($r = 0.62$, $p = 0.0008$). Level of *IL23* mRNA was significantly higher in inflamed ileal mucosa of CD subjects with abnormal level of HADS (11-21) compared to subjects with normal (0-7) and borderline abnormal (8-10) HADS scores ($P = 0.007$).

Conclusion: Significantly higher degree of stress, depression and anxiety was identified in patients with CD and UC. Patients with increased expression of *IL17F* mRNA and *IL23* mRNA level in inflamed ileal CD mucosa had higher PSS and abnormal levels of HADS, indicating the association between psychological abnormalities, immune dysregulation and inflammation in IBD patients.

Disclosure: Nothing to disclose.

P0281

THE UK INFLAMMATORY BOWEL DISEASE BIORESOURCE: PROGRESSING FROM GENETICS TO FUNCTION AND CLINICAL TRANSLATION IN CROHN'S DISEASE & ULCERATIVE COLITIS IN ADULTS, YOUNG PEOPLE AND CHILDREN

L. Pele^{1,2}, R. Simpkins^{1,2}, C. Thorbinson^{1,2}, R. Shawky^{1,2}, S. Hearn³, H. Uhlig³, M. Parkes^{1,2,4}, UK IBD Genetics Consortium ¹NIHR IBD BioResource, Cambridge, United Kingdom, ²University of Cambridge, Department of Medicine, Cambridge, United Kingdom, ³University of Oxford, Translational Gastroenterology Unit, Oxford, United Kingdom, ⁴NIHR Cambridge Biomedical Research Centre, Cambridge, United Kingdom

Contact E-Mail Address: laetitia.pele@bioresource.nihr.ac.uk

Introduction: Inflammatory Bowel Disease (IBD), comprising Crohn's disease (CD) and (UC), affects ~500,000 people in the UK causing relapsing intestinal inflammation, with 25% of patients presenting before the age of 18 years. Accelerating research into the causes CD and UC across all ages is essential for clinical translation but requires access to large and well-characterised cohort of patients.

For that purpose, the UK IBD Genetics Consortium and the NIHR BioResource launched IBD BioResource in 2016 and the Paediatric IBD BioResource (PIBD) in 2022.

The aim is to build a large national platform of 50,000 adults with CD or UC and 5,000 paediatric onset IBD patients with rich genetic and phenotypic data to facilitate downstream translational research.

Aims & Methods: Building the IBD BioResource panel: Following patient enrolment at UK participating hospitals, phenotype data are collected through a clinical data sheet based on the Montreal classification, medication response and surgical history while health and lifestyle information are obtained via a patient questionnaire. Plasma, serum and DNA samples are collected – the latter for genetic analysis (GWAS), including whole genome / exome sequencing (WGS / WES).

Recently diagnosed patients provide further biological sampling including stool, biopsy tissue and whole blood for RNA and longitudinal follow-up of their medical course through clinical records and from the subjects / parents themselves.

Accessing the IBD BioResource panel: The panel of patients and their data is open to any investigators from science or industry. Submitted research proposals or data access applications are reviewed by the NIHR BioResource Scientific Advisory Board or the Data Access Committee, respectively, and approvals granted on scientific merits and projected benefit to patients. These studies may involve access to data only, access to data and existing samples or patient recall studies.

Results: Recruitment: IBD BioResource is open in > 90 participating hospitals across the UK and has recruited ~36,000 patients with established IBD and > 400 patients who are new to their diagnosis. To date ~21,000 samples have been sent for GWAS analyses and ~32,000 for WGS/WES.

The opening of PIBD was approved in January 2022, with Oxford Children's Hospital being the first site opening in March and recruiting their very first paediatric IBD patient in April. A further eight tertiary hospitals across the UK will open in the coming months.

Research translation: Since the launch of the IBD BioResource, 60 research applications have been received. These studies cover a full range of research activity including:

1. Analysis of existing genetics and clinical data
2. Access to existing banked serum samples from patients on biologics
3. Assessing the contribution of infection to IBD pathogenesis
4. Running surveys of the impact of certain aspects of IBD on quality of life
5. Recall studies of patients selected by genotype for functional genomics

6. Recall studies to develop early diagnostic tests
7. Aiding recruitment to observational studies and intervention studies
8. Aiding recruitment to commercial drugs trials

Conclusion: The IBD BioResource and its network are on course to facilitate IBD Research through access to their panel and furthering knowledge / understanding of IBD for the benefit of all Crohn's and colitis patients.

Disclosure: Nothing to disclose.

P0282

INVESTIGATION OF SOMATIC MUTATIONS IN BIOPSIES FROM PATIENTS WITH INFLAMMATORY BOWEL DISEASE

I.J. Hidding¹, S. Hu¹, J. Björk¹, S. Andreu-Sánchez², R.A.A. Ruigrok³, H. van Dullemen¹, M.C. Visschedijk¹, G. Dijkstra¹, E.A.M. Festen¹, A. Vich Vila¹, R.K. Weersma¹

¹University Medical Centre Groningen, Gastroenterology and Hepatology, Groningen, Netherlands, ²University Medical Centre Groningen, Genetics, Groningen, Netherlands,

³University of Groningen & University Medical Center Groningen, Gastroenterology and Hepatology, Genetics, Groningen, Netherlands

Contact E-Mail Address: i.j.hidding@umcg.nl

Introduction: Genome wide association studies have identified over 200 risk loci for Inflammatory Bowel Disease (IBD)^{1,2}. Additional studies have shown an inflammation dependent effect on gene expression³ and it has been shown that inflammation increases the rate of which somatic variants are introduced in the gut of patients diagnosed with IBD⁴. The effect of these somatic variants on IBD pathogenesis is poorly understood.

We hypothesise that these somatic variants can affect the inflammation and thereby can explain at least some of the difference in disease heterogeneity and therapy response between patients.

Aims & Methods: Here we investigated the impact of these somatic variants on IBD by analysing the variants on a variant, gene and pathway level. Biopsies (n=547, UC=232, CD=315) have been taken from patients diagnosed with IBD (n=272, UC=122, CD=150). We sequenced bulk RNA data from the biopsies and whole-exome data from the blood of these same patients. GATK Mutect2 was used to call somatic variants from the comparisons. As healthy controls were not available, comparisons were performed on an inflammation, disease and location basis by linear regression model and multiple testing correction.

Additionally, the data was corrected for gene expression as the detecting of somatic variants is dependent on a high enough level of gene expression. Genes enriched with somatic mutations were grouped for pathway analysis.

Results: Biopsies consisted of 50+ different cell types and the number of somatic variants per biopsy ranged from 9 475 to 53 551 (mean=27 137, std=6 540).

Within sample enrichment was performed to analyse genes enriched with somatic mutations regardless of phenotype. XIAP is the gene with most somatic variants found across all biopsies (mean=80, std=35.7), this gene is linked to very early onset IBD as a monogenic cause for disease.

Comparing the number of somatic variants per gene in biopsies from inflamed tissue with biopsies from non-inflamed tissue resulted in 104 significant genes after correcting for age, sex, BMI and gene expression, one of which DUOX2 (adj. p-value = 0.004) is a gene associated with IBD and has a significantly higher number of somatic variants in inflamed biopsies compared to non-inflamed biopsies.

Additionally, 440 genes showed a significant difference in the number of somatic variants when comparing ileum versus colon biopsies. CD36 (nominal p-value = 1.8e-05) was the most significant gene when compar-

ing CD to UC. This gene is associated with inflammation and the difference in variants could show a difference in the inflammation mechanism between UC and CD.

Additionally, variant annotation showed a number of pathogenic and likely pathogenic variants from the Clinvar database ranging from 0 to 21 per sample (mean=7, std=5.8), showing that variants with a confirmed pathogenic effect can remain undetected from standard genetic screening. However, Clinvar annotation is based on germline variants and not somatic, which means any pathogenic effect on genomic level might not have the same impact on a local level.

Conclusion: Overall, our study has shown that somatic mutations can have a large impact on the genes in cells in the gut of patients with IBD, through pathogenic mutations and accumulation of mutations in genes related to IBD. Although, it is not expected that every mutation has an effect, overall trends in increased mutations can be interpreted as a biological effect and should be investigated further.

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P0283

TOWARDS A PERSONALIZED APPROACH IN ULCERATIVE COLITIS: ROLE OF OCTN1 IN PREDICTING DISEASE SEVERITY AND INDIVIDUAL RESPONSE TO THERAPY

P. Puca¹, V. Petito², L. Masi¹, L.R. Lopetuso³, G. Pani⁴, M. Fidaleo⁵, F. Del Chierico⁶, G. Cammarota⁴, D. Pugliese⁷, A. Gasbarrini⁸, F. Scalfaferrì⁹

¹Università Cattolica del Sacro Cuore, Rome, Italy, ²Catholic University of Sacred Heart, Department of Internal Medicine, Gastroenterology Division, Roma, Italy, ³Fondazione Policlinico Universitario "A. Gemelli" IRCCS - Università Cattolica di Roma, Surgical and Medical Sciences Department, Roma, Italy, ⁴Catholic University, Fondazione Policlinico Gemelli, Internal Medicine and Gastroenterology, Rome, Italy, ⁵Università di Roma La Sapienza, Rome, Italy, ⁶Children Hospital Bambino Gesù IRCCS, Unit of Human Microbiome, Rome, Italy, ⁷Fondazione Policlinico Universitario "A. Gemelli" IRCCS, CEMAD – IBD UNIT - Unità Operativa Complessa di Medicina Interna e Gastroenterologia, Dipartimento di Scienze Mediche e Chirurgiche, Rome, Italy, ⁸Fondazione Policlinico Universitario Gemelli IRCCS, Università Cattolica, Internal Medicine, Gastroenterology and Liver Diseases, Rome, Italy, ⁹Catholic University of Rome Dept. of Internal Medicine Dept. of Gastroenterology, Internal Medicine, Gastroenterology Division, IBD Unit, Roma, Italy

Contact E-Mail Address: pgpuca@gmail.com

Introduction: Ulcerative colitis is a chronic invalidating disease, whose therapeutic strategies include amino-salicylates, steroids, probiotics, immune-modulators, biologics, fecal microbiota transplantation and surgery. Though, in clinical practice, there are no evidence available about

elements that could predict response to each of the above-mentioned therapies. Our group thinks that OCTN1, an organic cation transporter directly involved in innate immunity, with its variants (C503L homozygous, heterozygous or T503F), could have a role in predicting individual response to biologic therapies (antiTNFa and vedolizumab).

Aims & Methods: In this prospective and retrospective study, we enrolled a cohort of 90 patients with active ulcerative colitis (50 in treatment with antiTNF agents and 40 with vedolizumab), determining their OCTN1 genotype and evaluating their clinical response to therapy, calculated with clinical Mayo score, after six weeks (T1) and six months (T2).

Results: Left colitis at diagnosis was more frequent in C503L patients (61.7% left colitis vs 38.3% pancolitis) than patients than in patients with T503F (32.5% left colitis vs 62.5% pancolitis). At the same way, the average age at diagnosis was sensibly lower in patients with T503F genotype (35.5 years C503L vs 33.3 years heterozygous vs 28.9 years T503F).

We used clinical response at T2 (6 months) as a primary outcome of our study. Among patients under antiTNFa therapy, patients with C503L genotype were divided into 8 no responders and 6 responders (43% responders vs 57% no responders), whilst patients with T503F genotype were divided into 10 responders and 2 no responder (80% responders vs 20% no responders). On the contrary, patients under vedolizumab therapy showed different trend: patients with C503L genotype were divided into 15 responders and 4 no responders (78.9% responders vs 21.1% no responders), whilst patients with T503F genotype were 3 responder and 1 no responder.

Conclusion: Patients with T503F genotype present an overall worse course of disease, with higher rate of pancolitis and younger age at diagnosis. Furthermore, the presence of the mutation (allele T) could have a role in increasing the response rate to antiTNFa.

Disclosure: No conflict of interest to declare.

P0284

ELEVATED ARTIFICIAL SWEETENER BODY LEVELS ARE ASSOCIATED WITH CROHN'S DISEASE.THE ENIGMA STUDY

J. Hu^{1,2,3}, Y. Ruan^{1,3}, W. Lin^{1,4}, G. Trakman^{5,6}, J. Zhang^{4,3,1}, J.J. Teh⁷, S. Kang⁷, A. Hamilton⁵, A.W.O. Brien⁵, J.Y.L. Ching^{1,4}, J. Sung⁸, J. Yu^{1,4}, M. Morrison⁷, M.A. Kamm^{5,6}, S.C. Ng^{1,4,9,3}

¹The Chinese University of Hong Kong, Department of Medicine and Therapeutics, Hong Kong, China, ²Institute of Digestive Disease, The Chinese University of Hong Kong, Hong Kong, China, ³Microbiota I-Center (MagIC), Hong Kong, China, ⁴The Chinese University of Hong Kong, State Key Laboratory of Digestive Disease, Li Ka Shing Institute of Health Sciences, Hong Kong, China, ⁵St Vincent's Hospital, Department of Gastroenterology, Melbourne, Australia, ⁶The University of Melbourne, Department of Medicine, Melbourne, Australia, ⁷The University of Queensland Diamantina Institute, Faculty of Medicine, Brisbane, Australia, ⁸Nanyang Technological University, Lee Kong Chian School of Medicine, Singapore, Singapore, ⁹Centre for Gut Microbiota Research, Faculty of Medicine, The Chinese University of Hong Kong, Hong Kong, China

Contact E-Mail Address: jielunhu@cuhk.edu.hk

Introduction: Food additives, including artificial sweeteners, have been epidemiologically and experimentally linked to an increased risk of developing Crohn's disease (CD). This is thought to be mediated by sweeteners altering the microbiota to be more pro-inflammatory.

However, the physiological fate of these sweeteners has not been fully evaluated. We aimed to determine the level of commonly consumed artificial sweeteners in urine, stool and serum samples of patients with CD compared with controls.

Aims & Methods: We included a total of 317 subjects [(184 CD patients), 40 first-degree relatives of CD (FDR), 52 non-related healthy household members of CD patients (HHM) and 41 healthy controls (HC)] from Australia and Hong Kong. Consumption of common artificial sweeteners (aspartame, sucralose and saccharin) was quantified using a validated 26-item food additive questionnaire, and their concentration in stool, urine and serum samples quantified using mass spectrometry based on a newly developed and validated standard operating procedures.

Results: Aspartame, sucralose and saccharin concentrations in urine, stool and serum samples were consistent with their known metabolism. Only saccharin was detectable in serum, and no significant differences were observed between groups.

However, the CD group had a greater saccharin concentration in urine than HC ($P<0.001$) and the sucralose and aspartame concentrations in stool were also significantly greater in CD than HC ($P=0.007$ and $P=0.041$, respectively). There was a positive correlation between sucralose stool concentration (the main exposure pathway for sucralose) and sucralose intake assessed by validated questionnaire that captured past 12 months intake ($R^2=0.4431$, $P<0.001$).

Conclusion: In the first human study that quantifies artificial sweetener levels concentrations of artificial sweeteners in urine and stool were increased in Crohn's disease compared with healthy controls. Sucralose and aspartame in stool may play a role in the pathogenesis of Crohn's disease inflammation.

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P0285

MORE SEVERE CROHN'S DISEASE CLINICAL PRESENTATION IN AN INFLAMMATORY BOWEL DISEASE (IBD) CENTER OF EMERGENCY DEPARTMENT DURING COVID-19 PANDEMIC

G. Oliviero^{1,2}, A. Facchiano¹, A.D. Guarino¹, C. Elmo¹, B. Manzo¹, M. Mautone¹, G. Vicinanza¹, L. Donnarumma¹, A. Cuomo¹
¹ASI Salerno, Umberto I Hospital - Gastroenterology Unit, Nocera Inferiore, Italy, ²University of Salerno, Department of Medicine and Dentistry - Gastroenterology Unit, Salerno, Italy

Contact E-Mail Address: giovanni.olivierounina2@gmail.com

Introduction: COVID-19 outbreak and consequential restrictive measures have strongly influenced clinical management of several chronic diseases, causing lengthening of waiting times for visits, follow-up and procedures, particularly conditioning the clinical presentation.

In this short case series study, we aim to demonstrate how COVID-19 pandemic has influenced Crohn's disease (CD) clinical course by increasing the number of patients with more severe symptoms at presentation.

Aims & Methods: In our study we observed the clinical presentation of all previously diagnosed, or subsequently confirmed, CD patients who accessed the emergency department and first time visited in our operative gastrointestinal unit from January 2020 to December 2021. The absolute percentage of all symptoms was reported and compared to a CD population admitted to emergency department during a previous two-years period (January 2018 to December 2019).

All data were collected from years-related databases based on information contained in medical records. Student T test was used to compare the difference in clinical presentation among the two groups. P values <0.05 were considered statistically significant.

Results: A total of 91 CD patients were first time visited in the two-year period 2020-2021. The median age of patients was 31.7 years (23-35) and 57.8 % (63 out of 109) were female. The most frequent clinical presentations

at first medical examination were abdominal pain in 82 patients (90.1%), tiredness/fatigue in 80 patients (87.9%), diarrhoea in 54 patients (59.3%) and abdominal bloating/distension in 61 patients (67.0%). A severe clinical presentation with intestinal obstruction or perforation occurred in 10 (10.9%) and 5 (5.4%) patients, respectively. In the two-year period 2018-2019, a total of 145 CD patients were first time visited; the median age was 32.8 years (25-36) and 61.5% (83 out of 135) were female.

At the first medical examination abdominal pain reported in 128 (88.3%) and tiredness/fatigue in 125 patients (86.2%) appeared to be the most common symptoms followed by diarrhoea in 85 patients (58.6%) and abdominal bloating/distension in 87 patients (60.0%). No severe presentation symptoms were recorded in 2018-2019 two-years period.

Hence, abdominal pain ($p=0.035$) and tiredness/fatigue ($p=0.049$) were statistically higher in patients observed during two-year period 2020-2021, moreover diarrhoea, abdominal bloating/distension, obstruction and perforation clinical pattern were more frequent although not reaching the statistical significance.

Conclusion: Our data suggest a change in clinical presentation of CD patients with an increase of all symptoms including severe presentation, such as intestinal obstruction and/or perforation in 2020/2021 two-year period, likely as direct or indirect consequence of COVID19 outbreak. Further clinical investigation is needed to confirm this observation.

Disclosure: Nothing to disclose.

P0286

COVID19 VACCINATION COVERAGE IN FLEMISH PATIENTS WITH IMMUNE-MEDIATED INFLAMMATORY DISEASES

L. Fierens¹, J. Joly², E. De Dycker³, T. Vanhoutvin⁴, P. De Munter^{5,6}, J. Sabino^{1,3}, S. Vermeire^{1,3}, P. De Haes^{4,5}, P. Verschuere^{2,7}, M. Ferrante^{1,3}

¹Catholic University Leuven, Department of Chronic Diseases and Metabolism, Leuven, Belgium, ²University Hospitals Leuven, Department of Rheumatology, Leuven, Belgium, ³University Hospitals Leuven, Department of Gastroenterology and Hepatology, Leuven, Belgium, ⁴University Hospitals Leuven, Department of Dermatology, Leuven, Belgium, ⁵Catholic University Leuven, Department of Microbiology, Immunology and Transplantation, Leuven, Belgium, ⁶University Hospitals Leuven, Department of General Internal Medicine, Leuven, Belgium, ⁷Catholic University Leuven, Department of Development and Regeneration, Leuven, Belgium

Contact E-Mail Address: liselotte.fierens@kuleuven.be

Introduction: Patients with immune-mediated inflammatory diseases (IMIDs) are at higher risk for infectious diseases, especially when receiving immunosuppressive treatments. In 2018, we set up the prospective COL-OSSeUM registry in order to track and optimize their vaccination coverage for influenza, pneumococci and hepatitis B. Once COVID19 vaccines became available, national authorities provided IMID patients priority access, but data on actual COVID19 vaccination coverage in this population are missing.

Aims & Methods: We evaluated the COVID19 vaccination coverage of IMID patients through the COL-OSSeUM registry. This registry contains data from 1488 consecutive IMID patients with IBD, rheumatic (RHEU) or dermatological inflammatory conditions (DER) recruited at a tertiary referral centre between August and December 2018 (Fierens L, *J Crohns Colitis* 2022). Global vaccination rates were assessed at baseline as well as in 2021/2022 after the implementation of a vaccination module (Vaccinnet) in the electronic patient health record. For the present study, both basic and booster COVID19 vaccination coverage until March 2022 were reviewed. Reasons

for non-vaccinations were collected by contacting patients directly. Vaccination rates were compared with those of the adult Flemish background population (source: laatjevaccineren.be).

Results: In total, 1430 adult IMID patients (44.90% male, median age 53.94 years, 789 IBD, 604 RHEU, 37 DER) were included in the present study. By March 2022, 96.78% of IMID patients had received the COVID19 basic vaccination (96.07% IBD, 98.01% RHEU, 91.89% DER) and 91.75% at least one COVID19 booster vaccination (89.23% IBD, 95.36% RHEU, 86.49% DER). COVID19 vaccination coverage was significantly higher for RHEU patients than for IBD/DER patients (basic 98.01% vs. 95.88%, $p=0.024$; booster 95.36% vs. 89.10%, $p<0.001$). Compared to the background population, COVID19 coverage rate was higher in our IMID patients (basic 96.78% vs. 92.95%, $p<0.001$; booster 91.75% vs. 83.77%, $p<0.001$). Factors associated with COVID19 vaccination in univariate analysis are shown in Table 1.

In multivariate analysis, basic COVID19 vaccination was associated with age above 50 years [Odds ratio 3.66 (95% CI 1.82-7.39), $p<0.001$], use of thiopurines/methotrexate [2.76 (1.06-7.20), $p=0.038$] and compliance with other recommended vaccinations [3.60 (1.84-7.06), $p<0.001$]. Booster COVID19 vaccination was associated with age above 50 years [4.74 (2.99-7.53), $p<0.001$], use of thiopurines/methotrexate [2.13 (1.21-3.74), $p=0.009$] and compliance with other recommended vaccinations [3.11 (2.05-4.72), $p<0.001$]. Main reasons for absence of COVID19 vaccination included skepticism (29/46, 63.04%) and fear for adverse events (13/46, 28.26%).

		Age above 50	Sex	Higher education level	Compliance with other recommended vaccinations	Any immunosuppression	Systemic steroids	Thiopurines / methotrexate	Biological therapy	Small molecules
ALL (n=1430)	Basic vaccination	$p<0.001$	$p=0.479$	$p=0.243$	$p<0.001$	$p=0.939$	$p=1.000$	$p=0.007$	$p=0.057$	$p=0.397$
	Booster vaccination	$p<0.001$	$p=0.996$	$p=0.379$	$p<0.001$	$p=0.686$	$p=0.109$	$p<0.001$	$p=0.074$	$p=0.780$
IBD (n=789)	Basic vaccination	$p=0.001$	$p=0.274$	$p=0.099$	$p=0.002$	$p=1.000$	$p=0.089$	$p=0.628$	$p=0.700$	$p=1.000$
	Booster vaccination	$p<0.001$	$p=0.731$	$p=0.038$	$p<0.001$	$p=0.214$	$p=0.642$	$p=0.566$	$p=0.808$	$p=0.270$
RHEU (n=604)	Basic vaccination	$p=0.042$	$p=0.550$	$p=1.000$	$p=0.006$	$p=1.000$	$p=1.000$	$p=0.067$	$p=0.017$	$p=1.000$
	Booster vaccination	$p<0.001$	$p=0.232$	$p=0.428$	$p=0.003$	$p=1.000$	$p=0.815$	$p=0.110$	$p=0.030$	$p=0.618$
DER (n=37)	Basic vaccination	$p=0.072$	$p=0.584$	$p=1.000$	$p=0.554$	$p=0.562$	$p=1.000$	$p=0.632$	$p=1.000$	not applicable
	Booster vaccination	$p=0.010$	$p=0.159$	$p=1.000$	$p=0.377$	$p=1.000$	$p=1.000$	$p=0.538$	$p=1.000$	not applicable

Table 1: Factors associated with basic and booster COVID19 vaccination in univariate analysis.

Conclusion: In IMID patients, COVID19 vaccination coverage was higher compared to the background population. Factors independently associated with vaccination coverage included older age, the use of thiopurines or methotrexate, and compliance with other recommended vaccinations.

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P0287

INFLAMMATORY BOWEL DISEASE AND SOLID ORGAN TRANSPLANTATION: A SINGLE CENTRE EXPERIENCE

J.I. Alves da Silva¹, S. Archer¹, D. Falcão², D.G. Ferreira³, P. Lago¹, C. Caetano¹, I. Pedroto¹, M. Salgado²

¹Centro Hospitalar Universitário do Porto, Porto, Portugal,

²Centro Hospitalar e Universitário do Porto, Gastroenterologia, Porto, Portugal, ³Centro Hospitalar Universitário do Porto, Gastroenterology, Amadora, Portugal

Contact E-Mail Address: sararcher_@hotmail.com

Introduction: Managing solid organ transplant (SOT) IBD patients represents a vexing problem, mainly due to concerns of immunosuppression and biologic therapies.

Aims & Methods: Retrospective analysis of 19 SOT-IBD patients between 2001-2021 in a Portuguese tertiary centre.

Results: Ten patients (53%) were male, 7 (37%) ulcerative colitis (UC), 10 (52%) Crohn's Disease (CD) and 2 (11%) unclassified colitis. Five patients (26%) were submitted to kidney transplant(KD) and 14 (76%) to liver transplant(LT). Nine patients (47%) were diagnosed with IBD after transplant, with 4 IBD post-KT. Tacrolimus and MMF were the most commonly used antirejection treatments.

Concerning CD patients, 9 were non-stricturing non-penetrating (4 ileocolic and 5 colonic), 1 was stricturing (jejuno-ileal) and 3 had perianal disease.

Three patients achieved remission under mesalazine (UC), 3 under steroids, 3 under azathioprine (AZT) and 7 under biologics. Two UC patients were submitted to colectomy due to medical therapy failure. Eight (42%) patients experienced treatment with biologics, 2 of them combined with AZT (infliximab+AZT). Five patients (26%) experienced only one biologic (3 treated only with infliximab and 2 with vedolizumab). Three patients (15%) experienced two or more biologics (1 failed to vedolizumab and is currently under ustekinumab; 1 failed to adalimumab, developed infliximab immunogenicity and is currently under vedolizumab; 1 failed to combined AZT plus infliximab, to adalimumab and to vedolizumab).

Two/8 treated with combination biologic and antirejection therapy experienced infectious complications: CMV colitis and campylobacter en-

terocolitis, both under infliximab+tacrolimus. One CD patient with LT was diagnosed with intestinal diffuse large B-Cell lymphoma (tacrolimus and recent AZT).

Conclusion: The majority of patients presented colonic disease. The risk of infection and neoplasms (mainly lymphoproliferative) should be considered in the management of this patients – that probably explains why vedolizumab was preferred in this population.

Disclosure: Nothing to disclose.

P0288

THE DISEASE SEVERITY INDEX FOR INFLAMMATORY BOWEL DISEASE IS ASSOCIATED WITH PSYCHOLOGICAL SYMPTOMS, QUALITY OF LIFE, AND PREDICTS A MORE COMPLICATED DISEASE COURSE

A. Swaminathan¹, D. Fan², G. Borichevsky³, T. Mules⁴, E. Hirschfeld³, C. Frampton³, A. Day⁵, C.A. Siegel⁶, R.B. Geary⁷
¹University of Otago, Department of Medicine, Christchurch, New Zealand, ²Christchurch hospital, Department of Gastroenterology, Christchurch, New Zealand, ³University of Otago, Christchurch, New Zealand, ⁴Christchurch hospital, Christchurch, New Zealand, ⁵University of Otago, Department of Paediatrics, Christchurch, New Zealand, ⁶Dartmouth-Hitchcock Medical Center, Lebanon, United States, ⁷University of Otago Dept. of Medicine, Christchurch, New Zealand

Contact E-Mail Address: akhilesh.swaminathan@gmail.com

Introduction: Individuals with inflammatory bowel disease (IBD) follow a heterogeneous disease course and experience higher rates of stress, anxiety and depression compared to those without IBD.^{1,2} The Disease Severity Index (DSI)³ is a novel tool that aims to incorporate measures of IBD activity, patient reported outcomes and clinical phenotype to estimate overall disease severity. However, the ability of the DSI to predict disease complications and the presence of psychosocial comorbidity has not previously been investigated.

This study prospectively assessed the associations between the DSI and psychological symptoms, quality of life (QoL) and disease outcomes in a cohort of patients with IBD.

Aims & Methods: Patients with IBD undergoing ileocolonoscopy for disease assessment in Canterbury, New Zealand were followed prospectively for 12 months. DSI, psychological symptoms (perceived stress (perceived stress scale, PSS-10), depression (patient health questionnaire, PHQ-9), anxiety (generalised anxiety disorder scale, GAD-7)) and QoL (inflammatory bowel diseases questionnaire, IBDQ-32) scores were assessed at baseline. Endoscopically active disease included individuals with a simple endoscopic score for Crohn's disease (SES-CD) >2 and ulcerative colitis endoscopic index of severity (UCEIS) ≥2. Logistic regression was used to identify variables predicting a complicated IBD course at 12 months (composite endpoint of need for escalation of biological/immunomodulator for disease relapse, recurrent corticosteroid use, IBD-related hospitalisation and surgery). Variables reaching a pre-defined significance of p<0.01 were incorporated into multivariable regression analyses to develop a final model to predict the composite study endpoint.

Receiver operating characteristics (ROC) analyses identified the optimal DSI set point to predict a complicated disease course. This threshold was then used as a categorical value in place of a continuous DSI score in the final multivariable prediction model to assess the risk of reaching the composite study endpoint at 12 months of follow up.

Results: One hundred and seventy-two patients were recruited (100 Crohn's disease (CD), 91 female). Median age of participants was 46 years (IQR 35-59), median DSI was 21 (IQR 11-32), median IBDQ-32 was 169 (IQR 135-196) and 97 patients had endoscopically active disease at baseline.

The DSI was significantly higher in patients with symptoms of moderate-severe stress (PSS-10 >14, $p < 0.01$, $n = 84$), depression (PHQ-9 ≥ 10 , $p < 0.01$, $n = 48$), anxiety (GAD-7 ≥ 10 , $p < 0.05$, $n = 34$) and impaired quality of life (IBDQ-32 <168, $p < 0.01$, $n = 84$). The composite study endpoint was observed in 49 patients (29 Crohn's disease, 20 ulcerative colitis (UC)).

Only the baseline DSI (odds ratio (OR) = 1.05, 95% CI 1.01-1.07) and endoscopically active disease (OR = 6.12, 95% CI 1.85-20.26) were associated with a complicated IBD course on multivariable logistic regression analyses and were used in the final prediction model (Table 1). Using this model, subgroup analyses stratified by IBD subtype showed that the DSI was associated with a complicated disease course in patients with CD (OR = 1.10, 95% CI 1.04-1.16) and UC (OR = 1.08, 95% CI 1.04-1.12).

A DSI of 23 was the optimal threshold for predicting a complicated IBD course (Area under the ROC (AUROC) = 0.84, $p < 0.01$; Sensitivity 84%; Specificity 72%) and was strongly predictive of reaching the composite study endpoint (OR = 8.31, 95% CI 3.38-20.46) when incorporated into the final prediction model.

Sub-group analyses confirmed no significant differences in the performance of the DSI in predicting the composite study endpoint between individuals with CD and UC (AUROC_{difference} = 0.08, $p > 0.05$). A DSI >23 was also associated with a significantly elevated risk of having a complicated IBD course at 12 months in individuals with inactive or mild disease activity (SES-CD <7, UCEIS <5) at baseline (OR = 11.75, 95% CI 3.47-39.81) when using the final multivariable prediction model.

Factors selected for multivariable analysis*	Odds ratio (95% CI)	p value
Current steroid use at baseline assessment	0.78 (0.18-3.20)	0.71
Steroid use in the year prior to baseline assessment	1.97 (0.61-6.23)	0.26
Current biological use at baseline assessment	1.71 (0.61-4.77)	0.31
Inflammatory bowel diseases questionnaire (IBDQ-32)	1.00 (0.98-1.03)	0.82
Patient health questionnaire-9 (PHQ-9)	1.06 (0.95-1.17)	0.31
Disease severity index (DSI) ^{continuous variable}	1.05 (1.01-1.07)	0.01 **
Subjectively active IBD at baseline (HBI >4, SCCAI >5)	0.99 (0.29-3.33)	0.99
Objectively active IBD at baseline (SES-CD >2, UCEIS >2)	6.12 (1.85-20.26)	<0.01 **

Table 1. Multivariable logistic regression analysis for baseline factors associated with a complicated IBD course at 12 months. IBD = inflammatory bowel disease. HBI = Harvey-Bradshaw index. SCCAI = simple clinical colitis activity index. SES-CD = simple endoscopic score for Crohn's disease. UCEIS = ulcerative colitis endoscopic index of severity. *Selected for multivariable analysis ($p < 0.01$ on univariable regression analyses).

**Selected for final prediction model.

Conclusion: The DSI is associated with psychological distress, impaired QoL, and predicts a more complicated disease course in patients with IBD. Even in individuals in endoscopic remission or with mild disease activity, a DSI >23 is significantly associated with IBD-related complications during 12 months of follow up. The DSI is a novel tool that can be incorporated into routine IBD assessment and has the potential to allow clinicians to provide more accurate and holistic patient care.

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A.S.D. has served on advisory boards for Janssen, Abbvie and Nestle (all unrelated to this manuscript).

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C.A.S. has equity interest as a co-founder of MiTest health, LLC (software company). Technology developed by MiTest Health, LLC has been licensed to Takeda (unrelated to this manuscript).

R.B.G. has received research grants, served on advisory boards, and received honoraria for educational activities for Janssen, Abbvie and Zespri (unrelated to this manuscript).

P0289

CYTOMEGALOVIRUS IN INFLAMMATORY BOWEL DISEASE: USEFULNESS OF A POSITIVE RESULT WITH DIFFERENT DIAGNOSTIC TECHNIQUES IN TREATMENT CHOICE

I. González Díaz¹, E. Martín Arranz¹, C.J. Suárez Ferrer^{1,2}, J.L. Rueda García¹, M. Sánchez Azofra¹, J. Poza Cordon^{1,2}, C. Amiana Roig¹, C. Amor Costa¹, M.D. Montero Vega³, L. Guerra Pastrán⁴, M.D. Martín-Arranz^{1,2}

¹Hospital Universitario La Paz, Gastroenterology, Madrid, Spain,

²Health Research Institute Hospital Universitario La Paz-IdiPaz, Gastroenterology, Madrid, Spain, ³Hospital Universitario La Paz, Microbiology, Madrid, Spain, ⁴Hospital Universitario La Paz, Pathology, Madrid, Spain

Contact E-Mail Address: irenegonzalezdiaz@gmail.com

Introduction: Cytomegalovirus (CMV) infection can worsen the prognosis of patients with active inflammatory bowel disease (IBD) and be a cause of steroid or immunosuppressive-refractory disease.

Several methods are available for the diagnosis of CMV infection, with variable sensitivities and specificities. The most reliable methods for the diagnosis are immunohistochemistry (IHC) and CMV polymerase chain reaction (PCR) in colonic tissue. Clinical significance of isolated positive PCR remains unclear.

Aims & Methods: The aim of this study is to review CMV-positive IBD patients, diagnosed by PCR and/or IHC, the adopted therapeutic approach and their clinical evolution.

We conducted a retrospective, cohort study. All biopsy samples sent from colonoscopy to check for CMV from 2017 to 2021 were reviewed. Patients with a diagnosis of CMV by PCR and/or IHC were included. Primary endpoint was describing the diagnostic techniques used and the clinical course of CMV+ patients.

Secondary endpoint was whether CMV diagnosis conditioned any baseline treatment changes/escalation. Non-IBD patients were excluded. Variables including demographics, disease related information, baseline treatment, clinical outcomes and need for antiviral treatment were collected.

Results: Out of 451 submitted biopsies, we detected 51 positive PCRs (11.3%) and 31 positive IHCs (6.7%), 11 of non-IBD patients were excluded. 44 biopsies were included in the final analysis. Of 39 PCR+ samples only 13 (36.1%) were IHC+. However, most patients with IHC+ (18) had PCR+ (13, 95.5%). Intranuclear bodies were seen in 8 of PCR+ (20.5%) patients and in 10 (55.5%) of IHC+ samples.

38 patients (86.4%) were diagnosed with ulcerative colitis (UC), while 5 (11.3%) had Crohn's disease (CD) and 1 (2.3%) unclassified IBD. Most patients had moderate-severe clinical activity (31, 70.5%) and also severe endoscopic activity (27, 71.1% of UC Mayo 3 and 100% of CD SES-CD >8). In total, 19 patients (43.2%) fulfilled criteria for steroid-refractory disease.

All of them were treated regardless of the technique used to detect CMV (17 PCR+, 8 PCR+/IHC+ and 2 PCR-/IHC+). Short-term remission occurred in 10 (52.6% patients), 3 (15.8%) required surgery and the remaining patients (6, 31.6%) needed treatment escalation to achieve long-term remission. In patients with non steroid-refractory disease, CMV was treated in severe flare-ups (9, 36%) and in 3 (33.3%) remission was achieved with antiviral treatment only. Patients who did not receive antiviral treatment (17) had mild clinical activity, CMV was assumed to be an innocent bystander and 13 (76.5%) patients remitted without baseline treatment changes. In 11 (84.6%) patients with PCR and IHC+ antiviral treatment was started. Remission rate was 45.5% (5 patients). Only 2 (15.4%) patients of this group were not treated, they had mild flare-up and responded to conventional treatment. 12 (52.2%) patients with isolated PCR+ received antiviral treatment, 8 (66.7%) with steroid refractory disease. No significant differences were observed in remission rates or in the need for surgery between isolated PCR+ treated patients (remission: 38.5%, surgery: 15.4%) and isolated PCR + untreated patients (remission: 69.2%, surgery: 7.7%).

Conclusion: In our study one third of patients with PCR+ had also IHQ+. Most of the patients who received antiviral treatment had steroid refractory disease or had both PCR and IHQ positivity. In patients with isolated PCR and a mild flare, not starting treatment could be considered.

Disclosure: Nothing to disclose.

P0290

NEUTROPHIL-LYMPHOCYTE RATIO ROLE TO PREDICT DISEASE ACTIVITY AND SEVERITY IN ULCERATIVE COLITIS

S. Berrag¹, T. Adiou¹, S. Ouahid¹, A. Touibi¹, H. Igorman¹, R. Laroussi¹, M. Moussaa¹, M. Tamzaourte¹

¹Military Hospital Mohamed V of Rabat, Gastroenterology 1, Rabat, Morocco

Contact E-Mail Address: sanaa.berrag@gmail.com

Introduction: Usual inflammatory biomarkers have been routinely used to evaluate activity and severity in ulcerative colitis (UC). But these parameters have a humble precision in reflecting UC disease activity. Therefore, finding non-invasive accessible and cost-effective biomarkers that can be used to evaluate disease activity is strongly needed for optimal management of UC.

Aims & Methods: The aim of this study is to evaluate the utility of neutrophil-lymphocyte ratio (NLR) as simple and cost-effective non-invasive biomarkers for detecting disease activity in UC patients. We conceived a retrospective study including 69 UC patients classified into two groups according to Mayo score (active UC and inactive UC). Patients were enrolled from the gastroenterology I department Military Hospital Mohamed V of Rabat over a period of 3 years (June 2019 to January 2022). The White blood cell count (WBC), NLR, LMR, C-reactive protein (CRP) and fecal calprotectin (FC) were measured.

Results: A total of 69 UC patients were included. The mean NLR values of the inactive and active patients were 1.61 ± 0.41 and 2.74 ± 1.130 , respectively ($p < 0.0001$). The NLR levels of active patients were significantly higher compared to patients with inactive UC. Spearman's correlation analysis indicated a significant positive correlations between NLR and WBC ($r = 0.289$, $p = 0.016$), faecalcalprotectin ($r = 0.578$, $p = 0.00$) and CRP ($r = 0.257$, $p = 0.033$) in the among all UC patients.

In UC active patients, NLR showed a significant positive correlation with faecalcalprotectin ($r = 0.337$, $p = 0.048$) and CRP ($r = 0.333$, $p = 0.05$). However, we found no correlation between the NLR and CRP, Faecalcalprotectin or WBC count in patients with inactive UC. A linear regression model showed that NLR remained an independent predictor of disease activity (OR: 2.8, 95%CI: 0.98–3.43, $p = 0.05$). ROC curve analysis suggested that

the optimum cut-off NLR value for active UC was 2.46, with sensitivity and specificity of 79.4 % and 66.7 % respectively (AUC: 0.46).

Conclusion: High NLR level is associated with active disease in UC. It can be considered as an additional marker to evaluate activity in UC

Disclosure: Nothing to disclose.

P0291

EFFECT OF TRANSITION CARE ON CLINICAL OUTCOMES AND TREATMENT ADHERENCE IN PATIENTS WITH INFLAMMATORY BOWEL DISEASE: AN OBSERVATIONAL PROSPECTIVE STUDY

O.M. Nardone¹, M. Martinelli², A. Testa³, A. Rispo³, R. de Sire³, A. Caiazzo³, G. Calabrese³, M.T. Fioretti², E. Miele², A. Staiano², F. Castiglione³

¹University of Naples Federico II, Department of Public Health, Naples, Italy, ²University of Naples Federico II, Department of Translational Medical Science, Naples, Italy, ³University of Naples Federico II, Department of Clinical Medicine and Surgery, Naples, Italy

Contact E-Mail Address: Olga.nardone@libero.it

Introduction: Inflammatory bowel diseases (IBD) are chronic diseases with an increasing incidence in the paediatric population. Given the lifelong impact of these diseases, the transition from paediatric to adult healthcare in patients with IBD is essential to ensure the continuity of care.

Aims & Methods: We aimed to evaluate the impact of structured transition from pediatric to adult IBD services on objective patient outcomes including disease flares, admission rates, hospitalization and surgery. We further assessed the rate of medication adherence and the quality of life pre-and post-transition.

An observational, prospective study was conducted in a tertiary IBD centre and included adolescent/young adult (aged ≥ 17 years) with a confirmed diagnosis of IBD before 16 yo and in clinical remission who underwent "structured transition" ("joint transition care"). We collected demographics and clinical data in the previous 12 months before the transition and 12 months after. Patients completed the following questionnaires at recruitment: the Morisky Medication Adherence Scale and the short form health survey (SF36) Questionnaire.

Results: We recruited 41 patients (aged 18–20) in clinical remission based on Crohn's Disease Activity Index [CDAI] score 117 ± 145 for Crohn's Disease [CD] and pMayo 2.7 ± 1.4 for ulcerative colitis [UC] who had recently transitioned to adult care and completed 12 months follow-up. Demographic details were summarized in Table 1.

Characteristics	Patients (n 41)
UC	22 (54%)
CD	19 (46%)
Female	27 (66%)
Smokers	5 (12%)
L1	4 (10%)
L2	3 (7%)
L3	12 (29%)
B1	13 (32%)
B2	6 (14%)
B3	0
Perianal disease	6 (14%)
E1	2 (5%)
E2	3 (7%)
E3	17 (41%)
Duration disease (months)	68.8 ± 35.6

Table 1.

There was a significant reduction in the number of outpatient visits and in the rate of flares in the 12 months post-transition (outpatient visits pre-transition 2.3 ± 0.7 , post-transition 1.8 ± 0.8 , $p=0.005$) (exacerbations pre-transition: 1.2 ± 0.9 , post-transition 0.6 ± 0.7 , $p=0.005$) (flares pre-transition 1.2 ± 0.9 , post transition 0.6 ± 0.7 , $p=0.001$). While, there was no statistically significant difference between patients' Body Mass Index (BMI) before (22.8 ± 3.4) and after transition (23 ± 3.5 ; $p=0.72$).

Similarly, no significant difference was observed in terms of hospitalization (hospitalization pre-transition 0.2 ± 0.5 , post-transition 0.2 ± 0.4 , $p=0.6$); surgery (surgery pre-transition 0.02 ± 0.15 , post-transition 0.10 ± 0.3 , $p=0.17$); medication adherence (adherence pre-transition 1.6 ± 0.5 , post-transition 1.6 ± 0.5 , $p=0.7$); quality of life (SF-36 pre-transition 100 ± 6 , post-transition 101 ± 5 , $p=0.2$).

Conclusion: Attendance at dedicated transition clinics can contribute to the achievement of the continuity of care. Transition patients have similar BMI, rate of hospitalization, surgery, adherence to medications and quality of life pre and 12 months post-transition clinic.

Whilst there was a significant reduction in the rate of flares and thereby in the number of outpatient visits in the 12 months post-transition since most patients were in clinical remission.

Disclosure: Nothing to disclose.

P0292

RADIOLOGIC EVALUATION OF FILGOTINIB TREATMENT IN PERIANAL FISTULIZING CROHN'S DISEASE USING A NOVEL SCORING SYSTEM

J. Rimola¹, K.B. Gecse², A. Serone³, J.-F. Colombel⁴, G.R. D'Haens⁵, T. Masior⁶, M. McKevitt³, X. Ren³, D.A. Schwartz⁶, W. Reinisch⁷

¹Hospital Clínic Barcelona, Department of Radiology, Barcelona, Spain,

²Amsterdam University Medical Center, Department of Gastroenterology and Hepatology, Amsterdam, Netherlands,

³Gilead Sciences, Foster City, United States, ⁴Icahn School of

Medicine at Mount Sinai, Gastroenterology, New York City, United States, ⁵Galapagos, NV, Mechelen, Belgium, ⁶Vanderbilt University

Medical Center, Division of Gastroenterology, Hepatology and Nutrition, Nashville, United States, ⁷Medical University of Vienna,

Department of Internal Medicine IV, Division of Gastroenterology and Hepatology, Wien, Austria

Contact E-Mail Address: jrimola@clinic.cat

Introduction: The Van Assche Index (VAI) was developed to evaluate the effectiveness of interventions on perianal fistula activity in Crohn's disease using magnetic resonance imaging (MRI).¹

A modified VAI (mVAI) was introduced to improve measurement of clinical response and intra- and interrater reliability², but recent studies suggest that further optimization is needed.³

Aims & Methods: The Perianal Fistula Activity Index (PFAI) was developed as part of a proof of concept study conducted in patients with perianal fistulizing Crohn's disease that assessed clinical and radiologic efficacy of filgotinib (FIL) (DIVERGENCE 2; NCT03077412).⁴

At the patient level, the total PFAI comprises an Inflammation Sub-Score and Anatomy Sub-Score (see Table). The PFAI differentiates from prior scoring systems by identifying all fistula tracts and branches visible on MRI at baseline and conducting pairwise scoring after treatment, aiming to allow a more comprehensive assessment of disease, including overall inflammatory burden and providing greater sensitivity to change. Pelvic MRIs conducted at baseline and Week 24 were scored using all three indices by a blinded central reader to enable index comparison.

This trial was initiated prior to the publication of the MAGNIFI-CD activity index.⁵

Results: MRIs of patients receiving FIL 100 mg, FIL 200 mg, or placebo (PBO) were scored at baseline (N=57) and week 24 (N=31) (Table). At baseline, all indices were generally balanced across treatment groups with higher scores (greater disease severity) in the FIL 200 mg group. Greater decreases were observed at week 24 in the FIL 200 mg group using the PFAI (-5.1) than the other indices (VAI, -2.1; mVAI, -2.4). At week 24, greater decreases were observed in the PFAI inflammation sub-score (FIL 200 mg: PFAI -4.1, VAI -1.6, mVAI -1.8; FIL 100 mg: PFAI -1.7, VAI -1.3, mVAI -1.0; PBO: PFAI -0.5, VAI -1.0, mVAI 0.3) than the anatomy sub-score (FIL 200 mg: PFAI -1.0, VAI -0.5, mVAI -0.6; FIL 100 mg: PFAI -0.4, VAI -0.2, mVAI -0.2; PBO: PFAI 0.3, VAI 0.2, mVAI 0.3).

Conclusion: In this small phase 2 study, the Perianal Fistulizing Activity Index was shown to enable a higher dynamic range and may be more sensitive to change in comparison to the modified Van Assche Index. More pronounced decreases in the PFAI were observed in the FIL 200 mg group compared to placebo. Use of the PFAI Inflammation subscore may be a useful tool in assessing the effectiveness of interventions on perianal fistulas in Crohn's disease. Additional studies evaluating the Perianal Fistulizing Activity Index are warranted.

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P0293

PREVALENCE AND CLINICAL FACTORS ASSOCIATED WITH NON-ALCOHOLIC FATTY LIVER DISEASE (NAFLD) IN PATIENTS WITH INFLAMMATORY BOWEL DISEASE (IBD)

M. Lopes¹, **D. Shintaku**¹, **A.C. de Oliveira**¹, **R. Fedatto Beraldo**¹, **G. Rodrigues Godoi**¹, **N. Castelhanos**¹, **D. Vulcano**¹, **E.C. de Oliveira**¹, **G. Herrerias**¹, **J. Baima**², **W. Barbosa**¹, **G. Faria Silva**¹, **L. Sassaki**¹
¹São Paulo State University, Internal Medicine, Botucatu, Brazil,
²UNESP Botucatu / UNINOVE Bauru, Botucatu, Brazil

Contact E-Mail Address: ma.lopes@unesp.br

Introduction: Inflammatory Bowel Disease (IBD) is an inflammatory and chronic disease, as well as non-alcoholic fatty liver disease (NAFLD). The pathogenesis of both diseases is related to gut dysbiosis and systemic inflammation, therefore, current literature has shown that IBD patients are at high risk for NAFLD. In addition, it has been observed an increase in NAFLD's incidence in the general population, however, there are few studies evaluating NAFLD's prevalence in IBD patients. This study aimed to evaluate prevalence of NAFLD and identify the clinical factors associated with it in IBD patients.

Aims & Methods: This cross-sectional, descriptive, observational study included 104 IBD patients from an IBD public outpatient in Brazil. Laboratory evaluation and clinical data were collected. The presence of NAFLD was evaluated by ultrasonography. The exclusion criteria were as follows: preexisting liver disease, history of alcohol intake >20g/day for women and >30g/day for men, and glucocorticoids treatment >20mg/day. Statistical analysis: descriptive statistics and association tests.

Results: In total, 104 patients were included, of which 50 (48.08%) were CD's patients and 54 (51.92%) UC patients. Median age was 44.83±14.31 years and the time from diagnosis was 11.41±7.82 years. Mostly, the patients were women (62.5%) and Caucasian (72.12%). Regarding the char-

acteristics of the diseases, 42% of patients with CD have ileocolonic involvement, 42% penetrating disease and 56% perianal involvement; also, most UC patients have pancolitis (62.96%). Mostly, the patients were in clinical (59.62%) and endoscopic (50.08%) remission.

Regarding medical treatment, the most used drugs were biological therapy (57.63%) and azathioprine (47.46%) in CD, and mesalamine (31.12%), azathioprine (46.67%) and biological therapy (51.11%) in UC. NAFLD group consists of 45 (43.27%) patients: 37.78% had mild steatosis; 48.89% moderate and 13.33% intense. Development of NAFLD was associated with body mass index (BMI) and laboratory biomarkers (Table 1).

	No NAFLD (n=59)	NAFLD (n=45)	P
Body Mass Index (BMI)	24.5±4.26	29.17±3.78	<0.0001
Hemoglobin	13.66±1.32 g/dL	14.48±1.62 g/dL	0.0057
AST	24.55±6.36 U/L	28.12±13.14 U/L	0.0295
ALT	18.17±7.55 U/L	27.67±16.54 U/L	<0.0001
Ferritin	84.91±143.06 ng/mL	185.57±333.95 ng/mL	0.0189
Fasting glucose	86.30±9.25 mg/dL	96.85±21.07 mg/dL	0.0054
Triglycerides	120.05±71.37 mg/dL	174.97±118.81 mg/dL	0.0016
HDL cholesterol	58.07±15.01 mg/dL	47.81±16.11 mg/dL	0.0169
Insulin	8.41±5.13 µIU/mL	13.37±8.53 µIU/mL	0.0011

Table 1. Comparison of clinical and laboratory biomarkers among IBD patients with and without NAFLD.

When comparing patients with the presence or absence of NAFLD, there was no difference between the groups regarding time since diagnosis (p=0.3595), previous surgery (p=0.5934), clinical activity (p=0.6361), endoscopic activity (p=0.0576) or medical treatment. However, in the NAFLD group, mostly, the patients were men (51.11% vs 48.89, p=0.0123) and the median age was higher (48.42±12.87 vs 42.03±14.84, p=0.0239).

Conclusion: We observed a high prevalence of NAFLD in patients with IBD. NAFLD group had higher levels of BMI, AST, ALT, fasting glucose and blood insulin, which are also associated with metabolic syndrome. Early diagnosis and appropriate nutritional orientation are necessary to prevent NAFLD related complications.

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P0294

E-CONSULTS IN INFLAMMATORY BOWEL DISEASE (TELEIBD): FACILITATING COMMUNICATION BETWEEN SPECIALIZED AND PRIMARY CARE

C. Pradera Cibreiro¹, M. Ramos Alonso¹, M. Fernández López¹, G. Molina Arriero¹, M.V. Mauriz Barreiro¹, V. Ollero Pena¹, A. Echarr Piudo¹

¹Centro Hospitalario Universitario de Ferrol, Gastroenterology, Ferrol, Spain

Contact E-Mail Address: marta.ramos.alonso@sergas.es

Introduction: According to current literature, incidence and prevalence of Inflammatory bowel disease (IBD) are increasing in the last years ^{1,2}.

Although, inflammatory bowel disease is unusual in primary health care, besides its symptomatology resembles to other pathologies such functional disorders. Taken together with workload and derivation time to specialist medical staff, can be a determining factor in delays in diagnosis and medical complications ³.

The electronic consultations allows the specialist medical staff a quickly and telematic evaluation due to the analytical and clinical results from primary care (PC) ^{4,5}.

Aims & Methods: This is a retrospective study that evaluates the results of TELEII (telematic circuit care) in patients with high diagnostic suspicion of IBD between PC and IBD Unit of our health area from its implementation in August 2019 to October 2020.

The number of telematic consultations, average time to resolution, adaptation to referral criteria, complementary tests requested and diagnostic confirmation were evaluated.

TELEII establishes the issuance of a telematic consultation through the electronic clinical history when a patient meet previously established criteria.

Specialized IBD physician who evaluate the case, can advise a diagnostic or therapeutic attitude either by electronic form or face-to-face with the patient.

Results: A total number of 77 care consultations from 77 patients (58,4% females) have been made. The average age were 49,2 years and the average reponse time were 7,5 days.

After teleconsultation, 46 patients (59.7%) were not requested medical test. Lower gastrointestinal endoscopy (LGE) was performed in 25 patients, blood and faecal calprotectin testing in 7 patients, magnetic resonance (MR) or computer tomographic (CT) enterography in 6 patients.

Taking to account the criteria for referral to a specialist, a total of 15 patients (19,5%) fully met the criteria, 13 patients (16,9%) partially met the criteria and 49 patients (63,6%) did not meet it. The main reason for not meeting the criteria were the inadequate use of TELEII (53,1%).

Of the 25 LGE requested, 3 were suggestive of Ulcerative Colitis (UC) and 1 of Crohn's Disease (CD). Diagnosis of CD was confirmed in 2 patients, using MR or CT enterography.

Diagnoses were reached in 4 patients, 3 of the group that met referral criteria (20%) and 1 of the group that partially met it (7.7%).

The diagnosis was not achieved in any patient who did not partially and/or fully meet the referral criteria.

Conclusion: E-consult allows a faster and easier contact between primary care and IBD specialists. TELEIBD can be a useful tool to reduce the time between suspicion of IBD and its diagnosis and beginning of treatment. Training primary care physicians in the referral criteria of the pathway is essential to improve the functioning of the circuit.

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P0295

BOWEL URGENCY COMMUNICATION GAP BETWEEN HEALTH CARE PROFESSIONALS AND PATIENTS WITH ULCERATIVE COLITIS IN THE US AND EUROPE: COMMUNICATING NEEDS AND FEATURES OF IBD EXPERIENCES (CONFIDE) SURVEY

S. Travis¹, A. Potts Bleakman², D.T. Rubin³, M.C. Dubinsky⁴, R. Panaccione⁵, T. Hibi⁶, T. Hunter Giblee², C. Kayhan², E.J. Flynn², C. Sapin², C. Atkinson⁷, S. Schreiber⁸

¹University of Oxford, Oxford, United Kingdom, ²Eli Lilly and Company, Indianapolis, United States, ³University of Chicago Medicine Inflammatory Bowel Disease Center, Chicago, United States, ⁴Icahn School of Medicine, New York, United States, ⁵University of Calgary, Calgary, Canada, ⁶Kitasato University, Kitasato Institute Hospital, Tokyo, Japan, ⁷Adelphi Real World, Bollington, United Kingdom, ⁸University Hospital Schleswig-Holstein, Kiel, Germany

Contact E-Mail Address: Simon.Travis@ndm.ox.ac.uk

Introduction: Moderate to severe ulcerative colitis (UC) is associated with substantial quality of life burdens¹. The Communicating Needs and Features of IBD Experiences (CONFIDE) study aims to increase understanding of the impact of symptoms on the lives of patients with moderate to severe UC and Crohn's disease and to investigate gaps in communication with healthcare professionals (HCPs) in the United States (US), Europe (EUR), and Japan. This report focuses on patients with moderate to severe UC and HCPs from the US and EUR.

Aims & Methods: Online, quantitative, cross-sectional surveys of patients with UC and HCPs were conducted in the US and EUR (France, Germany, Italy, Spain, and UK). HCP surveys included physicians and non-physician HCPs responsible for making prescribing decisions. Moderate to severe UC was defined based on treatment, steroid use, and/or hospitalization history. Data collected included perspectives on the experience of patients with UC.

Results: A total of 200 US (62% male, mean age 40.4 years) and 556 EUR patients (57% male, mean age 38.9 years), and 200 US and 503 EUR HCPs completed the survey. According to US and EUR patients, the top 3 symptoms currently (past month) experienced were diarrhoea (63% and 50%), bowel urgency (47% and 30%) and increased stool frequency (39% and 30%). Blood in stool was reported as currently experienced by 27% and 24% of US and EUR patients, respectively. Among patients currently experiencing bowel urgency, 47% of US and 27% of EUR patients discuss this symptom at every appointment. Among those who do not discuss bowel urgency at every appointment, 74% and 75% of US and EUR patients would like to discuss this symptom more frequently with their HCP. A total of 30% and 43% of US and EUR patients that ever experienced bowel ur-

gency were not comfortable reporting it to their HCP, with 62% and 58% of these US and EUR patients feeling embarrassed talking about this symptom (Table). HCPs in both the US and EUR ranked diarrhoea (74% and 65%), blood in stool (69% and 65%) and increased stool frequency (38% and 34%) as the top 3 symptoms most reported by patients. According to US and EUR HCPs, the top 4 symptoms proactively discussed in routine appointments were blood in stool (93% and 94%), diarrhoea (90% and 91%), increased stool frequency (82% and 82%) and bowel urgency (76% and 82%). Among HCPs who did not proactively discuss bowel urgency, 47% of US and 40% of EUR HCPs expect patients to bring this up if it is an issue.

	I feel embarrassed talking about it	I feel like my HCP doesn't understand it	I don't feel like my HCP can help me with it	There isn't enough time in our appointments to talk about it	I feel like I'm wasting my HCP's time	I don't know how to explain it to my HCP	I don't know how to explain it to my HCP	My HCP makes me feel nervous/intimidated	Other
US patients, n=37	62%	5%	22%	22%	22%	11%	11%	5%	11%
EUR patients, n=107	58%	13%	22%	21%	14%	20%	11%	8%	4%

Table. Reasons for patients not feeling comfortable discussing bowel urgency with their HCPs
(Patients with UC that reported ever experiencing bowel urgency related to their UC and who were not comfortable reporting bowel urgency to their HCP)

Conclusion: Communication characteristics and gaps were similar between US and EUR patients and HCPs. Bowel urgency is the second-most reported symptom by patients with moderate to severe UC. However, this symptom is not among the HCP-perceived top 3 most reported symptoms. Although a substantial proportion of patients reported a desire to discuss bowel urgency more frequently with their HCP, some patients reported feeling embarrassed talking about it. Many HCPs who do not proactively discuss this symptom expect patients to bring this up. A communication gap was identified and highlights the under-appreciation of bowel urgency as an important symptom of UC^{2,3}.

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P0296

THE IMPACT OF BOWEL URGENCY ON THE LIVES OF PATIENTS WITH ULCERATIVE COLITIS IN THE US AND EUROPE: COMMUNICATING NEEDS AND FEATURES OF IBD EXPERIENCES (CONFIDE) SURVEY

S. Schreiber¹, A. Potts Bleakman², M.C. Dubinsky³, D.T. Rubin⁴, T. Hibi⁵, R. Panaccione⁶, T. Hunter Gible², C. Kayhan², E.J. Flynn², C. Sapin², C. Atkinson⁷, S. Travis⁸

¹University Hospital Schleswig-Holstein, Kiel, Germany, ²Eli Lilly and Company, Indianapolis, United States, ³Icahn School of Medicine, New York, United States, ⁴University of Chicago Medicine Inflammatory Bowel Disease Center, Chicago, United States, ⁵Kitasato University, Kitasato Institute Hospital, Tokyo, Japan, ⁶University of Calgary, Calgary, Canada, ⁷Adelphi Real World, Bollington, United Kingdom, ⁸University of Oxford, Oxford, United Kingdom

Contact E-Mail Address: s.schreiber@mucosa.de

Introduction: Moderate to severe ulcerative colitis (UC) exerts a significant burden on patients' lives¹. Patients with UC report that bowel urgency has a substantial negative impact on their quality of life and psychosocial functioning, however, this symptom is missing from most disease activity indices².

The Communicating Needs and Features of IBD Experiences (CONFIDE) study aims to increase understanding of the impact of symptoms, including bowel urgency, on the lives of patients with moderate to severe UC and Crohn's disease in the United States (US), Europe (EUR), and Japan. These data focus on patients with moderate to severe UC in the US and EUR.

Aims & Methods: Online, quantitative, cross-sectional surveys of patients with moderate to severe UC were conducted in the US and EUR (France, Germany, Italy, Spain, and UK). Data included patient perspectives on their UC symptoms and the impact on their daily lives. Moderate to severe UC was defined based on treatment, steroid use, and/or hospitalization history. Descriptive statistics summarise the data.

Results: A total of 200 US patients (62% male, mean age 40.4 years) and 556 EUR patients (57% male, mean age 38.9 years) completed the survey, with 77% and 54% currently receiving advanced therapies (biologic or novel oral therapy), respectively.

The top 3 symptoms currently (past month) experienced by US and EUR patients were diarrhoea (63% and 50%), bowel urgency (47% and 30%) and increased stool frequency (39% and 30%). Among patients who have ever experienced bowel urgency, 93% of US and 89% of EUR patients reported doing so at least once a month over the past 3 months.

Among patients who have ever experienced urge incontinence (bowel urgency-related accidents), 86% of US and 71% of EUR patients reported doing so at least once a month over the past 3 months (Table).

A total of 69% and 65% of all US and EUR patients with UC, respectively, reported wearing a diaper/pad/protection at least once a month in the past 3 months due to fear/anticipation of urge incontinence.

For patients receiving advanced therapies, similar patterns were observed for frequency of bowel urgency and urge incontinence as well as wearing diaper/pad/protection due to fear/anticipation of urge incontinence.

Among both US and EUR patients, the most common UC-related reasons for declining participation in social events were bowel urgency (43% and 30%) and fear of urge incontinence (40% and 32%).

Similarly, the most common reasons for declining participation in work/school and sports/physical exercise were bowel urgency and fear of urge incontinence.

Conclusion: Bowel urgency, which was the second-most frequently reported symptom, has an extensive impact on the lives of patients with moderate to severe UC. In this younger patient population, including patients receiving advanced therapies, almost two thirds of US and EUR

patients reported wearing diapers/pads/protection at least once a month in the past 3 months due to fear/anticipation of urge incontinence. Even if patients were not currently experiencing bowel urgency, the persistent impact of UC was demonstrated by the use of diaper/pads/protection. Both US and EUR patients reported bowel urgency and fear of urge incontinence as the top reasons for declining participation in social events, work/school, and sports/physical exercise.

	Frequency of bowel urgency (all patients who have ever experienced bowel urgency)		Frequency of urge incontinence (all patients who have ever experienced urge incontinence)		Frequency of diaper/pad/other protection use due to fear/anticipation of urge incontinence (all patients)	
	US patients (n=123)	EUR patients (n=250)	US patients (n=90)	EUR patients (n=175)	US patients (n=200)	EUR patients (n=556)
At least once a month, n (%)	114 (93)	222 (89)	77 (86)	124 (71)	137 (69)	361 (65)
Less frequently than monthly, n (%)	7 (6)	19 (8)	5 (6)	25 (14)	15 (8)	60 (11)
Not in the last three months, n (%)	2 (2)	9 (4)	8 (9)	26 (15)	48 (24)	135 (24)

* Percentages are rounded and as a result totals may not add up to 100%

Table. Frequency of bowel urgency, urge incontinence and diaper/pad/other protection use over the past 3 months*

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P0297

QUALITY CRITERIA IN SCREENING COLONOSCOPY FOR COLORECTAL CANCER IN INFLAMMATORY BOWEL DISEASE

E. Afecto¹, A. Ponte¹, J.P. Laranjeira Correia¹, M.M. Estevinho¹, S. Sousa-Fernandes¹, J.C. Silva¹, T. Freitas¹

¹*Centro Hospitalar de Vila Nova de Gaia/Espinho, Vila Nova de Gaia, Portugal*

Contact E-Mail Address: joaopaulo_laranjeira@hotmail.com

Introduction: Extensive and long-lasting inflammatory bowel disease (IBD) carries an increased risk of colorectal cancer (CRC). Despite this, CRC screening in IBD is not uniform, in part due to the absence of validated quality criteria. In this sense, a group of experts reviewed the evidence and proposed quality criteria in this context. This work intended to audit the fulfillment of the proposed quality criteria in the IBD population of a tertiary center in Portugal.

Aims & Methods: We retrospectively included patients with IBD who underwent CRC screening colonoscopy. Pre-, intra- and post-procedure criteria were evaluated, namely surveillance interval, inflammatory activity, information provided, informed consent, use of polyethylene glycol and liquid diet the day before the procedure, sedation, cecal/ileal intubation rate, adenoma detection rate [ADR], chromoendoscopy, validated scores, directed/random biopsies, withdrawal time, Boston Bowel Preparation scale, photo-documentation, follow-up instructions and identified lesions, visualization and/or resection technique).

Results: Included 84 patients, 70.2% men, mean age 55.2 years, of which 67.9% had ulcerative colitis. The majority (72.6%) underwent the exam at the appropriate interval. Of the total, 9.5% had inadequate preparation and 7.1% had significant inflammatory activity. All procedures were performed under sedation, with a cecal intubation rate of 96.4%. Chromoendoscopy was performed in 89.3%, with an ADR of 21.3%. Withdrawal time was not evaluated. The lesions identified were evaluated by the Paris classification in 31.4% and the resection technique was always described.

In the report, inflammation was evaluated using validated scores (70.4%), photodocumentation was performed (97.5%), number/location of biopsies were described (93.8%), complications were described (0 cases) and follow-up instructions were given (25 %).

Conclusion: Although the results are satisfactory, some points such as the systematic use of the Paris classification and inflammatory activity scores still need to be improved. Follow-up instructions are provided by the treating physician and as such are not provided systematically in our reports. Audits are a vital tool for improving quality in endoscopy and its implementation should be widespread.

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P0298

SARCOPENIA AS A PREDICTIVE MARKER IN INFLAMMATORY BOWEL DISEASE

E. Afecto¹, S. Sousa-Fernandes¹, C. Rocha¹, J.P. Laranjeira Correia¹, M.M. Estevinho¹, A. Ponte¹, T. Freitas¹

¹Centro Hospitalar de Vila Nova de Gaia/Espinho, Vila Nova de Gaia, Portugal

Contact E-Mail Address: joapaulo_laranjeira@hotmail.com

Introduction: Sarcopenia can occur in chronic conditions such as Crohn's Disease (CD) and has been associated with worse clinical and surgical outcomes. In this study, the authors aim to assess the prevalence of sarcopenia in CD patients and determine its prognostic value.

Aims & Methods: Patients with CD undergoing intestinal ultrasound (IUS) in our center were prospectively included. Patients with other potential causes for sarcopenia were excluded. Demographic, clinical and ultrasound data were collected. Anthropometric data were recorded: body mass index, thickness of the femoral quadriceps (by ultrasound) and the time required to transverse 4 meters. Sarcopenia was defined as a composite outcome of decreased muscle mass (quadriceps thickness <34mm in women or <36mm in men) and function (abnormal if >3.2s to transverse 4m). Patients were evaluated for symptoms (Harvey-Bradshaw score - HBI) and complications (abscess/phlegmon, fistula, stenosis, hospitalization, surgery or therapeutic intensification) at 0/3/6 months.

Results: A total of 52 patients were included (50% men), mean age 46.3 years, most with ileal disease (94.2%, L1 or L3 from Montreal classification). Almost half (48.1%) of patients had low muscle mass and 11.5% had sarcopenia. The majority (54%) had inactive IUS disease and a mean initial HBI of 2.6 (75% in clinical remission). At follow-up, 10 patients (18.5%) had an event at 3 months and 4 (7.4%) at 6 months. Muscle thickness at baseline correlates with clinical response at 3 months ($p=0.007$) and inversely with baseline HBI ($p=0.008$, $r=2.75$). Sarcopenia is associated with reduced clinical response at 3 months ($p=0.02$).

Conclusion: The assessment of muscle mass by ultrasound and function is simple to perform in an outpatient setting and allows for the identification of patients who probably need more intensive therapeutic interventions and more frequent monitoring.

Disclosure: Nothing to disclose.

P0299

INDICATIONS, OUTCOMES AND OTHER ASPECTS RELATED TO THE USE OF THE ENDOSCOPIC CAPSULE IN THE PEDIATRIC AGE

T. Gómez Escribano¹, L.M. Palomino Pérez², M. Velasco Rodríguez-Belvis², J.A. Vázquez Gómez², E. Cañedo Villaroya², G. Domínguez Ortega², A. de la Mano Hernández², R.A. Muñoz Codoceo²

¹Universidad Autónoma de Madrid, Madrid, Spain, ²Hospital Infantil Universitario Niño Jesús, Gastroenterología y Nutrición, Madrid, Spain

Contact E-Mail Address: laura_palomino_perez@hotmail.es

Introduction: Video capsule endoscopy (ECV) has marked a turning point in the diagnostic imaging of small bowel lesions in the last two decades. It is a safe and well-tolerated diagnostic test for children but most studies of ECV apply to adults. The literature available today on the clinical use of ECV in the pediatric population is very limited.

Aims & Methods: The aim is to review the indications for ECV in the paediatric population and to analyse the therapeutic impact of its outcomes. Single-centre descriptive and retrospective study of a cohort of patients under 18 years of age who underwent VCE in a tertiary hospital from March

2017 to January 2022. Demographic, anthropometric, clinical and analytical data were collected. The study was considered complete in those in whom the arrival of ECV to the cecum was objectified. The statistical study was performed using SPSSv.28 software.

Results: Sixty patients, 53% female, aged 10.7 ± 4.37 years were included. The main indication for ECV was inflammatory bowel disease (IBD) in 34 (56.7%) patients, followed by gastrointestinal bleeding of unknown origin in 8 (13.3%). In 9 patients (15%) the self-degrading capsule was previously administered, with VCE being contraindicated in 3 (5%) due to delayed expulsion and/or deformation of the capsule.

Most children underwent liquid diet preparation the previous day (95%) and the study was complete in 45 (75%) of cases, with a higher proportion of complete studies in children with liquid diet preparation vs. those taking laxatives or a combination of laxatives and liquid diet ($p=0.017$). In 30 patients (50%) ECV was swallowed voluntarily, with differences according to age: oral ingestion was more frequent in older children (13.34 ± 3.18 years), while placement by upper endoscopy (EDA) was more frequent in younger children (7 ± 2.87 years) ($p<0.001$).

Among the 57 patients studied with ECV, 5 (8.8%) had complications: capsule retention in 3 (5.3%) and minor bleeding in 2 (3.5%) due to traumatic injury related to EDA placement. A lower proportion of complications was observed in the absence of pathological lesions in the small intestine ($p<0.001$). In 9 (15%) of the children the performance of ECV changed the diagnosis, supported by other complementary tests in all but one (88.8%). In relation to treatment, in 13 (20%) patients treatment was changed, with ECV being the only test that conditioned such a change in 5 (38.7%).

Conclusion: In our centre, VCE placement by UGE was significantly more frequent in the younger patients. Also, those who received an exclusively liquid diet the day before the VCE were more likely to have a complete exploration. Furthermore, ECV has an impact on the diagnosis and therapeutic approach to paediatric patients with digestive pathology and, although the rate of complications is higher than that described in adults, it is a safe and non-invasive technique.

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P0300

POSSIBILITIES FOR DIFFERENTIAL DIAGNOSIS OF NOSOLOGICAL FORMS OF INFLAMMATORY BOWEL DISEASE USING ERYTHROCYTE AND BLOOD SERUM MEMBRANE FATTY ACIDS

M.V. Kruchinina^{1,2}, I.O. Svetlova^{1,2}, N.V. Abaltusova¹, A.V. Borisova¹, M.V. Shashkov³, A.S. Sokolova⁴, I.N. Yakovina⁵, A.A. Shestov⁶, A.A. Gromov¹

¹Research Institute of Internal and Preventive Medicine - Branch of the Institute of Cytology and Gen, Siberian Branch of the Russian Academy of Sciences, Novosibirsk, Russian Federation,

²Novosibirsk State Medical University, Novosibirsk, Russian Federation, ³Boreskov Institute of Catalysis, Siberian Branch of the Russian Academy of Sciences, Novosibirsk, Russian Federation,

⁴Vorozhtsov Institute of Organic Chemistry, Siberian Branch of the Russian Academy of Sciences, Novosibirsk, Russian Federation,

⁵Novosibirsk State Technical University, Novosibirsk, Russian Federation, ⁶University of Pennsylvania, Perelman School of Medicine, Philadelphia, United States

Contact E-Mail Address: kruchmargo@yandex.ru

Introduction: The differential diagnosis of nosological forms in patients with inflammatory bowel diseases (IBD) is now crucial for the individual management of the patient, as each clinical case involves specific therapeutic strategies and prognoses [1].

Nevertheless, non-classical forms of both ulcerative colitis (UC) and Crohn's disease (CD) still pose a diagnostic problem, since there is no single "gold standard" for the diagnosis of IBD [1].

Therefore, between 5% and 15% of cases of IBD do not meet the strict criteria for either UC or CD [2], and in 14% of patients diagnosed with both UC and CD, the diagnosis changes over time [3].

Aims & Methods: The purpose of this research: To study erythrocyte (Er) membrane fatty acids' (FA) and blood serum (BS) FAs' levels in patients with different nosological forms of IBD (UC, CD, unclassified colitis (UCC) for possible use in differential diagnosis as biomarkers.

Materials and methods: 110 patients (average age 37.7±12.1 years) with IBD and 53 subjects of the comparison group (43.3±11.7 years) have been examined. The group of patients with IBD included patients with UC – 50 people, with CD – 41 people and 19 patients with UCC. In 42 patients (84%) with UC, 34 patients with CD (82.9%) and 11 people with UCC (57.9%), an exacerbation of the disease has been detected. The study of the composition of FAs of Er membranes and BS has been performed using a gas chromatography-mass spectrometry (GC/MS) system based on the Agilent 7000B Triple Quadrupole (USA).

Results: A study of FA levels in groups with different nosological forms of IBD using complex statistical analysis, including machine learning techniques, has made it possible to create diagnostic models that differentiate between CD, UC and UCC in the acute stage with a high degree of accuracy. The most significant for distinguishing active UC from exacerbation of CD were serum levels of C18:1;t9 (p=0.0006); C22:4n-6 (p=0.004); C20:2n-6 (p=0.009); omega-3/omega-6 PUFA ratio (p=0.02); C20:5n-3 (p=0.03) acids; the sum of two omega-3 PUFAs – C20:5n-3 and C22:6n-3 (p=0.03) acids, as well as the content of C12:0 of Er (p=0.04) (AUC 0.89; sensitivity 0.91; specificity 0.89; diagnostic accuracy 0.91). The revealed differences may be due to a greater violation of the regulation of PUFAs' desaturation in CD than in UC [4], differing profiles of significant cytokines, adiponectins in different nosological forms of IBD, which is associated with FAs' levels of serum and erythrocytes [5, 6].

The following BS FAs have been found to be relevant in distinguishing active UC from the acute stage of UCC: C18:3n-3; saturated (pentadecanoic, palmitic, stearic, arachidic); monounsaturated (C16:1;9, C18:1;9); omega-6 PUFA (C16:2, 20:4) (p=0.00000011-0.033) (AUC 0.995; sens. 0.98; spec.

0.96; diagnostic accuracy 0.97) An increase in the level of saturated FAs in UC is associated with a macrophage inflammation and lipotoxicity [7].

The levels of the following FAs were the most significant for differentiating patients with active CD from exacerbations of UCC: C18:3n-3; C16:1;9; C18:1;9; sum of SFAs; sum of USFAs; C18:0; sum of MUFAs; SFAs/USFAs ratio; SFAs/PUFA; C18:2n-6; sum of omega-6 PUFAs; C12:0; C20:0 (p=0.000000017-0.03) (AUC 0.914; sens. 0.90; spec. 0.87; diagnostic accuracy 0.91).

The significance of different lists of FAs for distinguishing UCC from UC and CD indirectly reflects the heterogeneity of patients with unclassified colitis.

Conclusion: The proposed approach seems promising for the purposes of differential diagnosis of nosological forms of IBD.

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P0301

DELAYED IBD DIAGNOSIS LEADS TO WORSE OUTCOMES OVER YEARS, WITH MULTIPLE IMPLICATIONS ON SERVICE DELIVERY

A. Rao¹, A. Bazarova², P. Mitra³, S. Majumder^{4,1,5}, T.L. Parigi^{4,1}, S. Ghosh⁶, M. Iacucci^{7,4,1}, U.N. Shivaji^{7,4,1}

¹University Hospitals Birmingham NHS Foundation Trust, Gastroenterology, Birmingham, United Kingdom, ²University of Cologne, Institute for Biological Physics, Köln, Germany, ³University of Birmingham, Biomedical Sciences, Birmingham, United Kingdom, ⁴Institute of Immunology and Immunotherapy, University of Birmingham, Immunology and Immunotherapy, Birmingham, United Kingdom, ⁵University of Birmingham, India Institute, Birmingham, United Kingdom, ⁶College of Medicine and Health, University College Cork, APC Microbiome, Ireland, Cork, Ireland, ⁷National Institute for Health Research NIHR Birmingham Biomedical Research Centre, University Hospitals Birmingham, Gastroenterology, Birmingham, United Kingdom

Contact E-Mail Address: abs.rao@doctors.org.uk

Introduction: Delays in diagnosis could be patient-related and health-system related. It has been reported that such delays increase overall complications in Inflammatory Bowel Diseases (IBD). The aim of our study was to report on the impact of delays on IBD-related adverse outcomes (AOs), as most hospitals currently face challenges with long waiting lists in the post-Covid-19 era.

Aims & Methods: New patients referred for suspected IBD to a single tertiary care centre between Jan 2013 to Dec 2017 were identified using EMR. For purposes of the study, a cut-off time was set by investigators for each delay-type based on best average hospital waiting times. The reasons for delays in patient journey until start of treatment and data on pre-defined AOs (steroid & other rescue therapies, hospitalisations, surgery) were recorded for each patient until end of June 2021.

The data were analysed using multiple Pearson correlations and Cox proportional Hazard model to determine whether there is a difference in survival without AOs between patients with and without a delay.

Results: Total of 105 patients were identified using stringent criteria (M=58; median age = 32y) with a long median follow-up of 55 months. The most frequent presenting complaints were abdominal pain (44, 41.9%), loose stools (40, 38.1%), bloody diarrhoea (37, 35.2%) and bleeding per rectum (33, 31.4%) and only 16% declared a family history. 65, 27 and 13 patients had final diagnosis of Ulcerative colitis, Crohn's disease and Unclassified colitis respectively, and analysed collectively.

In our cohort, the longest delay-types noted were - patients seeking medical attention (median= 4 months; range 1 to 84 months), arranging gastroenterology clinic review after referral from primary care (median=5 weeks; range 1 to 30 weeks), and waiting for index endoscopy (median=3 weeks; 1 to 36 weeks).

Patient stratification based on delay-type, using specific cut-off times for each showed a statistically significant difference in survival without AOs for all (when comparing delay v/s no delay).

- delay in seeking medical attention (cut-off=1m; $p=0.004$)
- delay in GP referral to specialty review (cut-off=1w; $p=0.048$)
- delay in index endoscopy (cut-off= 4w; $p=0.01$)
- delay in starting treatment (cut-off= 4w; $p=0.03$)

Conclusion:

- Several bottlenecks of delays increase AOs in IBD over the follow-up period.
- A delay as short as a week, between GP referral to specialty review, is significant in determining AOs; this has implications on specialist IBD centres particularly in the post-Covid period.

- Endoscopy units should prioritise suspected IBD patients to reduce AOs, which is likely to have implications on service delivery and planning.
- Long delays observed in patients seeking medical attention highlights the need for both primary and secondary care to undertake patient education in the community.

Disclosure: Nothing to disclose.

P0302

SYSTEMATIC REVIEW AND META-ANALYSIS: MICROSCOPIC COLITIS IS A RISK FACTOR FOR LOW BONE DENSITY

A. Rancz^{1,2}, B. Teutsch^{1,3}, M.A. Engh¹, D. Veres⁴, L. Földvári-Nagy⁵, B. Eröss^{1,3,6}, N. Hosszúfalusi², M.F. Juhász³, P. Hegyi^{1,3,6}, E. Mihály²

¹Centre for Translational Medicine, Semmelweis University, Budapest, Hungary, ²Semmelweis University, Department of Internal Medicine and Hematology, Budapest, Hungary, ³Institute for Translational Medicine, Medical School, University of Pécs, Pécs, Hungary, ⁴Semmelweis University, Department of Biophysics and Radiation Biology, Budapest, Hungary, ⁵Eötvös Loránd University, Department of Genetics, Budapest, Hungary, ⁶Heart and Vascular Center, Semmelweis University, Division of Pancreatic Diseases, Budapest, Hungary

Contact E-Mail Address: rancz.anett@gmail.com

Introduction: Microscopic colitis (MC), is a chronic inflammatory bowel disease characterized by watery diarrhea, which substantially decreases the patient's quality of life.

Moreover, low bone density (LBD) has been associated with the disease. Furthermore, many risk factors contribute to the random coincidence of the two conditions.

Aims & Methods: Our primary aim is to assess if MC is a risk factor for LBD. We also estimated the proportions of bone mineral changes in the MC population. Our protocol was prospectively registered in PROSPERO (CRD42021283392).

We directed our literature search in five databases from inception to the 16th of October, 2021 (Pubmed, Embase, Cochrane, Scopus, Web of Science). All articles were eligible which describe histologically confirmed MC patients. We used the random-effect model to calculate pooled odds ratios (ORs) and pooled event rates with 95% confidence intervals (CI).

We assessed the risk of bias with the aid of the QUIPS tool for the prognostic question, and we applied the JBI Critical Appraisal Checklist for Prevalence Studies in the proportional measurements. To ascertain the quality of evidence for our outcomes we followed the recommendations of the GRADE working group.

Results: The systematic search yielded a total of 3046 articles. Four articles were found eligible for our quantitative synthesis. Three of them used age- and sex-matched controls to evaluate the occurrence of LBD among MC patients. We analyzed 111 MC patients with 67 LBD cases in comparison to 265 controls with 110 LBD cases. The odds for having LBD was threefold higher (OR=2.96, CI: 1.15–7.59) in the presence of MC.

The rate investigation results showed that from 276, 182 and 182 MC patients a total of 189, 92 and 20 patients had LBD, osteopenia and osteoporosis, respectively. The proportion of LBD was 0.68 (CI: 0.56–0.78), osteopenia was 0.51 (CI: 0.43–0.58) and osteoporosis was 0.11 (CI: 0.07–0.16) among the MC patients.

Most of the studies carried a high risk of bias due to the low number of study participants, while the certainty of the evidence was very low owing to the small sample sizes and because of the use of a surrogate outcome, measuring the bone mineral density.

Conclusion: LBD is strongly associated with MC, and the appearance of LBD is tripled in the presence of MC. There is a crucial need for further prospective studies with high patient numbers and long follow-up periods on this topic.

Disclosure: Nothing to disclose.

P0303

NON-INVASIVE ASSESSMENT OF NON-ALCOHOLIC FATTY LIVER DISEASE IN PATIENTS WITH INFLAMMATORY BOWEL DISEASES

S. Dragasevic¹, A. Djajic², T. Milovanovic (former Alempijevic)¹, S. Rajic³, L. Toncev³, S. Djuranovic¹, A. Milutinovic¹, M. Stojkovic Lalosevic¹, M. Stulic¹, S. Lukic¹, D. Popovic¹

¹University Clinical Center Serbia, Belgrade, Serbia/School of medicine, University of Belgrade, Clinic for Gastroenterology and Hepatology, Belgrade, Serbia, ²School of Medicine, University of Belgrade, Belgrade, Serbia, ³University Clinical Center Serbia, Clinic for Gastroenterology and Hepatology, Belgrade, Serbia

Contact E-Mail Address: dragasevicsanja@gmail.com

Introduction: Inflammatory bowel disease (IBD) is characterized by a chronic inflammatory process, which includes Crohn's disease (CD) and ulcerative colitis (UC). Non-Alcoholic Fatty Liver Disease (NAFLD) occurs in up to 40% of patients with CD and UC with the accumulation of fat in hepatocytes that affects more than 5% of the liver parenchyma. Due to the rapidly increasing prevalence of IBD, there is a tendency for NAFLD detection at the earliest period of development despite the fact that often appears without symptoms and is frequently misdiagnosed.

Although abdominal ultrasonography is an initial non-invasive diagnostic method, in order to make it faster and easier to diagnose, Hepatic Steatosis Index (HSI) and NAFLD Liver Fat Score (NAFLD-LFS) are used in clinical practice.

Aims & Methods: The aim of the study was to assess the prevalence of NAFLD using non-invasive scores in patients with newly diagnosed IBD. The study included 110 patients with CD and 113 with UC. The presence of NAFLD was assessed using two scores HSI and NAFLD-LFS. Statistical analysis was performed in the software program SPSS 21.0 (IBM SPSS Statistics, Chicago, USA).

Results: According to HSI values, the diagnosis of NAFLD was marked as highly-suspicious in 30.1% of UC patients and 37.3% of CD patients. According to NAFLD-LFS values, NAFLD is highly-suspicious in 51.3% of UC patients and in 57.3% of CB patients. The results showed no statistically significant difference in the frequency of NAFLD morbidity between CD and UC patients. For HSI $p=0.2975$, and for NAFLD-LFS $p=0.3052$.

Conclusion: Non-invasive NAFLD scores have proven to be fast, simple, and easy to apply in clinical practice. They could potentially be considered as a screening method for diagnosis of NAFLD in IBD patients and could influence further therapy modalities.

Disclosure: Nothing to disclose.

P0304

TRYPTOPHAN DEGRADATION PRODUCTS AS UNIFYING BIOMARKERS OF SEVERITY AND LONG-TERM DISEASE CONTROL IN CHRONIC INFLAMMATORY DISEASES

D. Harris^{1,2}, N. Engelbogen³, C. Ogris⁴, S. Sari¹, A. Franke¹, F. Tran^{5,1}, J. Labrenz¹, R. Junker³, M. Kisiela¹, C. Conrad⁶, S. Schuchardt⁷, B. Hoyer⁸, P. Rosenstiel¹, S. Schreiber⁶, S. Szymczak⁹, S. Waschina², K. Aden^{1,6}

¹Kiel University, University Hospital Schleswig-Holstein, Institute of Clinical Molecular Biology, Kiel, Germany, ²Kiel University, Nutriinformatics, Kiel, Germany, ³University Hospital Schleswig-Holstein, Institute of Clinical Chemistry, Kiel, Germany, ⁴Helmholtz Zentrum München, Institute of Computational Biology, Neuherberg, Germany, ⁵University Medical Center Schleswig-Holstein, Campus Kiel, Department of Internal Medicine I, Kiel, Germany, ⁶University Hospital Schleswig-Holstein, Department of Internal Medicine I, Kiel, Germany, ⁷Fraunhofer Institute for Toxicology and Experimental Medicine, Department of Bio and Environmental Analytics, Hannover, Germany, ⁸Kiel University, University Hospital Schleswig-Holstein, Rheumatology, Kiel, Germany, ⁹Lübeck University, Institute for Medical Biometry and Statistics, Lübeck, Germany

Contact E-Mail Address: d.harris@ikmb.uni-kiel.de

Introduction: Tryptophan (Trp) metabolism is altered in inflammatory bowel disease (IBD), with an increased demand for Trp via the kynurenine pathway. Serum Trp levels negatively correlate with disease activity in ulcerative colitis and Crohn's disease patients, suggesting that altered Trp metabolism may indicate the degree of chronic inflammation.

Whether increased Trp degradation is specific to IBD or reveals a generalized pattern among chronic inflammatory diseases (CIDs) is unknown.

Aims & Methods: We used several clinical cohorts to assess the association of Trp metabolism with CIDs.

Cohort #1: Serum Trp measurement in a multi-observation, cross-sectional cohort that includes patients diagnosed with CIDs of the gastrointestinal tract (IBD), musculoskeletal system (rheumatoid diseases, RD), and skin ($n=1410$ CID; 291 healthy controls, $n=28,849$ observations). Serum Trp measurement was performed within clinical routine laboratory diagnostics.

Cohort #2: Targeted serum metabolomics on Trp and its derivatives in $n=267$ CID patients and $n=200$ healthy controls.

Cohort #3: Targeted serum metabolomics in a longitudinal therapy response cohort, $n=133$ CID patients (IBD, $n=88$; RD, $n=36$, skin, $n=15$; 15 biological therapies).

We performed serum metabolomics at baseline, week 2, 6, and 14. Therapy responders were identified as patients who adhered to their respective biologic therapy for 12 months following initial administration. All targeted metabolomics assays were performed by LC-MS/MS using the MxP Quant 500 kit (Biocrates).

Results: Serum Trp levels were decreased in the cross-sectional cohorts across IBD and all musculoskeletal disease, yet slightly higher in serum of psoriasis patients relative to healthy controls. Trp levels correlated with disease activity in IBD patients and RD patients. Intriguingly, Trp levels appear to destabilize with disease progression, as demonstrated by the increase in Trp variability over time with therapy escalation to biologic therapy.

We assess the ratio of Trp/aromatic amino acids to normalize for dietary Trp intake, finding Trp to represent roughly one third of the aromatic amino acids in healthy controls (0.32 ± 0.03), with a significant reduction in this ratio across all CIDs tested.

Most strikingly, in our longitudinal cohort, this ratio increased over time in therapy adherers, but not non-adherers ($p = 0.0038$ and 0.39 , respectively), suggesting restoration of Trp metabolism occurs early in responders to biologic therapy – i.e., within the first 14 weeks upon therapy administration.

Conclusion: Tryptophan metabolism is perturbed across CIDs, suggesting that aberrant tryptophan metabolism is a universal feature underlying chronic inflammation. Further, early restoration of aberrant tryptophan metabolism only occurs in patients within 12-month therapy adherence indicating a unique pattern of metabolic healing that indicates thorough disease control in CID patients.

Disclosure: Nothing to disclose.

P0305

ENDOSCOPIC SCORES AS PREDICTORS OF TREATMENT FAILURE IN ULCERATIVE COLITIS

A.I. Ferreira^{1,2,3}, T. Lima Capela^{1,2,3}, S. Xavier^{1,2,3}, C. Arieira^{1,2,3}, T. Cúrdia Gonçalves^{1,2,3}, F. Dias de Castro^{1,2,3}, M.J. Moreira^{1,2,3}, J. Berkeley Cotter^{1,2,3}

¹Hospital Senhora da Oliveira – Guimarães, Gastroenterology Department, Guimarães, Portugal, ²Life and Health Sciences Research Institute (ICVS), School of Medicine, University of Minho, Braga, Portugal, ³ICVS/3B's, PT Government Associate Laboratory, Guimarães/Braga, Portugal

Contact E-Mail Address: tiagolimacapela@gmail.com

Introduction: The endoscopic Mayo score (MS) is the most frequent score used for the evaluation of inflammatory activity in Ulcerative Colitis (UC), varying from 0 to 3 points. Recently the DUBLIN score (DS) emerged, which varies from 0 to 9 points and results from the product of the MS and the disease extent, according to Montreal classification, E1-E3.

Aims & Methods: In this study we aimed to evaluate and compare the predictive ability of MS and DS for long term treatment failure. A retrospective and unicentric study was conducted, including patients with left-sided or extensive UC, asymptomatic and without the need for steroid therapy or therapy changes in the 6 months prior to undergoing total colonoscopy with calculation of MS and DS.

Treatment failure was evaluated, defined by the need for therapy changes and/or hospitalization because of disease exacerbation, over a follow-up period of a minimum of 24 months and a maximum of 84 months.

Results: A total of 204 patients were included, 104 (51%) females and with a mean age at diagnosis of 36.4 ± 12.7 years. In the initial evaluation, 48 (23.5%) were being treated with anti-TNF α medication. The mean values of MS were 1.0 ± 1.1 points and of DS were 2.2 ± 2.6 points.

During follow-up, 32 (15.7%) patients experienced treatment failure and patients initially treated with anti-TNF α medication had 2.3 times higher risk of treatment failure ($p=0.042$). MS values (AUC 0.809; $p<0.001$; with sensitivity of 0.938 and specificity of 0.529 for values equal or superior to 1) and DS values (AUC 0.789; $p<0.001$; with sensitivity of 0.844 and specificity of 0.581 for values equal or superior to 2) had good discriminative abilities in predicting treatment failure. There were no statistically significant differences in the discriminative ability between both scores ($p=0.340$).

Conclusion: MS and DS had good discriminative abilities in predicting treatment failure. However, the integration of the disease extent in the DS as a complement of MS in the evaluation of UC was not associated with a higher predictive ability of long term treatment failure.

Disclosure: Nothing to disclose.

P0306

METAGENOMIC ANALYSIS OF A SIGNATURE GUT MICROBIOME BIOMARKER IN CROHN'S DISEASE ACROSS FIVE POPULATIONS

J. Zhang^{1,2,3}, W. Zhu^{1,2,3,4}, Q. Sun^{1,2,3}, M. Zhang^{1,3}, C. Liu^{1,3}, J.Y.L. Ching^{1,2}, J. Zheng^{1,2,3}, M. Morrison⁵, M.A. Kamm^{6,7}, F.K. Chan^{1,3,8}, S.C. Ng^{1,2,3,9}

¹The Chinese University of Hong Kong, Department of Medicine & Therapeutics, Hong Kong, Hong Kong, China (SAR), ²The Chinese University of Hong Kong, State Key Laboratory of Digestive Disease, Li Ka Shing Institute of Health Sciences, Hong Kong, Hong Kong, China (SAR), ³Microbiota I-Center (MagIC), Hong Kong, Hong Kong, China (SAR), ⁴The Chinese University of Hong Kong, Department of Anaesthesia and Intensive Care and Peter Hung Pain Research Institute, Hong Kong, Hong Kong, China (SAR), ⁵The University of Queensland Diamantina Institute, Faculty of Medicine, Brisbane, Australia, ⁶St Vincent's Hospital, Department of Gastroenterology, Melbourne, Australia, ⁷The University of Melbourne, Department of Medicine, Melbourne, Australia, ⁸The Chinese University of Hong Kong, Faculty of Medicine, Hong Kong, Hong Kong, China (SAR), ⁹The Chinese University of Hong Kong, Centre for Gut Microbiota Research, Faculty of Medicine, Hong Kong, Hong Kong, China (SAR)

Contact E-Mail Address: zhangjingwang12@gmail.com

Introduction: There is a need for non-invasive biomarkers to facilitate early and accurate diagnosis of Crohn's disease (CD). Here, we identified fecal microbial signatures in CD and examined their potential role as non-invasive biomarkers for CD.

Aims & Methods: We included 484 subjects (266 CD; 218 age- and sex-matched healthy controls) from three cohorts (two from Hong Kong and one from Australia). We performed shotgun metagenomic sequencing of stool samples and analyze bacterial composition.

We identified bacterial features associated with disease phenotype using Boruta algorithm. We used random forest algorithm for diagnostic model construction.

We further validated the performance of the model in three public datasets including 136 CD cases and 110 controls.

Results: Bacterial diversity and richness were significantly lower in CD than controls (all $P<0.01$). Principal Coordinates Analysis (PCoA) showed that the bacterial clusters in CD and controls were distinctly separated ($P<0.001$).

Compared with control samples, the genera *Firmicutes* was depleted while *Proteobacteria* and *Fusobacteriawere* enriched in CD samples. In a discovery cohort, we identified nine bacterial species that differentiated CD from controls with an area under the receiving-operator curve (AUC) of 0.90.

The discriminative ability of these nine bacterial markers was validated in an independent cohort of 300 subjects from Hong Kong and 120 subjects from Australia with AUCs of 0.76 and 0.81, respectively.

Ecological network analysis of these nine bacteria markers in three different cohorts showed co-occurring (positive) correlations among CD-depleted bacteria and co-excluding (negative) correlations among CD-enriched and CD-depleted bacteria in all three cohorts.

In our validation cohort utilizing metagenomic datasets from the United States, Netherlands, and Mainland China, our bacteria markers showed that CD can be distinguished from controls with AUCs of 0.892, 0.844 and 0.966, respectively.

Conclusion: We presented metagenomic profiling of CD fecal microbiomes across five populations and identified a universal microbial signature for CD diagnosis. This may serve as a non-invasive biomarker for early CD detection and monitoring.

Disclosure: Siew Chien Ng and Francis Ka Leung Chan are the scientific co-founders and sit on the board of Directors of GenieBiome Ltd. Siew Chien Ng has served as an advisory board member for Pfizer, Ferring, Janssen, and Abbvie and a speaker for Ferring, Tillotts, Menarini, Janssen, Abbvie, and Takeda. She has received research grants from Olympus, Ferring, Janssen and Abbvie. Francis Ka Leung Chan has served as an advisor and lecture speaker for Eisai Co. Ltd., AstraZeneca, Pfizer Inc., Takeda Pharmaceutical Co., and Takeda (China) Holdings Co.

P0307

ENDOSCOPIC FEATURES OF NON-IBD COLITIS

F. Pigò¹, H. Bertani¹, S. Mangiafico¹, G. Grande¹, S. Russo¹, S. Cocca¹, M. Lupo¹, R. Conigliaro¹

¹Azienda Ospedaliero Universitaria of Modena, Endoscopic Unit, Modena, Italy

Contact E-Mail Address: giuseppgrande1984@gmail.com

Introduction: The term non-IBD colitis refers to a heterogeneous group of inflammatory diseases of the colon which may be differentiated from Crohn's disease and Ulcerative Colitis by their clinical, endoscopic, and histological characteristics. Previous studies on the endoscopic aspect of non-IBD colitis are scarce, with incomplete clinical and histological information necessary for diagnosis.

Aims & Methods: The aim of this retrospective study was to describe the endoscopic appearance of non-IBD colitis in an out-patients cohort.

All cases of non-IBD colitis, in an outpatient base setting from 2018 to 2021, with a colonoscopy performed in the previous three months and complete clinical information, were enrolled. Diagnosis was based on following characteristics: age, sex, symptoms (onset, duration, severity), comorbidities, history of exposure to drugs during the three months preceding the consultation, smoking and alcohol habits, allergies, pathological familial history, laboratory evaluations, stool cultures, imaging, bowel preparation, colonoscopy findings, histologic findings, follow-up of at least six months.

The endoscopic appearance was described with various terms: hyperaemia/erythema (spots or coalescent areas of red mucosa), oedema (areas of swollen mucosa), erosions (small, shallow sores, often surrounded by a ring of red tissue, with irregular shape, like long, ragged marks), ulcers (breaks in the lining of the mucosa, small like aphthae or big with a star-shape or longitudinal), mucopurulent exudate strictly adherent to the underlying mucosa.

Results: 101 patients (63 males, age 54 years $\pm$ 19 SD) performed an outpatient colonoscopy with a final diagnosis of non-IBD colitis associated with drug-exposition in 54 cases, food allergies in 11 cases, recent or active gastrointestinal infections in 12 cases, ischemic colitis in 10 cases, segmental colitis associated diverticulosis (SCAD) in 8 cases, obstructed defecation syndrome in 4 cases and microscopic colitis in 2 cases. Drug exposition was associated with hyperaemia, erosions/ulcers in 88% of cases with involvement of right colon in 73% of cases. Recent infection was related with erosions in 60% of cases with distribution in the left colon and rectum in 88% of cases. Food allergies were associated with red spot areas/erosions in 67% of cases with involvement of all the colon. Ischemic colitis was associated with ulcers in 86% of cases located in the right or left colon. SCAD has a crescentic fold pattern (hyperemia/eodema) in 75% of cases, always in left colon. Hyperemia, erosions, and loss of vascularity were described in 90% of cases of faecal obstruction in the rectum. 2 cases of microscopic colitis presented with oedema, hyperemia in the whole colon.

Conclusion: In an out-patient cohort, drug- associated colitis is the most frequent cause of non-IBD colitis. In an appropriate clinical, laboratory and histological context, small lesions as red spot, hyperaemia and ero-

sions could be associated with drug expositions, recent infection, and food allergies. Ulcers of the colon are more frequent with ischemic colitis or drug exposition.

Disclosure: Nothing to disclose.

P0308

RELATIONSHIP BETWEEN INTESTINAL ULTRASOUND, FECAL CALPROTECTIN AND HARVEY BRADSHAW INDEX IN THE ASSESSMENT OF INFLAMMATORY ACTIVITY IN CROHN'S DISEASE

Á. Montero-Moreton¹, I. Bastón-Rey^{2,3}, C. Calvino-Suarez^{2,3}, D. de la Iglesia-García^{2,3}, R. Ferreiro-Iglesias^{3,2}, S. Maestro Antolin¹, F. Santos-Santamarta¹, A.G. Pérez-Millán¹, J.E. Domínguez Muñoz^{2,3}, M. Barreiro de Acosta^{2,3}

¹Complejo Asistencial Universitario de Palencia, Gastroenterology, Palencia, Spain, ²University Hospital of Santiago de Compostela, Department of Gastroenterology, Santiago de Compostela, Spain, ³Health Research Institute of Santiago de Compostela (IDIS), Santiago de Compostela, Spain

Contact E-Mail Address: manubarreiro@hotmail.com

Introduction: Crohn's disease (CD) is an inflammatory bowel disease with chronic course and exacerbations. Diagnosis and follow-up are based on clinical activity, biomarkers, ileocolonoscopy and imaging techniques. Intestinal ultrasound (IUS) has been shown to have high sensitivity and specificity analyzing inflammatory activity in CD.

Aims & Methods: The aim of our study is to correlate IUS parameters with clinical activity and biomarkers in CD.

METHODS: Retrospective, observational, single-center study was designed. Adult patients with CD who underwent IUS between September 2020 and May 2021 were included. Exclusion criteria was exclusive colonic involvement. Examination was done by ultrasound machine (Hitachi Ascendus) with low frequency curved-array (1-5 MHz) and high-frequency linear-array (5-13 MHz) transducers.

Examination assessed bowel wall thickness, mesenteric fat hypertrophy, lymph nodes, hyperemia on color Doppler flow measured as Limberg index and length of affected segment (cm). Clinical activity score for CD was assessed by Harvey Bradshaw index (HBI). Biomarkers parameters studied were C-reactive protein (CRP) and faecal calprotectin (FC). Results are shown as percentages, median and interquartile range (IQR). Data were analysed using Spearman's correlation analysis.

Results:

		CRP	Faecal Calprotectin	Harvey Bradshaw Index
IUS parameters	Wall thickness	0.29 (0.12-0.44) *	0.35 (0.18-0.50) *	0.09 (-0.09-0.27)
	Limberg Index	0.38 (0.21-0.52) *	0.56 (0.42-0.67) *	0.11 (-0.06-0.29)
	Mesenteric fat hypertrophy	0.35 (0.18-0.50) *	0.43 (0.27-0.57) *	0.13 (-0.05-0.30)
	Lymph nodes	0.33 (0.16-0.48) *	0.43 (0.27-0.57) *	0.15 (-0.03-0.32)
	Length (cm)	0.27 (0.10-0.43) *	0.36 (0.22-0.53) *	-0.005 (-0.18-0.17)

CRP, C Reactive Protein. IUS, Intestinal Ultrasound
*p<0.05

Table 1.

121 patients were consecutively included (median age 45.6 years (IQR 33.4 – 59.6), 56.2% female). 78.5% had ileal disease and 21.5% ileocolonic involvement. At the time of IUS 17.4% of patients were not taking any maintenance treatment, 13.2% were on azathioprine, 48.8% on anti-TNF (61% adalimumab; 39% infliximab) and 8.3% on ustekinumab. 85.1% patients had HBI <6, 14.1% had moderate activity. Median CRP level was 0.334 mg/

dl (IQR 0.06-1.12), FC was 141 µg/g (IQR 35-386). Median wall thickening was 4.7 mm (range 4.1-5.6), 68.6% of patients had mesenteric fat hypertrophy and 73.55% had lymph nodes. Limberg index was 0 in 20.7%, 1 in 23.1%, 2 in 37.2% and 3 in 19% of patients. IUS determined treatment modification in 60.3% of cases: 19% started biological therapy, 15.7% changed biological target, 14.9% underwent intensification or reinduction of biological treatment, in 1.7%, treatment reduction was decided.

The Spearman's correlation between IUS parameters, clinical and biochemical markers is presented in Table 1. IUS parameters were significantly associated with faecal calprotectin and CRP level, specially Limberg Index and faecal calprotectin ($r=0.56$, $p<0.05$) and Limberg Index and CRP level ($r=0.38$, $p<0.05$). No correlation was observed between HBI and IUS parameters.

Conclusion: Through this study, significant correlation between IUS and biomarkers was observed in CD. IUS has been shown to be useful for monitoring CD activity in order to optimize patients treatment.

Disclosure: Nothing to disclose.

P0309

SMOKING AND COLITIS-ASSOCIATED COLORECTAL NEOPLASIA: EXPLORING THE RELATIONSHIP

A. Wijnands¹, S.G. Elias², E. Dekker³, H.H. Fidder¹, F. Hoentjen⁴, J.R. ten Hove¹, J.P.W. Maljaars⁵, A.E. Van Der Meulen - De Jong⁵, E. Mooiweer⁶, R.J. Ouweland¹, C.Y. Ponsioen³, F.D.M. van Schaik¹, H.-P.D. Schultheiss¹, M. Severs¹, B. Oldenburg¹

¹University Medical Centre Utrecht, Department of Gastroenterology and Hepatology, Utrecht, Netherlands, ²Julius Center for Health Sciences and Primary Care, University Medical Centre Utrecht, Department of Epidemiology, Utrecht, Netherlands, ³Amsterdam UMC, Department of Gastroenterology and Hepatology, Amsterdam, Netherlands, ⁴Radboud University Medical Center / University of Alberta, Dept of Gastroenterology and Hepatology, Nijmegen / Edmonton, Netherlands, ⁵Leiden University Medical Center, Department of Gastroenterology and Hepatology, Leiden, Netherlands, ⁶Hospital St Jansdal, Department of Gastroenterology and Hepatology, Harderwijk, Netherlands

Contact E-Mail Address: A.M.Wijnands-3@umcutrecht.nl

Introduction: Prior studies examining the effect of smoking on the risk of colitis-associated colorectal neoplasia (CRN) report conflicting results. Few studies evaluated the effect of smoking in a multivariable model and none investigated a dose-response-relationship.

We aimed to investigate the association between smoking, including possible dose-effects, and CRN in patients with inflammatory bowel disease (IBD).

Aims & Methods: We performed a prospective multicenter cohort study including adult patients with colonic IBD enrolled in a surveillance program between 2011 and 2021 (NCT01464151). The prospective follow-up period was five years. Data collection was completed until 07-2021 for all patients. The effects of smoking status (ever versus never) and pack-years at study entry on recurrent events of CRN (including indefinite, low-grade, and high-grade dysplasia and colorectal cancer) were evaluated by uni- and multivariable Prentice, Williams, and Peterson (PWP) total-time Cox proportional hazard models. In the multivariable model, adjustment for extensive disease, dysplasia prior to or at index (indefinite for dysplasia or low-grade dysplasia), primary sclerosing cholangitis, male sex, first-degree relative with colorectal cancer, and age (continuously) was performed. A PWP-total time Cox proportional hazards model assumes that the occurrence of a first event increases the likelihood of recurrent events,

the maximum number of evaluated recurrent events was three due to otherwise too few data. To account for left truncation, disease duration at study index was used as the timescale in our model.

Results: In total, for 501 of the included 576 patients at least one follow-up procedure was available (median follow-up 5 years). CRN occurred at least once during follow-up in 105 patients. Smoking status at baseline was ever smoking for 246 patients (49%), with a median number of pack-years of 9 (p25-p75 4-20, range 78). In univariable and adjusted analyses smoking status (ever versus never) was not associated with recurrent CRN risk (adjusted hazard ratio 0.97, 95% confidence interval 0.70-1.36). An increase in the number of pack-years was associated with an increased risk of recurrent CRN (adjusted hazard ratio per 10 pack-years 1.16, 95% confidence interval 1.02-1.31). Separate adjusted analyses per IBD type did not reveal differences (Table 1).

Variable	Total cohort (n=501)		UC or IBD-U (n=277)		CD (n=224)	
	HR (95% CI)	p	HR (95% CI)	p	HR (95% CI)	p
Univariable analyses						
Ever smoking (reference = never)	1.19 (0.88-1.61)	0.26	1.26 (0.84-1.90)	0.27	1.18 (0.69-2.01)	0.53
Pack-years (per 10 pack-year increase)	1.25 (1.11-1.42)	<0.05	1.23 (1.05-1.45)	<0.05	1.19 (0.96-1.49)	0.11
Adjusted analyses¹						
Ever smoking (reference = never)	0.97 (0.70-1.36)	0.88	0.99 (0.63-1.54)	0.96	0.80 (0.43-1.51)	0.48
Pack-years (per 10 pack-year increase)	1.16 (1.02-1.31)	0.27	1.09 (0.91-1.30)	0.36	1.05 (0.81-1.36)	0.73

¹: HR adjusted for extensive disease, first degree relative with colorectal cancer, primary sclerosing cholangitis, male sex, age (per year increase, restricted cubic spline with four knots), and prior or index CRN.
Abbreviations: CD=Crohn's disease; CI=confidence interval; CRN=colorectal neoplasia; HR=hazard ratio; IBD-U=inflammatory bowel disease-unclassified; n=number; UC=ulcerative colitis

Table 1: PWP-total time Cox proportional hazards model (timescale IBD disease duration)

Conclusion: This study suggests that an increase in pack-years is associated with a higher risk of recurrent CRN in patients with IBD after adjustment for confounders. No association was observed for smoking status. The suggestion of a dose-effect may be an extra motivation for patients to quit smoking.

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FS: advisory boards Takeda, Dr. Falk, Galapagos.

ED: I have endoscopic equipment on loan of FujiFilm and Olympus, receive a research grant from FujiFilm. I have received honorarium for consultancy from FujiFilm, Olympus, GI Supply, CPP-FAP, PAION and Ambu, and speakers' fees from Olympus, GI Supply, Norgine, IPSEN, PAION and FujiFilm.

P0310

SARCOPENIA IS A POOR PROGNOSTIC FACTOR FOR ENDOSCOPIC REMISSION IN PATIENTS WITH CROHN'S DISEASE

M. Grova¹, F. Crispino², M.F. Maida³, A. Vitello³, S. Renna⁴, A. Casà¹, L. Tesè¹, F.S. Macaluso⁵, A. Orlando¹

¹"Villa Sofia-Cervello" Hospital, Palermo, Italy, ²Gastroenterology & Hepatology Section, PROMISE, Palermo, Italy, ³S. Elia-Raimondi Hospital, Caltanissetta, Gastroenterology and Endoscopy Unit, Caltanissetta, Italy, ⁴"Villa Sofia-Cervello" Hospital, Palermo, Italy, ⁵"Villa Sofia-Cervello" Hospital, Palermo, Italy

Contact E-Mail Address: mauro.grova@gmail.com

Introduction: Sarcopenia is defined as depletion in lean muscle mass with loss of muscle strength and has been associated with poor prognosis in various diseases, including malignancies and chronic inflammatory diseases. As Crohn's disease (CD) is frequently associated with malnutrition and subsequent changes in body composition, sarcopenia has generated much interest in the last years.

Aims & Methods: Our aim was to investigate its role in predicting clinical and endoscopic outcomes in a cohort of Crohn's disease (CD) patients. All consecutive CD patients who started biological therapy between 2014 and 2020 and who had undergone abdominal magnetic resonance or computed tomography within 6 months from the beginning of the therapy were enrolled. Muscle mass was assessed through a simple and fast surrogate index (total psoas area index, TPAI), measured at the third lumbar level (L3).

Patients were grouped into sex-stratified quartiles, and patients in the lowest sex-stratified TPAI quartile were considered as being sarcopenic. Univariate and multivariate analyses were used to evaluate whether sarcopenia could predict steroid-free clinical remission (SFCR), endoscopic remission (ER), hospitalisation and surgery after twelve months of biological therapy.

Results: 358 patients were included. Sarcopenic patients were older (45.6±15.5 vs 39.2±14.6; p=0.001), with lower body mass index (22.2±4.0 vs 23.9±4.5; p=0.001), higher Charlson Comorbidity Index (1±1.3 vs 0.6±1.3; p=0.020), longer disease duration (12.8±10.1 vs 10.2±8.3; p=0.015) and higher age at diagnosis (32.7±13.5 vs 29.0±13.0; p=0.024) than non-sarcopenic patients.

After twelve months of biological therapy, sarcopenic patients had higher SES-CD (5.6±6.7 vs 2.8±4.9; p=0.008) and Rutgeerts score (3.2±1.2 vs 1.7±1.6; p=0.001), and consequently lower rates of endoscopic remission (23.5% vs 47.1%; p=0.014). Conversely, sarcopenia was not associated with SFCR (65.5% vs 70.4%; p=0.391), hospitalisation (7.8% vs 8.2%; p=0.897) and surgery (2.2% vs 6.7%; p=0.108).

After multivariate analysis, sarcopenia was identified as a predictor of lack of ER (Odds Ratio [OR]=2.77, confidence interval [CI] 1.1-7.1; p=0.033), as well as smoking (OR 2.63, CI 1.2-5.9; p=0.018) and perianal disease (OR 2.61, CI 1.2-5.7; p=0.017).

Conclusion: Sarcopenia represents a poor prognostic factor for endoscopic outcomes in CD patients who start a biological therapy, and its assessment may represent an additional tool to improve decision making. Smoking and perianal disease were also associated with poor endoscopic outcomes.

Disclosure: Nothing to disclose.

P0311

ENDOSCOPIC AND HISTOLOGICAL PREDICTORS OF COMPLETE REMISSION AFTER THREE MONTHS OF CONVENTIONAL TREATMENT IN ULCERATIVE COLITIS BASED ON MAYO ENDOSCOPIC SCORE AND NANCY HISTOLOGICAL INDEX

Ø. Steinsbø¹, A. Carlsen¹, O.G. Aasprong², L. Aabakken³, E. Tvedt-Gundersen¹, R. Gjerde¹, L. Karlsen¹, T. Grimstad^{1,4}

¹Stavanger University Hospital, Department of Medical Gastroenterology, Stavanger, Norway, ²Stavanger University Hospital, Department of Pathology, Stavanger, Norway, ³Rikshospitalet-Radiumhospitalet HF, Dept. of Medical Gastroenterology, Oslo, Norway, ⁴University of Bergen, Department of Clinical Science, Bergen, Norway

Contact E-Mail Address: oyvind.steinsbo@outlook.com

Introduction: Mucosal activity and disease extent are risk factors in ulcerative colitis (UC). Whereas mucosal activity is assessed both endoscopically and histologically, disease extent is classified by endoscopic findings.

Persistent histologic activity in endoscopically normal/quiescent mucosa is common, suggesting that endoscopic and histological distribution may not be the same and that remission status may depend on the number of biopsy sites.

Aims & Methods: To assess complete remission after 3 months of conventional treatment in new-diagnosed patients, to measure the effect of increasing number of biopsy sites on the remission rates, and to evaluate the predictive value of endoscopic and histologic activity and distribution at baseline.

Clinical, biochemical, colonoscopy, and histological data were collected at baseline (V0) and after 3 months (V3). Rates of *clinical remission* (Partial Mayo Score (PMS) ≤ 2), *mucosal healing* (Mayo Endoscopic Score (MES) ≤ 1), *histologic healing* (Nancy Histological Index (NHI) ≤ 1 in rectum, left colon and right colon), *deep remission* (clinical remission plus mucosal healing), and *complete remission* (deep remission plus histologic healing) were determined. The association between baseline variables and complete remission was evaluated by logistic regression.

Results: The study included 180 newly diagnosed patients, 51 diagnosed with proctitis, 60 with left-sided disease and 69 with pancolitis. Disease activity scores at V0, given as median and interquartile range (IQR), were as follows: PMS 5 (3-7), MES 2 (2-3), NHI 1 (0-2) in right colon, NHI 2 (0-3) in left colon, and NHI 2 (2-3) in rectum. PMS, MES and NHI all decreased significantly from V0 to V3 (p < 0.005).

Mucosal healing	Histologic healing	Patients (n)	PMS	FC (mg/kg)
Yes	Yes (all segments)	83	0 (0-1)	28.5 (18-83)
	No	50	1 (0-3)	79 (27.5-387)
	Rectal healing only	27 of 50	1 (0-3)	158 (38.5-437)
No	Yes (all segments)	4	0.5 (0-2)	227 (65-358)
	No	43	3 (2-5)	1096 (157-3000)
	Rectal healing only	5 of 43	2 (0-3)	1096 (298-1524)

Table.

At V3 mucosal healing was achieved by 133 patients, in which 83 (62.4%) of them showed histologic healing and 50 (37.6%) showed histologic activity in at least one colorectal segment. PMSs and faecal calprotectin (FC) levels were significantly higher in the latter group (p < 0.005).

In the latter group, 27 (54%) of 50 showed histologic activity only in colonic segment(s) whereas rectal biopsies were scored NHI ≤ 1 (defined as *rectal healing*). PMSs and FC levels were also significantly higher in the rectal healing group than in the group achieving histologic healing in all colorectal segments (p < 0.005).

Deep remission rate was 62.8% (113 of 180) and complete remission rate 42.2 % (76 of 180). Deep remission plus NHI ≤ 1 in rectum $\pm$ colon was observed in 52.2% (94 of 180).

Assessing the predictive value of clinical, endoscopic, and histological activity scores at baseline, the sum of segmental NHI and MES were independently associated with complete remission.

Notably, the sum of segmental NHI was higher than expected in many patients with limited disease extent, as 28 (25%) of 112 patients with proctitis and left-sided colitis also had histologic activity in proximal colonic segments.

Conclusion: Histologic activity in endoscopically normal or quiescent mucosa was common. The endoscopic evaluation of the proximal extent of the inflammation was frequently underestimated, and one-third achieving endoscopic mucosal healing had persistent histologic activity.

The complete remission rate was dependent on the number of biopsy sites and was increased by 10% if only rectal biopsies were evaluated.

Disclosure: Nothing to disclose.

P0312

VISCERAL OBESITY, DEFINED ACCORDING TO THE ANTHROPOMETRIC CRITERIA, IS NOT ASSOCIATED WITH A WORSE INFLAMMATORY BOWEL DISEASE COURSE AND DOES NOT LEAD TO AN ADDITIONAL INCREASE IN PROINFLAMMATORY RESPONSE

A. Niezgódka-Klósak¹, K. Korybalska², I. Miechowicz³, A. Dobrowolska¹, P. Eder¹

¹Poznan University of Medical Sciences, Department of Gastroenterology, Dietetics and Internal Medicine, Poznan, Poland, ²Poznan University of Medical Sciences, Department of Pathophysiology, Poznan, Poland, ³Poznan University of Medical Sciences, Department of Computer Science and Statistics, Poznan, Poland

Contact E-Mail Address: niezgodkaalina@gmail.com

Introduction: There is a growing body of evidence suggesting that visceral obesity can have a negative impact on inflammatory bowel disease (IBD). However, routine assessment of visceral obesity using the most frequently applied cross-sectional imaging methods is limited due to their costs, low availability, and lack of validation of diagnostic criteria.

Aims & Methods: To assess the prevalence of visceral obesity defined by International Diabetes Federation (IDF) anthropometric criteria in IBD patients and its relationship with IBD clinical course, disease phenotype, and proinflammatory response.

252 participants were prospectively enrolled into the study - 182 patients with IBD and 70 healthy people constituting the control group. According to the IDF criteria, we divided patients into subgroups with and without visceral obesity based on the waist circumference (waist circumference threshold for visceral obesity in Europe: ≥ 94 cm in men; ≥ 80 cm in women). IBD clinical activity was assessed using the Harvey-Bradshaw Index (for Crohn's disease) and the Partial Mayo Score (for ulcerative colitis).

Disease phenotype was defined according to the Montreal classification. The need for steroid therapy at diagnosis and/or the need for immunosuppressive/biological treatment and/or major abdominal surgery were considered to define severe IBD course.

We performed waist and hip circumference measurements in all patients using the Seca-201[®] measure and body composition analysis using the bioelectrical impedance method (TANITA-MC980 MA[®]). Concentrations of selected proinflammatory adipocytokines (CRP, hslL-1 β , hslL-6, MCP-1, resistin, visfatin, leptin) were measured by a highly sensitive ELISA method.

Results: Patients with visceral obesity constituted 20% (n=36/182) of the study group. We found no differences between IBD patients with and without visceral obesity in terms of general characteristics, the risk of develop-

ing fistulising and/or stricturing phenotype, and fulfilling the predefined criteria of severe IBD course. Additionally, we found no differences in all measured proinflammatory adipocytokines among patients with IBD when stratified the study group according to the IDF criteria for visceral obesity (except for leptin).

At the same time - CRP, hslL-6, resistin, and MCP-1 concentrations were significantly higher in both IBD subgroups (with and without visceral obesity) when compared to healthy people. As for leptin, we noted a significantly higher concentration of this adipokine in patients with IBD with visceral obesity - both compared to those with IBD without obesity and healthy people.

Conclusion: Visceral obesity, defined by IDF anthropometric criteria, is a frequent phenomenon in IBD patients, however it does not adversely affect the clinical course or the disease phenotype. Moreover, visceral obesity is not an additional proinflammatory factor in IBD, as the concentrations of several adipocytokines were not different in patients with increased waist circumference compared to those without visceral obesity. Increased leptin concentration reflects the metabolic state of patients with excessive accumulation of adipose tissue and not the inflammatory activity.

Further studies are needed to verify the most optimal definition and the most accurate diagnostic method for visceral obesity in IBD. This, in turn, could allow estimating the potential clinical relevance of diagnosing visceral obesity in IBD in routine practice.

Disclosure: Nothing to disclose.

P0313

METABOLIC ASSOCIATED LIVER DISEASE AND SEX AS KEY FACTORS OF CARDIOVASCULAR RISK IN INFLAMMATORY BOWEL DISEASE

S. García Mateo^{1,2}, S.J. Martínez-Domínguez¹, S. Ballesta Martínez³, J. Espinosa Rueda³, C. Tejero Justes³, M.C. Aso Gonzalvo¹, B. Gallego Llera², E. Alfambra Cabreja², P.M. Baptista², C.J. Gargallo-Puyuelo¹, F. Gomollón^{1,2,4}

¹Lozano Blesa University Hospital, Gastroenterology and Hepatology, Zaragoza, Spain, ²IIS Aragón, Digestive Diseases, Zaragoza, Spain, ³Lozano Blesa University Hospital, Neurology, Zaragoza, Spain, ⁴University fo Zaragoza, Medicine, Zaragoza, Spain

Contact E-Mail Address: sgarciamateo7@gmail.com

Introduction: Atherosclerosis is the main factor for the development of cardiovascular (CV) events. Patients with systemic inflammatory conditions such as inflammatory bowel disease (IBD) are supposed to be at risk of early atherosclerosis. However, data are still contentious. IBD patients are also at risk of other comorbidities such as metabolic associated fatty liver disease (MAFLD), a well-recognized entity associated with increased CV risk.

Aims & Methods: The aim of this study is to demonstrate the impact of MAFLD on CV risk for IBD patients. Prospective cohort study of consecutive IBD outpatients (Leonnard-Jones criteria, > 1 year) was performed from October 2020 to April 2021. Of 947 patients, 50 with IBD who met criteria for MAFLD and 50 with IBD and without MAFLD were matched by sex, age and IBD location. Patients with a previous diagnosis of CV disease, type II Diabetes Mellitus and under treatment for dyslipidaemia were excluded. Fatty liver disease (FLD) was diagnosed by ultrasonography, controlled attenuation parameter (CAP[™]), fatty liver index (FLI), hepatic steatosis index (HSI) and lipid accumulation product (LAP).

To assess early atherosclerosis, alterations in Carotid Artery Intima-Media Thickness (CIMT) and SCORE as non-invasive CV risk test were performed in both groups. Statistical analysis was performed using SPSS version 26, a

binomial generalized linear model with logistic regression was performed, with CIMT alteration as dependent variable. For all tests, a two-sided p value <0.05 was considered significant.

Results: Of 100 IBD patients included, 51 (51%) were women with median age of 51.0 (IQR 41-59). There were 49 (49%) patients diagnosed of ulcerative colitis (UC) and 51 (51%) of Crohn's disease (CD). Most of the patients were former smokers (51 (51%)), had overweight or obesity (40 (40%) and 24 (24%) respectively), and an elevated waist-to-hip ratio (51 (51%)).

The most often disease location were ileocolonic disease for CD patients (43 (43%)) and pancolitis (29 (29%)) for UC. Extraintestinal disease was diagnosed in 29 (29%) of the patients. The therapies most often prescribed were mesalazine (35 (35%)) and anti-TNF (23 (23%)). Thirty-two patients (32%) had a steroid-dependent course, and 24 (24%) need surgery at any time of their course of disease.

Most of the patients had an abnormal CIMT (58 (58%)). Of all the variables obtained, only female sex (OR (CI 95%) 3.322 (1.03-10); p=0.033) and MAFLD (OR (CI 95%) 5.05 (1.71-14.92); p=0.003) were significantly associated with CIMT alterations. SCORE test did not associate with a significant CIMT alteration.

Among the different options to assess FLD, only ultrasonography and CAP were statistically associated with CIMT alterations (specificity 66%, sensitivity 62%, p=0.005).

Conclusion: Female sex and MAFLD are associated with early atherosclerosis, defined by CIMT alterations in IBD patients. Ultrasonography and CAP are better than biochemical test not only to predict FLD but also to assess CV risk.

Disclosure: Nothing to disclose.

P0314

EVALUATION OF ACUTE INFLAMMATORY AND STRUCTURAL CHANGES OF SACROILIITIS ON MR ENTEROGRAPHY: A DIRECT COMPARISON WITH SACROILIAC JOINT MRI

I. Ergenç¹, H.T. Kani¹, C.A. Gündoğmuş², R. Ergelen², N. Afsar³, G. Ekinç², M.P. Atagunduz⁴

¹Marmara University, School of Medicine, Gastroenterology, Istanbul, Turkey, ²Marmara University, School of Medicine, Radiology, Istanbul, Turkey, ³Marmara University, School of Medicine, Internal Medicine, Istanbul, Turkey, ⁴Marmara University, School of Medicine, Rheumatology, Istanbul, Turkey

Contact E-Mail Address: ergencilkay@gmail.com

Introduction: Patients with inflammatory bowel disease (IBD) are at increased risk of sacroiliitis. Nevertheless, sacroiliitis may go undiagnosed during follow-up. Two retrospective studies reported that detectable acute inflammatory and structural changes (fat metaplasia, ankylosis, and sclerosis) of inflammatory sacroiliitis are present in a significant proportion of IBD patients on MRE^{1,2}.

Aims & Methods: The study aims to investigate the acute inflammatory and structural changes of sacroiliitis as auxiliary findings on magnetic resonance enterography (MRE) and their presence on closely timed conventional magnetic resonance imaging (MRI) of the sacroiliac (SI) joint (MRI-SIJ). We screened IBD and spondyloarthritis (SpA) patients for the simultaneous presence of MREs and MRI-SIJs. Two radiologists blinded to the patient's identity and date of imaging evaluated MRI-SIJs and MREs on two separate occasions.

We used the SpondyloArthritis international Society (ASAS) / OMERACT definitions for MRI-SIJ. We implemented previously published standard definitions for bone marrow oedema, erosion, sclerosis, and fatty infiltration of SIJ in MREs that contains T1w and T1w post-gadolinium sequences.

Results: MRI-SIJ and MRE were present in 43 patients. The median time between the two modalities was 14 (0-89) days. Twelve patients had ASAS-defined sacroiliitis on MRI-SIJ. Radiologist-1 and radiologist-2 detected sacroiliitis on MRE in nine and eight out of these 12 patients, respectively (Table 1).

Both radiologists detected ankylosis and fatty metaplasia with a complete agreement, and sclerosis with an almost perfect agreement. Both radiologists agreed on erosions on MRI-SIJ in the same 10 cases. But the degree of agreement on erosions on MRE was weak. Radiologists did not identify acute inflammatory or structural changes on MRE in patients with a negative MRI-SIJ for these lesions.

On intra-reader analysis, Kappa values in detecting sacroiliitis on MRE-images for radiologist-1 and radiologist-2 were 0.927 (p< 0.001) and 1.000 (p< 0.001), respectively. Regarding structural changes, intra-reader Kappa value for both detecting fatty infiltration and ankylosis was 1.000 (p< 0.001) on MRE. On inter-reader analysis of both radiologists, kappa values for detecting sacroiliitis, fat metaplasia, ankylosis and sclerosis on MRE were 0.934 (P< 0.001), 1.000 (P< 0.001), 1.000 (P< 0.001), and 0.732 (p<0.001) respectively.

MRE vs. MRI-SIJ		MRE (n=43)		SI Joint MRI(n=43)		p
		Present n (%)	Absent n (%)	Present n (%)	Absent n (%)	
Radiologist 1	BME	9 (20.9)	35 (81.4)	12 (27.9)	31 (72.1)	0.125
	Fat metaplasia	13 (30.2)	30 (69.8)	13 (30.2)	30 (69.8)	1.000
	Sclerosis	5 (11.6)	38 (88.4)	5 (11.6)	38 (88.4)	1.000
	Ankylosis	1 (2.3)	42 (97.7)	1 (2.3)	42 (97.7)	1.000
Radiologist 2	BME	8 (18.6)	35 (81.4)	12 (27.9)	31 (72.1)	0.125
	Fat metaplasia	13 (30.2)	30 (69.8)	13 (30.2)	30 (69.8)	1.000
	Sclerosis	6 (14.0)	37 (86.0)	6 (14.0)	37 (86.0)	1.000
	Ankylosis	1 (2.3)	42 (97.7)	1 (2.3)	42 (97.7)	1.000

MRE: Magnetic resonance enterography; SI Joint MRI: Sacroiliac joint magnetic resonance imaging, BMO: Bone Marrow oedema (ASAS definition of sacroiliitis)

Table 1: Comparison of MRE and SI Joint MRI findings.

Conclusion: Our data supports that MRE is a useful diagnostic tool in the detection of both sacroiliitis and structural changes of SIJ. Along with intestinal findings, additional reporting of acute and structural inflammatory changes of the SI joint on a present MRE is extremely valuable and may alert gastroenterologists for the presence of previously not diagnosed axial SpA.

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Disclosure: Nothing to disclose.

P0315

NATURAL HISTORY AND IMPACT OF IBS-TYPE SYMPTOMS IN INFLAMMATORY BOWEL DISEASE DURING 6 YEARS OF LONGITUDINAL FOLLOW-UP

K.M. Fairbrass^{1,2}, P.J. Hamlin^{1,2}, D.J. Gracie^{2,1}, A.C. Ford^{2,1}

¹Leeds Gastroenterology Institute, St. James's University Hospital, Leeds, United Kingdom, ²Leeds Institute of Medical Research at St. James's, University of Leeds, Leeds, United Kingdom

Contact E-Mail Address: keeley.fairbrass@nhs.net

Introduction: The long-term natural history and impact of irritable bowel syndrome (IBS)-type symptoms on outcomes in inflammatory bowel disease (IBD) are uncertain. We assessed this in a longitudinal follow-up study of secondary care patients.

Aims & Methods: We assessed natural history of IBS-type symptoms in IBD via Rome III criteria applied at baseline, 2 years, and 6 years. We defined longitudinal disease activity as need for glucocorticosteroids or flare, escalation, hospitalisation, or intestinal resection. To assess healthcare utilisation, we recorded number of outpatient clinic attendances and investigations. We also collected anxiety, depression, and somatoform symptom scores, as well as quality of life scores during follow-up.

Results: Among 125 individuals with Rome III data at all three time points, only 41 (32.8%) never reported IBS-type symptoms. Fifteen patients (12.0%) had IBS-type symptoms at baseline that resolved, 19 (15.2%) had fluctuating symptoms, 35 (28.0%) had new onset symptoms, and 15 (12.0%) had persistent symptoms.

	Quiescent IBD	IBD with IBS-type Symptoms	IBD with Occult Inflammation	Active IBD	p Value
Glucocorticosteroid prescription or flare of disease activity (%)	59/126 (46.8)	49/82 (59.8)	31/70 (44.3)	24/30 (80.0)	0.002*
Multivariate HR for glucocorticosteroid prescription or flare of disease activity (95% CI)	1.00 (reference)	1.45 (0.96 – 2.18)	0.97 (0.60 – 1.56)	3.35 (1.93 – 5.81)†	<0.001
Escalation of medical therapy due to uncontrolled IBD activity (%)	58/127 (45.7)	43/83 (51.8)	33/77 (42.9)	34/42 (81.0)	<0.001*
Multivariate HR for escalation of medical therapy due to uncontrolled IBD activity (95% CI)	1.00 (reference)	1.15 (0.75 – 1.76)	1.00 (0.63 – 1.59)	3.01 (1.88 – 4.84)†	<0.001
Hospitalisation due to uncontrolled IBD activity (%)	16/127 (12.6)	20/83 (24.1)	14/80 (17.5)	18/61 (29.5)	0.028*
Multivariate HR for hospitalisation due to uncontrolled IBD activity (95% CI)	1.00 (reference)	2.36 (1.15 – 4.83)	1.34 (0.60 – 3.02)	2.56 (1.21 – 5.40)	0.041
Intestinal resection due to uncontrolled IBD activity (%)	6/127 (4.7)	8/83 (9.6)	5/80 (6.3)	11/62 (17.7)	0.021*
Multivariate HR for intestinal resection due to uncontrolled IBD activity (95% CI)	1.00 (reference)	1.76 (0.54 – 5.75)	1.08 (0.27 – 4.41)	3.61 (1.16 – 11.2)	0.096

* χ^2 for comparison across all four groups.

† $p < 0.01$ versus reference category.

Table 1. Clinical Outcomes of Patients According to IBD Activity Status (FC <250mcg/g) at Baseline.

Among more than 300 patients with IBD activity data, IBS-type symptoms were not associated with an increased likelihood of need for glucocorticosteroids or flare, escalation, hospitalisation, or intestinal resection. However, mean number of outpatient appointments and endoscopic investigations were significantly higher among those with IBS-type symptoms. Anxiety, depression, and somatoform symptom scores were significantly higher and quality of life scores significantly lower in those reporting IBS-type symptoms at least once during the study.

Conclusion: IBS-type symptoms affected more than two-thirds of patients with IBD during >6 years of follow-up and were associated with increased healthcare utilisation, and worse anxiety, depression, and somatoform symptom, and quality of life scores, but not adverse disease activity outcomes.

Disclosure: Nothing to disclose.

P0316

CHARACTERISTICS AND IMPACT OF ANXIETY AND DEPRESSION TRAJECTORIES IN INFLAMMATORY BOWEL DISEASE

K.M. Fairbrass^{1,2}, E.A. Guthrie³, C.J. Black^{1,2}, C.P. Selinger^{1,2}, D.J. Gracie^{1,2}, A.C. Ford^{1,2}

¹Leeds Gastroenterology Institute, St. James's University Hospital, Leeds, United Kingdom, ²Leeds Institute of Medical Research at St. James's, University of Leeds, Leeds, United Kingdom, ³Leeds Institute of Health Sciences, University of Leeds, Leeds, United Kingdom

Contact E-Mail Address: keeley.fairbrass@nhs.net

Introduction: There is increasing evidence that symptoms of anxiety and depression are associated with poor clinical outcomes in inflammatory bowel disease (IBD).

Aims & Methods: We report the trajectories of common mental disorders in IBD, the characteristics associated with these subgroups, and the effect on healthcare utilisation.

We collected complete demographic, symptom, psychological, and quality of life data in 771 patients, with repeat questionnaires at 3-monthly intervals, over 12-months of longitudinal follow up. Medical records were reviewed to collect data on disease extent and phenotype, medications, and healthcare utilisation. We recorded the number of reported flares, escalation of therapy, hospitalisation, intestinal resection due to IBD activity and death. We compared the characteristics of those with persistently normal or improving anxiety and depression trajectories with those with fluctuating, or persistently abnormal or worsening hospital anxiety and depression scale scores.

Results: Of 771 patients, persistently abnormal or worsening anxiety or depression trajectories were present in 105 (13.6%) and 53 (6.9%) of individuals, respectively. They were associated with increased antidepressant ($p < 0.001$) and opiate use ($p < 0.001$). These individuals were also more likely to have been newly diagnosed with IBD in the previous 12 months ($p = 0.001$ and 0.006 respectively), significantly more likely to report higher somatisation scores ($p < 0.001$), and had significantly lower quality of life scores ($p < 0.001$) compared with those with persistently normal or improving anxiety or depression trajectories. Individuals with worsening, or persistently abnormal anxiety or depression trajectories were also significantly more likely to require more IBD-related appointments, and more radiological and endoscopic investigations.

Conclusion: Persistently abnormal or worsening anxiety or depression trajectories were associated with higher rates of antidepressant or opiate use, more recent diagnosis of IBD, higher somatisation scores, and worse quality of life, as well as increased healthcare utilisation.

Disclosure: Nothing to disclose.

	Persistently normal or improving (n = 400)	Fluctuating (n = 266)	pvalue*	Persistently abnormal or worsening (n = 105)	pvalue*	pvalue**
Healthcare Utilisation According to HADS-anxiety Trajectories						
Mean number of IBD-related outpatient clinic appointments (SD)	1.0 (1.0)	1.0 (1.0)	0.024	1.5 (1.3)	<0.001	<0.001
Mean number of IBD helpline calls (SD)	1.6 (3.1)	1.8 (3.3)	0.03	3.3 (5.6)	<0.001	<0.001
Mean number of IBD-related radiological investigations (SD)	0.1 (0.4)	0.1 (0.4)	0.07	0.2 (0.5)	0.002	0.007
Mean number of IBD-related endoscopic investigations (SD)	0.1 (0.4)	0.2 (0.4)	0.38	0.3 (0.5)	0.002	0.008
Healthcare Utilisation According to HADS-depression Trajectories						
Mean number of IBD-related outpatient clinic appointments (SD)	1.0 (1.3)	1.2 (1.3)	0.01	1.6 (1.3)	<0.001	<0.001
Mean number of IBD-related radiological investigations (SD)	0.1 (0.4)	0.2 (0.4)	0.01	0.2 (0.4)	0.10	0.03
Mean number of IBD-related endoscopic investigations (SD)	0.1 (0.4)	0.2 (0.5)	0.002	0.2 (0.6)	0.10	0.005
*Mann-Whitney U for comparison of continuous data across 2 groups, **Kruskal-Wallis One-way ANOVA for comparison of continuous data across 3 groups.						

P0316 Table 1. Healthcare Utilisation of Patients According to HADS Anxiety and Depression Trajectories Over 12-month Longitudinal Follow-up.

P0317

AN OPTIMIZATION OF INFLAMMATORY BOWEL DISEASES DIAGNOSIS USING AN ARTIFICIAL INTELLIGENCE

I. Rasmagina¹, I. Bakulin¹, M. Skalinskaya¹, G. Mashevskiy², N. Shelyakina²

¹North-Western State Medical University n.a. I.I. Mechnikov, Propedeutics of Internal Diseases, Gastroenterology and Dietology n.a. S.M. Riss, Saint-Petersburg, Russian Federation, ²Saint-Petersburg Electrotechnical University, Saint-Petersburg, Russian Federation

Contact E-Mail Address: irenerasmagina@gmail.com

Introduction: Inflammatory bowel diseases (IBD), including ulcerative colitis (UC) and Crohn's disease (CD), are chronic immune-mediated diseases that usually occur in young patients and requires lifelong therapy and monitoring. Even in developed countries UC is diagnosed 1,5 years after the onset of the symptoms and CD - 3,5 years respectively. This delay in diagnosis may cause surgical complications development and severe course of IBD.

Aims & Methods: The aim of the study was to optimize the existing methods of IBD diagnosis and to create a decision support system (DSS) using artificial intelligence (AI).

300 medical histories (per 100 of UC, CD and (irritable bowel syndrome (IBS)) of patients that had been admitted to the gastroenterology department or managed in outpatient center of IBD of the NWSMU

n.a.I.I.Mechnikov (Saint-Petersburg, Russia) were analyzed. In order to determine the clinical and laboratory data that could be used in differentiation between IBS, UC and CD, we assessed gender, age, clinical symptoms of the disease (stool frequency, rectal bleeding, abdominal pain, night symptoms, weight loss, extraintestinal manifestations, fever, perianal manifestations, the history of abscesses, strictures, fistulae, surgical treatment), comorbidities, family history of autoimmune diseases and laboratory parameters (hemoglobin levels, WBC, serum protein, CRP and fecal calprotectin).

For diagnosis and differentiation of IBD, the DSS that was based on an adapted VGG16 convolutional neural network (CNN) with fast assess connections was developed. The CNN used digital endoscopic images as an input and the output was a conclusion about the presence and the type of pathology. The images were obtained with endoscope Olympus during the video colonoscopies of the patients with verified IBD and IBS.

Results: Clinical and laboratory data that were statistically significant for IBD verification were determined. The demarcation markers between IBD and IBS were loose stool, weight loss, C-reactive protein and fecal calprotectin levels ($p < 0,05$). The parameters that could help to differentiate the types of IBD were the presence of extraintestinal and perianal manifestations, anemia (more likely in patients with CD) and the presence of obvious blood in stool and leukocytosis for UC ($p < 0,05$).

In order to train the CNN to diagnose IBD, the endoscopic images were divided into two groups – images of normal mucosa and images of inflamed mucosa of the patients with UC and CD. The images were randomly divided into training ($n = 843$ images: 234 – normal mucosa, 600 – pathological mucosa) and control samples ($n = 210$ images: 60 – normal mucosa, 150 – pathology) in a 4:1 ratio. To differentiate the types of IBD, the images were divided in 9:1 ratio: training sample included 670 images (326 – CD, 344 – UC), control – 80 images (39 – CD, 41 – UC).

The CNN verified visually normal mucosa and mucosa with pathological changes with sensitivity 100%, specificity 91% and differentiated the type of IBD with sensitivity 88%, specificity 75%.

The DSS was implemented using Keras and TensorFlow open libraries in Python. The program included information about the patient, clinical and laboratory data and endoscopic image upload section.

Conclusion: DSS with the application of AI can be used as an additional tool to improve the accuracy of IBD diagnosis; however, future studies on the combination of clinical, laboratory and endoscopic data relevance for IBD diagnosis are needed.

Disclosure: Nothing to disclose.

P0318

USTEKINUMAB DRUG EXPOSURE IS NOT LINKED TO CHANGES IN BOWEL WALL THICKNESS, BUT DOES ASSOCIATE WITH TRANSMURAL REMISSION IN CROHN'S DISEASE

B. Verstockt^{1,2}, C. Maaser³, R.L. Wilkens^{4,5}, G. Maconi⁶, M.A. D'Agostino⁷, M. Nazar⁸, M. Lahaye⁹, O.J. Adedokun¹⁰, M. Le Bars¹¹, I. Bravatà¹², L. Ni¹³, M. Allocca¹⁴, F.A.E. de Voogd¹⁵, C. Palmela¹⁶, R. Vaughan¹⁷, T. Kucharzik³

¹Department of Gastroenterology and Hepatology, University Hospitals Leuven, KU Leuven, Leuven, Belgium, ²Translational Research in Gastrointestinal Disorders, Department of Chronic Disease, Metabolism, KU Leuven, Leuven, Belgium, ³Klinik für Allgemeine Innere Medizin und Gastroenterologie, Klinikum Lüneburg, Lüneburg, Germany, ⁴Gastro Unit, Section of Medicine, Hvidovre Hospital, Copenhagen, Denmark, ⁵Digestive Disease Center, Bispebjerg Hospital, Copenhagen, Denmark, ⁶Gastroenterology Unit, Department of Biomedical and Clinical Sciences, "Luigi Sacco" University Hospital, University of Milan, Milan, Italy, ⁷Rheumatology Unit, Fondazione Policlinico Universitario Agostino Gemelli IRCSS, Università Cattolica del Sacro Cuore, Rome, Italy, ⁸Janssen-Cilag Polska Sp. z o.o., Warsaw, Poland, ⁹Janssen-Cilag B.V., Breda, Netherlands, ¹⁰Janssen Research & Development, LLC., Spring House, Pennsylvania, United States, ¹¹Janssen-Cilag, Issy-les-Moulineaux, France, ¹²Janssen-Cilag S.p.A., Milan, Italy, ¹³Janssen-Cilag Russia, Moscow, Russian Federation, ¹⁴Department of Gastroenterology, Humanitas University, Milan, Italy, ¹⁵Department of Gastroenterology and Hepatology, Amsterdam University Medical Center, Amsterdam, Netherlands, ¹⁶Division of Gastroenterology, Surgical Department, Hospital Beatriz Ângelo, Loures, Portugal, ¹⁷Gastroenterology Department, The Royal Melbourne Hospital, Melbourne, Australia

Contact E-Mail Address: bram.verstockt@uzleuven.be

Introduction: STARDUST is a phase 3b randomized trial comparing treat-to-target (T2T) strategy vs standard of care (SoC) in patients (pts) with Crohn's disease (CD) treated with ustekinumab (UST), which incorporated intestinal ultrasound (IUS) for the first time as an exploratory endpoint. Little is known about the association between drug exposure pharmacokinetics (PK) and IUS outcomes pharmacodynamics (PD), previously reported with biomarker and endoscopic outcomes. We report Week (W)48 results from the IUS substudy, assessing IUS endpoints and their relationship with UST exposure.

Aims & Methods: Adult pts with moderate-severe active CD unresponsive to conventional therapy and/or 1 biologic, received intravenous (IV), weight-based UST ~6mg/kg at W0 at baseline (BL); then subcutaneous (SC) UST 90mg at W8. At W16, responders (pts with ≥70-point reduction in CD activity index [CDAI]) were randomized (1:1) to either T2T or SoC and received protocol-specified SC UST every 12W or every 8W. Key IUS endpoints assessed at W4, W8, W16 and W48 (central reading): IUS response (IUSR; ≥25% bowel wall thickness [BWT] reduction from BL); BWT change from BL (mm); transmural remission (TMREM; normalization of BWT [≤3.0mm overall]), vascularization, bowel wall echo-stratification and inflammatory mesenteric fat). All IUS parameters used the most affected bowel segment at BL. Serum samples were collected to measure UST concentration at W8, W16 and W48 using validated assays.

Results: Of 77/88 pts enrolled in the substudy, 71 had BL and ≥1 post-BL IUS assessment. Changes in BWT at W8 (compared with BL) correlated significantly with BWT changes at W16 ($r=0.62$, $p<0.001$) and W48 ($r=0.46$, $p<0.001$). Likewise, serum UST levels at W8 correlated significantly with serum UST levels at both W16 ($r=0.81$, $p<0.001$) and W48 ($r=0.43$, $p=0.002$). However, changes in BWT at W8 (compared with BL) did not correlate

with serum UST levels at W8, W16 and W48 ($p>0.05$) (Table 1). Quartile (Q) analyses revealed that pts with the lowest UST levels at W8 (Q1) had a numerically lower chance of achieving IUS response by W16 (12.5% Q1 vs 39.5% Q2-Q4).

In contrast, pts with the highest UST exposure at W8 (Q4) had the highest chance numerically of achieving TMREM by W16 (38.5% Q4 vs 8.7% Q1-Q3). UST drug exposure at W8 and W16 was not associated with IUS outcomes at W48, potentially due to the design of the STARDUST trial, where dose optimization begins between W16 and W48 in many patients.

	UST serum concentration W8	UST serum concentration W16	UST serum concentration W48
Change in BWT at W8 compared with BL	$r=-0.08$ $p=0.53$	$r=0.01$ $p=0.92$	$r=-0.05$ $p=0.72$
Change in BWT at W16 compared with BL	$r=-0.10$ $p=0.47$	$r=0.02$ $p=0.91$	$r=0.08$ $p=0.60$
Change in BWT at W48 compared with BL	$r=-0.18$ $p=0.22$	$r=-0.08$ $p=0.57$	$r=-0.05$ $p=0.74$

BL, baseline; BWT, bowel wall thickness; UST, ustekinumab; W, week

Table 1 Correlation between changes in BWT and UST drug exposure.

Conclusion: In contrast to convincing evidence regarding UST PK-PD relationships in the context of biomarker and endoscopic outcomes, the association between UST exposure and IUS parameters is rather limited. Validated IUS scoring systems in large (randomized) studies should help to unravel the potential association between drug exposure and transmural healing in CD.

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P0319

PROGNOSTIC MODEL FOR THE OCCURRENCE OF A COMPOSITE OUTCOME IN CROHN'S DISEASE PATIENTS UNDER INFLIXIMAB MAINTENANCE THERAPY

M.M. Estevinho¹, F. Magro^{2,2}, G. Catalano^{3,3}, M. Patita⁴, B. Arroja⁵, P. Lago⁶, I. Rosa⁷, H. Tavares de Sousa⁸, M.P. Ministro Santos⁹, A. Vieira⁴, J. Castela¹⁰, J. Moleiro¹¹, J. Roseira¹², E. Cancela¹³, P. Sousa¹⁴, F. Portela¹⁵, L. Correia¹⁶, M. Santiago¹⁷, S. Dias¹⁸, J. Afonso¹⁹, S. Danese²⁰, L. Peyrin-Biroulet²¹, C.C. Dias²²

¹Centro Hospitalar Vila Nova de Gaia Espinho, Gastroenterology, Vila Nova de Gaia, Portugal, ²Centro Hospitalar Universitário de São João, Gastroenterology, Porto, Portugal, ³IRCCS Ospedale San Raffaele, Milan, Italy, ⁴Hospital Garcia de Orta, Gastroenterology, Almada, Portugal, ⁵Hospital de Braga, Gastroenterology, Braga, Portugal, ⁶Centro Hospitalar Universitário do Porto, Porto, Portugal, ⁷Instituto Portugues de Oncologia de Lisboa, EPE Dept. de Gastroenterologie, Gastroenterology, Lisboa, Portugal, ⁸Centro Hospitalar Universitário do Algarve, Faro, Portugal, ⁹CH Tondela Viseu Serviço de Gastroenterologia, Gastroenterology, Viseu, Portugal, ¹⁰Núcleo Regional do Sul da Liga Portuguesa Contra o Cancro, Lisboa, Belgium, ¹¹Portuguese Oncology Institute of Lisbon, Gastroenterology, Lisbon, Portugal, ¹²Algarve University Hospital Center, Gastroenterology Department, Portimão, Algarve, Portugal, ¹³Gastroenterologia, Hospital S. Teotónio, Sever do Vouga, Portugal, ¹⁴Centro Hospitalar Tondela-Viseu, Dept. of Gastroenterology, Viseu, Portugal, ¹⁵Centro Hospitalar de Coimbra Serviço de Gastroentologia, Gastroenterology, Coimbra, Portugal, ¹⁶CH Lisboa Norte - Hospital Santa Maria, Lisboa, Portugal, ¹⁷Faculty of Medicine University of Porto, Porto, Portugal, ¹⁸Grupo de Estudo da Doença Inflamatória Intestinal, Porto, Portugal, ¹⁹Faculty of Medicine of Porto, Biomedicine - Unity Pharmacology and Therapeutics, Porto, Portugal, ²⁰Vita-Salute San Raffaele University - IRCCS San Raffaele Scientific Institute, Gastrointestinal Immunopathology, Milan, Italy, ²¹Inserm U1256, Nancy University Hospital, Inserm U1256 - Team 2 "Inflammation/Cellular Stress and Exposure to Environmental Risks", Vandoeuvre-les-Nancy, France, ²²Faculty of Medicine, University of Porto, Porto, Portugal

Contact E-Mail Address: mmestevinho@gmail.com

Introduction: Composite outcomes are frequently used as primary end-points in clinical studies, allowing smaller sample sizes and optimizing resources. A composite outcome incorporating clinical (need for surgery or hospitalization, new fistulae, abscess, or stricture) and drug-related items (>10 mg steroids per day, *de novo*AZA or methotrexate, AZA dose increase other than by weight fluctuation, swap/switch of biologics) has been reported for Crohn's disease (CD)¹.

Aims & Methods: To perform a sub-analysis of the DIRECT, a prospective, observational, multicenter study. Univariate and multivariate logistic regressions using clinical and analytical parameters were used to calculate the odds ratio (OR) of achieving the composite outcome in CD patients receiving infliximab (IFX) as maintenance therapy for two years. Fecal calprotectin (FC), C-reactive protein (CRP), and hemoglobin (Hb) levels were selected to develop a risk matrix.

Results: Overall, 285 CD patients were included; the composite outcome was reached in 57. The outcome was more common ($p < 0.05$) in patients with higher FC and CRP levels (cutoffs FC <250, 250-500 or >500 µg/g, and CRP <3, 3-10 or > 10 g/L) and in those presenting anemia during the follow-up (<12 or 13 g/dL, for women and men). These variables remained significant after adjusting for age at diagnosis, sex, disease location, and phenotype. On the other hand, IFX levels (≤ 3 µg/ml) and anti-IFX antibody-

ies (>1.7 µg/ml) did not significantly impact the development of the outcome. Regarding risk matrices, CD patients with FC <250, CRP <3, and without anemia at a single visit had an estimated probability of presenting the outcome of 6.1% (95%CI, 5.5-6.7%), while patients with FC >500, CRP >10 and anemia in at least two visits had a probability of 49.7% (95%CI, 46.3-53.1%).

Conclusion: This analysis corroborates the importance of FC, CRP, and Hb in CD monitoring, even when measured at a single time-point, and reinforces the relevance of risk matrices as point-of-care tools that may influence clinical management.

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P0320

CONTRAST-ENHANCED INTESTINAL ULTRASOUND: TIME TO REFRESH THE NON-INVASIVE MONITORING IN CROHN'S DISEASE

T. Lima Capela^{1,2,3}, A.I. Ferreira^{1,2,3}, V. Macedo Silva^{1,2,3}, M. Freitas^{1,2,3}, C. Arieira^{1,2,3}, T. Cúrdia Gonçalves^{1,2,3}, M.F. Castro^{1,2,3}, M.J. Moreira Basto^{1,2,3}, J. Berkeley Cotter^{1,2,3}

¹Hospital da Senhora da Oliveira, Gastroenterology Department, Guimarães, Portugal, ²Life and Health Sciences Research Institute (ICVS), School of Medicine, University of Minho, Braga, Portugal, ³ICVS/3B's, PT Government Associate Laboratory, Braga, Portugal

Contact E-Mail Address: tiagolimacapela@gmail.com

Introduction: Intestinal ultrasound (IUS) using contrast-enhanced imaging (CEUS) is an increasingly used non-invasive tool to evaluate Crohn's disease (CD) activity in addition to clinical, biochemical and stool parameters.

Aims & Methods: We aimed to assess the usefulness of CEUS in predicting inflammatory activity in CD patients and determine the relationship between its parameters and clinical, biochemical and stool parameters. Retrospective study including CD patients submitted to CEUS, with SonoVue® contrast, directed to the terminal ileum, performed by a single operator using an ultrasound Hitachi HI VISION Avius®, between April 2016 and March 2022. Qualitative and quantitative parameters from the conventional IUS analysis including wall thickness, stratification, colour Doppler and inflammatory fat were evaluated.

A quantitative measurement of contrast bowel wall enhancement, peak intensity (PI), was evaluated using CEUS. Clinical activity score was assessed by Harvey Bradshaw index (HBI). Biochemical (C-reactive protein (CRP)) and stool (fecal calprotectin (FC)) parameter were registered. The endoscopic activity was assessed with ileocolonoscopy by Simple Endoscopic Score for CD (SES-CD), graded as inactive (SES-CD <7) or active (SES-CD ≥7) and considered the gold-standard method to assess inflammatory activity.

Results: Of 57 patients, 31 (54.4%) were female with a mean age of 34±12 years. The majority had only ileal involvement (n=35, 61.4%) and the rest had ileocolonic involvement. Inflammatory, stricturing and penetrating

phenotypes were present in 24(42.1%), 22(38.6%) and 11(19.3%) patients, respectively. Only PI performed by CEUS was significantly different between patients with inactive and active endoscopic inflammatory activity (median, 5.4vs9.8, $P=0.012$, respectively) contrary to HBI (median, 4vs4, $P=0.836$, respectively), CRP (median, 754.5vs879.0, $P=0.742$, respectively), and FC (median, 10.3vs8.6, $P=0.281$, respectively). PI was significantly correlated with HBI ($r=0.301$, $P=0.023$), but not significantly correlated with CRP ($P=0.871$), and FC ($P=0.080$) values.

Conclusion: Contrast-enhanced Intestinal ultrasound is a more reliable tool to evaluate inflammatory activity in Crohn's disease than clinical, biochemical and stool parameters.

Disclosure: Nothing to disclose.

P0321

INFLUENCE OF CELIAC DISEASE ON THE COURSE OF INFLAMMATORY BOWEL DISEASE

G. Babayeva¹, G. Asadova², U. Makhmudov³, F. Quliyev², K. Ismayilova¹, T. Samadova¹, A. Hasanova¹, M. Mahammadaliyeva¹, O. Mirzazada¹, C. Abdulzade¹, H. Ibrahimli⁴
¹Azerbaijan State Advanced Training Institute for Doctors named after A. Aliyev, Terapiya, Baku, Azerbaijan, ²National Oncology Center, Invasive Diagnostics and Treatments, Baku, Azerbaijan, ³Modern Hospital, Gastroenterology, Baku, Azerbaijan, ⁴Azerbaijan State Advanced Training Institute for Doctors named after A. Aliyev, Healthcare Organization and its Management, Baku, Azerbaijan

Contact E-Mail Address: doctorabu@mail.ru

Introduction: Celiac disease is an autoimmune genetically determined disease associated with a violation of tolerance to cereals, leading to atrophy of the intestinal villi.

The combined course with IBD, as well as with other autoimmune diseases, its influence on the course of these pathologies is of particular interest in the development of the diagnosis and differential diagnosis, treatment and prevention of these pathologies.

Aims & Methods: To identify the prevalence of celiac disease in patients with inflammatory bowel disease and its impact on the clinical and endoscopic course, as well as changes in laboratory and pathomorphological parameters.

The study was conducted from January 2016 to January 2022, among 400 patients with IBD (MC 12 patients, women 8, men 4; UC 150 patients, women 71, men 79; CD 238 patients, women 120, men 118).

Patients underwent serological examination for celiac disease (in the blood AGA IgA, AGA IgG, DGP IgA, DGP IgG, anti-TTG IgA, anti-TTG IgG), endoscopy was performed with biopsy sampling for pathomorphological examination, and laboratory blood tests were performed (complete blood count, h/s CRP, homocysteine, vit. D, ANCA-indicators, α -TNF and IL-1b, IL-2, IL-4, IL-6, IL-8, IL-10, IL-18, total protein, albumin, iron, ferritin; urinalysis and urine albumin; fecal analysis and fecal calprotectin and lactoferrin).

Results: Results: 370 patients (92.5%) underwent serological testing for celiac disease and in 89 cases (22.3%) the result was positive, the number of positive endoscopic manifestations was 112 (28% /30.3%), the number of patients with positive pathological conclusion - 89 (22.3%/24%), the number of patients with concomitant autoimmune diseases - 64 (17.3%).

Overlap "IBD+Celiac disease" in 29 cases revealed markers of ANCA-associated vasculitis (anti-BPI, anti-lizosim, anti-elastaza, anti-Katepsin G). Indicators of the studied parameters before and after the gluten-free diet are presented in table 1, table 2 and table 3.

Activity indicators	CeD+ average value before/ after	CeD+ UC n=28 before/ after	CeD+ CD n=61 before/after	CeD- average value before/after	CeD- UC n=28 before/after	CeD- CD n=61 before/after
h/s CRP (N<1mg/L)	15,6 / 2,5	12,3 / 2,7	19,1 / 2,4	6,4 / 6,4	6,8 / 6,6	5,9 / 5,7
Plateles (N150 000 - 400 000/ mm ³)	460 / 360	431 / 322	488 / 368	327 / 313	315 / 311	338 / 322
Homocystein ((N<12 μ mol/L)	17 / 9,4	15,8 / 8,8	18,1 / 10,3	10,1 / 10,1	9,3 / 9,1	10,8 / 10,5
Vitamin D (N 30-100ng/ mL)	4,7 / 22,3	4,1 / 24,5	5,3 / 25,2	21 / 21	22,5 / 22,5	19,4 / 19,5
Albumin (in urina) (N<2mg/L)	42,9 / 12,9	34,8 / 14,8	47 / 17	8,1 / 8,0	12,5 / 12,1	3,7 / 3,5
Calprotectin ((N<50 μ g/g)	834,5 / 214,5	1312 / 212	745 / 225	385 / 385	596,4 / 596,4	173,2 / 173,2
Laktoterrin (N<7,5 μ g/g)	101,5 / 8,5	139,2 / 7,2	121,7 / 8,7	27 / 27	44,6 / 44,6	9,2 / 9,2
il-8 (N< 10 pg/ml)	44,4 / 10,1	43,8 / 8,8	49,0 / 10,4	24,9 / 22,4	24,1 / 23,9	25,6 / 24,1
il-18 (N< 261 pg/ ml)	292,2 / 212,1	293,1 / 223,5	291,2 / 211,2	279,9 / 265,2	280,1 / 273,6	279,6 / 274,1

Table 1. Changes in activity in some laboratory parameters before starting a gluten-free diet and after a gluten-free diet

Conclusion: Overlap "IBD+Celiac disease" in the study group of patients was 22.3%. Overlap "IBD+Celiac disease" had higher indicators for laboratory, endoscopic and morphological activity of IBD, and it is also possible to identify markers of ANCA-associated vasculitis (anti-BPI, anti-lizosim, anti-elastaza, anti-Katepsin G).

Disclosure: no conflict of interest.

P0322

PLASMA FATTY ACID BINDING PROTEIN 2, INTERLEUKIN-10 AND LIPOPOLYSACCHARIDES AS BIOMARKERS FOR MICROSCOPIC COLITIS

V. Kiudelis^{1,2}, G. Varkalaite², E. Vaitkeviciute², J. Arstikyte², J. Skieceviciene², J. Kupcinskas^{1,2}

¹Lithuanian University of Health Sciences, Department of Gastroenterology, Kaunas, Lithuania, ²Lithuanian University of Health Sciences, Institute for Digestive Research, Kaunas, Lithuania

Contact E-Mail Address: vytautas.kiudelis@lsmu.lt

Introduction: Microscopic colitis (MC) is a chronic inflammatory disease of the large intestine, characterised by histologic lesions and an absence of destructive mucosal damage on colonoscopy, in contrast with inflammatory bowel disease like ulcerative colitis (UC).

The pathogenesis of MC is still poorly understood and there are no non-invasive diagnostic markers to aid in disease diagnosis. Fatty acid binding protein 2 (FABP2) is expressed in enterocytes and colonocytes (although to a lesser extent)¹ and is released after intestinal injury. Interleukin-10 (IL-10) is an anti-inflammatory cytokine that is reduced in inflammatory bowel diseases.²

Lipopolysaccharides (LPS) are bacterial endotoxins that promote inflammation and their presence in systemic circulation represents impaired intestinal barrier function.³

Aims & Methods: Our aim was to investigate FABP2, IL-10 and LPS as possible non-invasive diagnostic biomarkers for MC and compare their profile between MC and UC. For this purpose, we used plasma obtained from 63

patients with active MC, 52 healthy controls, 43 patients with active and 43 with inactive UC. Hjortswang criteria were used to determine disease activity in MC patients and Mayo score in UC patients.

Plasma concentrations of FABP2, IL-10 and LPS were measured using Human FABP2/I-FABP Quantikine ELISA Kit (DFBP20; R&D systems, MN, USA), Human IL-10 Quantikine ELISA KIT (D1000B; R&D systems, MN, USA), and Human Lipopolysaccharides (LPS) ELISA Kit (CSB-E09945h; Cusabio, China). Statistical significance of concentration differences between groups was determined using the Mann-Whitney U test.

Results: Plasma concentration of FABP2 was lower in healthy controls (median 1365 mg/ml) when compared with MC (median 1680 pg/ml) but the results did not reach statistical significance. However, FABP2 concentration was significantly lower in the plasma of UC patients, both active (median 1272 pg/ml, $p = 0,004$) and inactive (median 1334 pg/ml, $p = 0,001$) when compared with MC patients. The difference in FABP2 concentration between healthy controls and active or inactive UC patients was not significant.

IL-10 plasma concentration was significantly lower in active UC (median 2,58 pg/ml) than in MC patients (median 3,89 pg/ml, $p = 0,006$) and healthy controls (median 4,79 pg/ml, $p = 0,005$). IL-10 concentration was also lower in the plasma of inactive UC (median 3,04 pg/ml) and MC patients when compared with healthy controls, but the results did not reach statistical significance.

The plasma concentration of LPS was similar across all the patient groups and no significant difference was observed.

Conclusion: Plasma FABP2, IL-10 and LPS did not distinguish MC patients from healthy controls in our study. IL-10 concentration in patients with active UC was lower when compared to MC patients and healthy controls.

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P0323

THE EFFECT OF INDUCTION THERAPY WITH INFLIXIMAB OR VEDOLIZUMAB ON HEPcidIN AND IRON STATUS IN PATIENTS WITH INFLAMMATORY BOWEL DISEASE

R. Loveikyte^{1,2}, A.R. Bourgonje², J.J. van der Reijden¹, M.L.C. Bulthuis³, L.J.A.C. Hawinkels¹, M.C. Visschedijk², E.A.M. Festen², H.M. van Dullemen², R.K. Weersma², H. van Goor³, A.E. Van Der Meulen - De Jong¹, G. Dijkstra²

¹Leiden University Medical Center, Department of Gastroenterology and Hepatology, Leiden, Netherlands, ²University Medical Center Groningen, Department of Gastroenterology and Hepatology, Groningen, Netherlands, ³University Medical Center Groningen, Department of Pathology and Medical Biology, Groningen, Netherlands

Contact E-Mail Address: r.loveikyte@lumc.nl

Introduction: Differentiating absolute iron deficiency from functional iron restriction is challenging in active Inflammatory Bowel Disease (IBD). Hepcidin, the systemic iron regulator, could be the key to the diagnosis and management of absolute iron deficiency. In this study, we assessed hepcidin as a diagnostic iron deficiency marker and we explored the relationship between hepcidin, inflammation, hypoxia, and iron deficiency in patients receiving induction therapy with infliximab (IFX) or vedolizumab (VEDO).

Aims & Methods: 130 patients with IBD, who received induction therapy with IFX or VEDO for active disease, were included in this cohort study. Clinical and biochemical data were extracted from medical records. Serum samples at baseline and week 6 of induction therapy were retrieved from the University Medical Center Groningen (UMCG) biobank and analysed for: hepcidin, inflammation (e.g., interleukins [IL] 6, 10, and Tumour Necrosis Factor- α [TNF- α]), oxidative stress (free thiols), and hypoxia (e.g., erythropoietin [EPO], Macrophage Inflammatory Protein-3 α [MIP-3 α]). Data were analysed by stratifying based on the response at week 14.

Response to therapy was defined by either General Physician's Assessment at week 14 of induction therapy, normalisation or at least a three-point decrease in clinical scores: Harvey-Bradshaw Index (HBI) for Crohn's Disease, Simple Clinical Colitis Activity Index (SCCAI) for ulcerative colitis. For comparison, serum samples from 50 age- and gender-matched healthy controls were obtained from the pre-donation biobank at the UMCG.

Results: At baseline, hepcidin correlated positively with ferritin and negatively with soluble Transferrin Receptor/log ferritin index [$\rho = 0.74$ and $\rho = -0.79$, respectively; $P < 0.001$ for both markers], while inflammation- and hypoxia-associated markers showed only marginal correlations. Hepcidin accurately identified absolute iron deficiency: $AUC_{(hepcidin)} = 0.89$ [95% CI: 0.82–0.95; $P < 0.001$]. In total, 75.4% of patients responded to the induction therapy. Induction with either IFX or VEDO decreased hepcidin [13.5 ng/mL vs. 9.5 ng/mL; $P < 0.001$], ferritin [45.5 ug/L vs. 37.0 ug/L, $P < 0.05$], and inflammatory markers at week 6, while transferrin increased [2.4 g/L vs. 2.5 g/L, $P < 0.001$].

In addition, hypoxia (i.e., EPO, MIP-3 α) and inflammatory markers such as faecal calprotectin, IL-6, IL-22, and TNF- α improved significantly. In contrast, none of these changes were observed in patients who did not respond to the therapy.

Conclusion: Hepcidin levels in IBD are primarily driven by iron status, even in an inflammatory state. Therefore, hepcidin could be a potential diagnostic iron deficiency biomarker that could assist therapeutic decision-making. In addition, induction therapy with either IFX or VEDO can reduce hepcidin levels, especially in patients who respond to the therapy.

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P0324

C-REACTIVE PROTEIN/ALBUMIN RATIO (CAR) AS A MARKER FOR DETECTING ACUTE SEVERE ULCERATIVE COLITIS IN EGYPTIAN PATIENTS

D. Header¹, R. Abd El Halim², M. Elkeleny², E. Bedewy², A. El Lakany²

¹Alexandria University, Faculty of Medicine, Gastroenterology, Alexandria, Egypt, ²Alexandria University, Alexandria, Egypt

Contact E-Mail Address: d.ahmedellakany@yahoo.com

Introduction: The C-reactive protein/albumin ratio (CAR) is an inflammatory marker that is considered to have prognostic value in many diseases as acute severe ulcerative colitis (ASUC). A high level of the CAR is associated with increased inflammatory burden, poor prognosis, and mortality.

Aims & Methods: Our aim in the present study was to investigate the diagnostic performance of the CAR in determining the clinical severity of acute severe ulcerative colitis (ASUC).

Materials and methods: A retrospective study on 200 UC patients that were admitted to the Gastroenterology unit of the Alexandria University, over an 8-year period from January 2012 to January 2020, was conducted. Patient demographic data, laboratory values, and clinical and endoscopic disease activity scores were evaluated. C-reactive protein (CRP) and albumin levels were recorded. The CAR was calculated to determine clinical severity.

Results: Of the 200 patients, 135 (67.5%) were men and 65 (32.5%) were women. Mean age was 43.5 ± 9.8 years. Patients were divided into groups with mild, moderate, or severe disease activity and there were statistically significant differences in the CAR, the erythrocyte sedimentation rate (ESR), CRP levels, and albumin levels ($p=0.001$; $p<0.05$).

With a cut-off value of 0.6, the CAR performed best in defining patients with severe disease, with an area under the curve (AUC) of 0.985, 98% sensitivity, 100% specificity, positive predictive value of 100%, and negative predictive value (NPV) of 97%, $p<0.001$. AUC values for the diagnosis of severe disease were 0.985, 0.88, 0.72, and 0.65 for the CAR, CRP, albumin, and the ESR, respectively.

Conclusion: There was a statistically significant association between the CAR and clinical disease activity in patients with UC. The CAR is a reliable and practical tool for detecting ASUC.

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Disclosure: Nothing to disclose.

P0325

RISK FACTORS OF CYTOMEGALOVIRUS COLITIS IN INFLAMMATORY BOWEL DISEASE

S. Nacer¹, F. Haddad¹, F.Z. Elrhaoussi¹, M. Tahiri Joutei Hassani¹, W. Hliwa¹, A. Bellabach¹, W. Badre¹

¹CHU Ibn Rochd, Casablanca, Morocco

Contact E-Mail Address: saramedstudies@gmail.com

Introduction: Patients with inflammatory bowel disease (IBD) are at an increased risk for cytomegalovirus (CMV) colitis. The major challenge is to differentiate between IBD flare and CMV colitis. Early detection and rapid initiation of antiviral treatment for CMV disease seems to reduce the mortality and colectomy rate.

Aims & Methods: The aim of this study was to identify risk factors for CMV colitis in IBD patients. We conducted a single center retrospective study between 2016 and 2021 including 130 active IBD (49 Crohn's disease (CD), 81 Ulcerative Colitis (UC)) patients with known CMV status. Disease activity of UC and CD was assessed by Mayo score and Harvey-Bradshaw Index (HBI) respectively.

CMV colitis was defined by the presence of clinical signs associated with inclusion bodies detected microscopically using haematoxylin and eosin (H&E) and/or CMV immunohistochemistry (IHC) staining and/or quantitative polymerase chain reaction (qPCR) in colonic biopsies with a cut-off

value of >250 copies/mg. Statistical analysis identified several independent risk factors for CMV colitis. P value <0.05 was considered statistically significant.

Results: Of the 130 patients with active IBD, 13 patients were diagnosed with CMV colitis. The median age was 36.7 years with a female to male ratio of 2. Positive CMV inclusion bodies in H&E staining were identified in 53.8% of patients. IHC staining was positive in 23% of patients and qPCR in 30.7% of patients.

The median disease duration in the CMV colitis group was shorter than that in the CMV negative group (26 versus 56 months; $p=0.001$). The median Mayo Score for patients with UC in CMV negative group was 7 compared with 10 in CMV colitis group ($p=0.026$). Patients with CD in the CMV negative group had a median HBI of 14 compared with 17 in CMV colitis group ($p=0.034$). Endoscopic findings include digging ulceration (3; 23%) longitudinal ulceration (4; 30.7%), and ulceration in map (2; 15.3%).

The presence of endoscopic ulcers turned out to be predictive factors for CMV colitis ($p=0.02$). Medications used in our patients included azathioprine, mesalazine, steroids, and anti-TNF α . They were 37.3%, 34.5%, 21.5%, and 10%, respectively. Among the 28 patients who received steroids, 7 (25%) were steroid-refractory colitis.

Higher steroid usage rate was observed in the CMV positive group compared with CMV negative group (30.8% vs 18.5%, $p=0.003$).

The use of more than two lines of immunosuppressive drugs ($p=0.001$) and steroid-refractory colitis ($p=0.001$) were risk factors for patients with IBD to develop CMV colitis.

All patients in the CMV colitis group received antiviral therapy. Nine patients showed an improvement of their clinical disease activity, 2 patients underwent a colectomy and 2 patients died because of sepsis.

Gender, age, C-reactive protein (CRP), administration of biologics (infliximab, adalimumab), antimetabolites (methotrexate, 6-mercaptopurin, azathioprine) or 5-aminosalicylates were not significantly associated with CMV colitis.

Conclusion: Overall, CMV colitis occurs in patients with UC rather than CD. The use of corticosteroid, combined immunosuppressants and severe IBD patients were identified as risk factors to CMV disease. A closely monitoring in these patients is needed to provide timely diagnosis and early antiviral treatment.

Disclosure: Nothing to disclose.

P0326

THE EFFECT OF RENIN-ANGIOTENSIN-ALDOSTERONE SYSTEM BLOCKING AGENTS ON THE 5- AND 10-YEAR DISEASE COURSE OF CROHN'S DISEASE PATIENTS WITH HYPERTENSION

C. Karime¹, J.G. Hashash², M.F. Picco², J.A. Murray³, F.A. Farraye²

¹Mayo Clinic Florida, Department of Internal Medicine, Jacksonville, United States, ²Mayo Clinic Florida, Inflammatory Bowel Disease Center, Department of Gastroenterology and Hepatology, Jacksonville, United States, ³Mayo Clinic, Gastroenterology and Hepatology, Rochester, United States

Contact E-Mail Address: chriskarime@hotmail.com

Introduction: An association between the proinflammatory renin-angiotensin-aldosterone system (RAAS) and inflammatory bowel disease (IBD) has been reported, suggesting that RAAS-blocking therapy may be beneficial in patients with IBD. Using surrogate markers of IBD severity, we aimed to retrospectively compare the 3-, 5-, and 10-year disease course of patients with Crohn's disease (CD) initiated on either angiotensin-converting enzyme inhibitor (ACEI) or angiotensin receptor blocker (ARB) therapy.

Aims & Methods: Patients with CD and hypertension who initiated therapy with an ACEI (n= 40, mean age 59.9, 55% male) or ARB (n= 40, mean age 59.9, 50% male) between 2000-2016 were enrolled and matched to controls (n= 40, mean age 57.8, 42.5% male). Matching was performed on age at CD diagnosis, CD duration before study entry, gender, body mass index, Montreal classification, and comorbid conditions (hypertension, nicotine dependence, diabetes).

Clinical (emergency department visits, hospitalizations, corticosteroid use, and biologic therapy use), radiological (computer tomography [CT], CT enterography, magnetic resonance imaging, magnetic resonance enterography), and procedural (endoscopic, IBD-related operations) data were collected as surrogate markers of IBD severity in the 3-, 5-, and 10-years following ACEI or ARB initiation. Statistical analysis was carried out by Kruskal-Wallis test followed by Dunn's post hoc test. A P-value of <0.05 was used as a criterion of statistical significance.

Results: Compared to matched controls, ARB-treated patients had a better overall 10-year disease course, with significantly fewer emergency department visits (0.91 vs. 1.70, p<0.05, - 47%) and corticosteroid prescriptions (1.06 vs. 2.88, p<0.01, - 63%). ACEI-treated patients had an overall worse disease course, with significantly more imaging studies (3.00 vs. 1.75, p<0.05, + 71%) and endoscopic procedures (2.70 vs. 1.78, p<0.01, + 52%) at 5-years, and significantly more imaging studies (6.19 vs. 3.50, p<0.05, + 77%), endoscopic procedures (5.91 vs. 3.78, p<0.01, + 56%), and IBD-related operations (0.59 vs. 0.18, p<0.05, +228%) at 10-years. ACEI-treated patients were more likely to initiate biologic therapy compared to both controls (56.0% vs. 32.3%) and ARB-treated patients (56.0% vs. 17.4%).

Conclusion: Given the known cardio- and reno-protective effect of RAAS blockade, use of ACEI and ARB therapy to manipulate proinflammatory RAAS activation in IBD is a potentially attractive option.

Our study indicates that RAAS-blocking agents may significantly affect the long-term disease course of patients with CD, even when initiated at a relatively older age. Whilst ARB therapy was found to have an ameliorating effect on CD course at 10-years, ACEI use was found to have a deleterious effect at 5- and 10-years following therapy initiation.

If confirmed in larger population studies, the presence of CD may influence choice of future antihypertensive therapy.

Variable	Average number of events per patient								
	3 years			5 years			10 years		
	CD-ACEI (n= 40)	CD-ARB (n= 40)	CD- Control (n= 40)	CD-ACEI (n= 40)	CD-ARB (n= 40)	CD- Control (n= 40)	CD-ACEI (n= 32)	CD- ARB (n= 33)	CD- Control (n= 40)
Emergency department visits (all)	1.25	1.50	1.90	2.52	2.30	2.60	5.34	3.91	6.1
Emergency department visits (abdominal pain)	0.58	0.48	0.48	1.05	0.60	0.75	2.34*	0.91*	1.70*
Hospitalizations (abdominal pain)	0.18	0.15	0.25	0.38	0.23	0.28	0.88	0.30	0.65
Systemic corticosteroid use (single instances)	0.63	0.35	1.00	1.53	0.45	1.28	3.72*	1.06*	2.88*
Abdominal imaging	2.05	1.55	1.25	3.00*	1.83*	1.75*	6.19*	2.73*	3.50*
Endoscopic procedures	1.45	0.90	1.05	2.70*	1.60*	1.78*	5.91*	2.61*	3.78*
Gastrointestinal operations	0.13	0.08	0.08	0.15	0.10	0.08	0.59*	0.15*	0.18*

Table 1: Summary of clinical, radiological, and procedural variables in the 3-, 5-, and 10-years following initiation of either ACEI or ARB therapy.

* = p < 0.05

Disclosure: Nothing to disclose.

P0327

A MARKER OF PROTEOLYTIC DEGRADATION OF CROSS-LINKED TYPE V COLLAGEN IS UPREGULATED IN PATIENTS WITH INFLAMMATORY BOWEL DISEASE

M. Pehrsson¹, L.E. Godskesen², S. Qubtan¹, M.A. Karsdal¹, A. Krag³, J. Kjeldsen², J.H. Mortensen¹

¹Nordic Bioscience A/S, Biomarkers and Research, Herlev, Denmark, ²Odense University Hospital, Dept. of Medical Gastroenterology, Odense, Denmark, ³Odense University Hospital, Dept. of Gastroenterology and Hepatology, Odense, Denmark

Contact E-Mail Address: mpe@nordicbio.com

Introduction: In inflammatory bowel disease (IBD), the continuation of wound healing results in excessive production of extracellular proteins capable of driving disease progression. Among these proteins are the fibrillar collagens and enzymes catalyzing collagen cross-linking. The excessive deposition of collagens and their subsequent cross-linking are critical processes in intestinal fibrosis, thought to affect all IBD patients to various degrees, potentially progressing the disease. The induction of proteolysis of the cross-linked collagens may lead to regression of intestinal fibrosis, though no tools are currently available for the objective assessment of these underlying processes.

Aims & Methods: We developed a novel sandwich enzyme-linked immunosorbent assay quantifying cross-linked and protease-degraded metabolites of type V collagen (NBH-276). Several technical parameters such as the measurement range, dilution recovery, spiking recovery, inter- and intra-variability, interference (hemoglobin, biotin, and lipid), and analyte stability were evaluated. The acceptance criteria for the technical validation of the assay were a recovery of 100% ±20 and an inter-intra variability of <15%.

We evaluated the formation of type V collagen (PRO-C5) and subsequent proteolytic release by the NBH-276 biomarker in an *in vitro* scar-in-a-jar model using human intestinal fibroblast (Cellbiologics). The fibroblasts were stimulated for up to 12 days with or without 20 ng/mL of TGF-β, followed by adding 0.5 ng/mL of either MMP-9 or MMP-13 for 48 hours.

The levels of protease degraded and cross-linked metabolites of type V collagen were investigated in the serum of patients with UC (n=47) and CD (n=39) from a prospective observational study conducted at Odense University Hospital and healthy controls (HC) (n=32).

The statistical difference and ability of NBH-276 to differentiate the biomarker levels between IBD patients and the HCs were performed by Kruskal-Wallis with Dunns test for multiple comparisons and ROC analysis. The biomarker levels of the *in vitro* model were evaluated by two-way ANOVA using Dunnet test for multiple comparisons. The statistical analysis was performed by Graphpad Prism 9.3.1 (Graph Pad Software, La Jolla, CA, USA)

Results: The technical validation of the NBH-276 assay demonstrated acceptable results with recoveries of dilution, spiking, interference, and analyte stability of 100±20%. The inter-intra assay variability was 14.4% and 5.3%, respectively, and a measurement range of 1.0 – 62.8 ng/mL. Human intestinal fibroblast stimulated with 20 ng/mL TGF-β had elevated levels of PRO-C5 compared to unstimulated cells on days 4, 8, and 12 (all: p < 0.01, [60.76 ng/mL, 57.73 ng/mL, 64.84 ng/mL]). The NBH-276 biomarker was unmeasurable in the cell supernatants.

Following MMP-9 or MMP-13 cleavage of the deposited cell matrix, the measured levels of NBH-276 increased 3.2-fold (p < 0.01) and 1.9-fold (p > 0.05), respectively, compared to the uncleaved control. The serum levels of NBH-276 were found significantly elevated in patients with UC or CD compared to the HCs (all: p < 0.0001, mean differences [3.87 ng/mL and 2.19 ng/mL]). The AUROC for NBH-276 separating UC or CD patients from HCs was 0.99 (all: p < 0.0001) (see Table 1 for sensitivity and specificity).

Biomarker	Matrix	P-value	Area under the curve	Sensitivity (95% Confidence interval)	Specificity (95% Confidence interval)
PRO-C5 (Type V collagen formation)	Cell supernatant	compared to unstimulated cells on days 4, 8, and 12: $p < 0.01$			
	Cell supernatant	compared to unstimulated cells: $p > 0.05$			
CTX-V (cross-linked and protease-degraded type V collagen)	Cleaved cell matrix	compared to uncleaved control: MMP-9, $p < 0.01$; MMP-13, $p > 0.05$			
	Serum UC patients	compared to healthy controls: $p < 0.0001$	0.99	100.0% (92.4 - 100.0)	96.9% (84.3 - 99.8)
	Serum CD patients	compared to healthy controls: $p < 0.0001$	0.99	100.0% (91.0 - 100.0)	96.9% (84.3 - 99.8)

Conclusion: Our study demonstrated the biological relevance of the novel CTX-V biomarker as a cross-linked and protease-degraded fragment of type V collagen. MMP-9 induced the release of CTX-V in the fibrotic human intestinal fibroblast *in vitro* model and subsequently showed relevance in UC and CD patients. The biomarker may potentially enable a noninvasive and objective quantification of proteolysis of cross-linked type V collagen in IBD patients.

Disclosure: Martin Pehrsson, Sahra Qubtan, Morten Asser Karsdal, and Joachim Høg Mortensen are all employed at Nordic Bioscience A/S, a small-medium biomedical company focused on the development of biomarkers.

P0328

HISTOLOGIC DISEASE ACTIVITY CORRELATES WITH ENDOSCOPIC SEVERITY IN PATIENTS WITH MODERATE TO SEVERE CROHN'S DISEASE

W. Reinisch¹, G. De Hertogh², M. Protic³, L.S. Chan³, F. Magro⁴, P. Pollack⁵, B. Feagan⁵, N. Harpaz⁶, R. Pai⁷

¹Medical University of Vienna, Dep. of Internal Medicine IV, Division of Gastroenterology and Hepatology, Wien, Austria, ²University Hospital Leuven, Pathology, Leuven, Belgium, ³Eli Lilly and Company, Indianapolis, United States, ⁴University Hospital São João, Porto, Portugal, ⁵Robarts Clinical Trials Inc., London, Canada, ⁶Icahn School of Medicine at Mount Sinai, New York City, United States, ⁷Mayo Clinic, Scottsdale, United States

Contact E-Mail Address: walter.reinisch@meduniwien.ac.at

Introduction: The role of histopathology evaluation in Crohn's disease (CD) is not precisely defined. Due to the heterogeneity of phenotypes, the discontinuity of distribution and the transmural nature of inflammation, the interpretation of histologic outcomes is complex.

Aims & Methods: To analyze how histology relates to established outcomes in CD, we examined association between histologic and endoscopic disease activity measured by frequently used scores (simple endoscopic score for Crohn's disease [SES-CD], Robarts histopathology index [RHI], global histological activity score [GHAS]) and the association between histologic or endoscopic severity with inflammatory biomarkers in a cohort of patients with moderate to severe CD. Patients (N=191) who were enrolled in a phase 2 randomized clinical trial (NCT02891226) in patients with moderate-to-severe CD were assessed at baseline (BL) for endoscopic disease location and severity as measured by SES-CD. Biopsies were obtained during BL endoscopy from the edge of the ulcers and the most inflamed mucosa in terminal ileum and 4 colonic segments (ascending, transverse, descending, rectum; N=10/patient, 2 per location with

the more severe score used), and scored by central readers blind to study treatment, timepoint, and response status using RHI and both modified and active GHAS (mGHAS: Q1, 3, 4, 5, 6; aGHAS: Q1, 4, 5, 6). Inflammatory biomarkers included fCLP and CRP; log-transformed values are used. Linear correlations between measures were determined using Pearson correlation coefficients (PCC) as exploratory analyses. Nominal p values are presented.

Results: SES-CD correlated well with all 3 histologic measures examined. While both fCLP and CRP correlated more closely with endoscopy than with histologic measures, fCLP had higher correlation with each histologic measure than CRP. 64% of patients had the same disease location at BL when measured by endoscopy or histology. Patients with endoscopic colonic disease displayed histologic ileal involvement in up to 20% of cases, while 13% of patients with endoscopic ileal disease demonstrated histologic colonic involvement (Table 1).

	Induction population N=191	Baseline endoscopic disease location			Total
		Colonic	Ileal	Ileal-colonic	
Baseline active histologic disease location	Colonic	46	0	12	58
	Ileal	3	21	15	39
	Ileal-colonic	10	4	42	56
	No active disease	5	5	7	17
	No biopsy	11	3	7	21
	Total	75	33	83	191

Number of patients with active disease at each location as determined by endoscopy or histology.

Active histologic disease at BL: modified Global Histologic Disease Activity Score >0 [GHAS; Q1, 3, 4, 5, 6] or sum of Robarts Histopathology Index [RHI] questions 2-4>0.

Modified GHAS: The score has been modified from the original publication by removing component 2 (architectural changes), 7 (presence of granuloma) and 8 (number of specific biopsies affected). Q1: Epithelial damage (0: Normal, 1: Focal Pathology, 2: Extensive Pathology); Q3: Infiltration of mononuclear cells in the lamina propria (0: Normal, 1: Moderately increase, 2: Severe increase); Q4: Infiltration of polymorphonuclear cells in the lamina propria (0: Normal, 1: Moderately increase, 2: Severe increase); Q5: Polymorphonuclear cells in epithelium (1: In surface epithelium, 2: Cryptitis, 3: Crypt abscess); Q6: Presence of erosion and/or ulcers (0: No, 1: Yes).

Active GHAS: modified GHAS excluding Q3. RHI: The score has been modified from original publication by removing component 1 (chronic inflammatory infiltrate). Q2: Lamina propria neutrophils (0: None, 1: Mild but unequivocal increase, 2: Moderate increase, 3: Marked increase); Q3: Neutrophils in epithelium (0: None, 1: <5% crypts involved, 2: <50% crypts involved, 3: >50% crypts involved); Q4: Erosion or ulceration (0: No erosion, ulceration, or granulation tissue, 1: Recovering epithelium + adjacent inflammation, 2: Probable erosion-focally stripped, 3: Unequivocal erosion, 4: Ulcer or granulation tissue).

Endoscopic disease location was determined by presence of any endoscopic lesions/inflammation at isolated ileum only, isolated colonic segments only, or at both ileal and colonic segments.

Histologic location was determined by presence of histologic inflammation at isolated ileum only, isolated colonic segments only, or at both ileal and colonic segments, independent of endoscopic activity.

Table 1: Disease location at baseline as measured by endoscopy or histology

Conclusion: Although histologic disease activity in CD, as determined by 3 different measures, correlates well with endoscopic assessment of disease, histologic involvement provides complementary information on disease distribution and extension. Further analyses are required to understand the additive role of mucosal histology in CD.

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P0329

THERAPEUTIC DRUG MONITORING OF VEDOLIZUMAB IN INFLAMMATORY BOWEL DISEASE PATIENTS - TUMMY TRIAL

M. Sivridas¹, L.J.J. Derijks¹, P. Boekema¹, A.A. Van Bodegraven², L. Gilissen³, T.E.H. Römkens⁴, D.R. Wong⁵, R. Creemers², F.C. Loeff⁶, T. Rispens⁶

¹*Máxima Medical Center, Veldhoven/Eindhoven, Netherlands,*

²*Zuyderland Medical Center, Sittard-Geleen, Netherlands,*

³*Catharina Ziekenhuis, Gastroenterology and Hepatology, Eindhoven, Netherlands,* ⁴*Jeroen Bosch Hospital, Den Bosch, Netherlands,* ⁵*Zuyderland Medical Centre, Clinical Pharmacy & Toxicology, Sittard-Geleen, Netherlands,* ⁶*Sanquin Diagnostic Services, Amsterdam, Netherlands*

Contact E-Mail Address: merve.sivridas@mmc.nl

Introduction: There is limited evidence for therapeutic drug monitoring (TDM) in inflammatory bowel disease (IBD) patients treated with vedolizumab (VDZ) during maintenance phase. An exposure-response relation has been reported in patients treated with VDZ in the GEMINI studies. Even though this relation has been proven, TDM is not general practice in managing VDZ.

Aims & Methods: This is a prospective, observational multicenter study of patients with IBD treated with VDZ in the maintenance phase. The aim of our study was to determine whether there is a correlation between VDZ trough levels and disease activity. Patient demographics, biomarkers and serum trough levels have been collected.

Clinical disease activity has been obtained by Harvey Bradshaw Index (HBI) for Crohn's disease (CD) and Simple Clinical Colitis Activity Index (SCCAI) for colitis ulcerosa (UC). Clinical remission was determined as HBI<5 and SCCAI <3. Biochemical remission was defined as <250 mg/kg.

Results: total of 149 patients (58 CD, 91 UC) were included. VDZ levels varied from 0.1 to 74.4 mg/L. The median VDZ level in CD patients in remission was 16.5 mg/L and 16,6 mg/L in UC patients. There was no significant correlation between trough VDZ level and clinical remission in both group of patients. Neither was there an association in biochemical remission and VDZ trough levels.

Conclusion: TDM in IBD patients showed a great interindividual variability in VDZ trough levels. In this population trough VDZ levels were not associated with clinical and biochemical remission during maintenance phase.

Disclosure: Nothing to disclose

P0330

DIETARY BEHAVIOR AND RISK OF ORTHOREXIA IN PATIENTS WITH INFLAMMATORY BOWEL DISEASE

F.M. Di Giorgio¹, S.P. Modica¹, M. Saladino¹, S. Muscarella¹, L.M. Amato¹, S. Ciminnisi¹, P.L. Almasio², M. Cappello¹

¹*University of Palermo, Gastroenterology and Hepatology Section, Promise, Palermo, Italy,* ²*University of Palermo, Promise, Palermo, Italy*

Contact E-Mail Address: francescam.digiorgio@libero.it

Introduction: Patients with inflammatory bowel diseases (IBD), Crohn's disease (CD) and ulcerative colitis (UC), have a strong perception on the role of food and many of them change their diet after diagnosis, adopting restrictions that can lead to anxiety, stress and nutritional deficiencies.

Orthorexia nervosa is a eating behavior that follows the pathological obsession for biologically pure and healthy food. Only a few studies have addressed the topic in patients suffering from disease of the gut and there are no studies in patients with IBD.

Aims & Methods: The aim of this study is to assess the risk of orthorexia in patients with IBD. The Donini standardized questionnaire ORTO-15 test was used to assess the risk of orthorexia in consecutive patients with IBD attending the clinic or hospitalized in a tertiary referral IBD center from southern Italy. Data regarding sex, age, marital and occupational status, weight, height, BMI, IBD type (UC or CD), time of diagnosis, IBD treatment, surgical history, disease activity, gluten or/and lactose intolerance and tobacco use were also collected.

Results: 48 patients, 22 CD and 26 UC, were enrolled. A risk of orthorexia (threshold value below 40) was found in 34 (70.8%) patients, 17 (50%) CD, 24 (70.6%) male and 10 (29.4%) female, mean age 50 ± 15 years, weight 66 ± 15 Kg, BMI 24 ± 5 . 19 (55.9%) patients were married and 15 (44.1%) were single/widowed/separated/divorced. 27 (79.4%) of them were employed and 7 (20.6%) unemployed. As far as concerns education, 13 (38.2%) patients had primary school /middle school degree and 21 (61.8%) had a high school or university degree.

Most of the patients (31 i.e. 91.2%) were on biologics and 3 (8.8%) on conventional therapy. 5 patients (15.7%) had been operated on. In 28 patients (82.4%) the disease was in remission/mild activity, in 6 (17.6%) in moderate/severe activity. Only 3 patients with orthorexia (8.8%) had a diagnosed food intolerance (lactose or gluten), 15 patients (44.1%) were smokers. Body weight (lower) and marital status (single) were significantly related to the risk of orthorexia while there were no significant correlations with IBD type or disease characteristics.

Conclusion: Orthorexia is common in IBD and is related to low body weight and single status. Though not yet recognized as an eating disorder, orthorexia can impact on life style and lead to unnecessary dietary restrictions. Appropriate counselling by trained dietitians is strongly warranted in IBD clinics.

Disclosure: Nothing to disclose.

P0331

RESPONSIVENESS OF FECAL CALPROTECTIN AND QUALITY OF LIFE QUESTIONNAIRES TO CHANGE IN POUCH DISEASE ACTIVITY. RESULTS FROM A PROSPECTIVE TRIAL

J. Ollech¹, H. Yanai², I. Avni-Biron³, Y. Snir¹, H. Banai¹, N. Wasserberg², I. White⁴, I. Dotan¹

¹Rabin Medical Center, Gastroenterology, Petah Tikva, Israel,

²RABIN Medical Center, Dr., Tel Aviv, Israel, ³Rabin Medical Center, IBD and Capsule Endoscopy, Sde Hemed, Israel, ⁴Rabin Medical Center, Petach Tikva, Israel

Contact E-Mail Address: jacob.eliezer.ollech@gmail.com

Introduction: Assessment of pouchitis is performed using the validated pouchitis disease activity index (PDAI). Including clinical, endoscopy and histology subscores, this is invasive, labour-intensive and time-consuming. We aimed to assess whether inflammatory biomarkers and quality of life questionnaires would reflect change in disease activity in these patients.

Aims & Methods: Patients with acute pouchitis were prospectively recruited at the Rabin Medical Center in Israel, a major referral center for patients with a J-pouch. Acute pouchitis was diagnosed clinically by the treating physician in a patient with compatible clinical symptoms – i.e., a combination of increase in the number of bowel movements from baseline, urgency, bleeding and pain. Patients were treated with a 2-week course of antibiotics – either metronidazole and ciprofloxacin or metronidazole and doxycycline.

Full PDAI including clinical, endoscopic and histologic evaluation was performed at baseline and following 2 weeks of antibiotic therapy. Patients had comprehensive laboratory tests including fecal calprotectin (FC) mea-

surements at both time points. Patients also filled quality of life questionnaires (short inflammatory bowel disease questionnaire - SIBDQ, inflammatory bowel disease [IBD] disk) at both time points.

Outcomes of interest included the responsiveness of FC and quality of life questionnaires to change in pouch disease activity according to the PDAI. Paired analyses were performed to compare results between the 2-time points.

Results: Twenty patients were prospectively enrolled. At enrollment, the median age was 36 years IQR [27-56], females 12 (60%). The median interval from closure of ileostomy was 7 years IQR [2-17]. Median PDAI score: 9 IQR [8-11.5], median FC: 661 ug/g IQR [425-1261], median C-reactive protein: 1.1 mg/dl IQR [0.5-1.8] and median hemoglobin: 13.2 g/dl IQR [12.1-14.1].

Following 2 weeks of antibiotic treatment, PDAI decreased significantly from a median of 9 to 5 ($p=0.007$). This was mainly attributed to significant differences in both the clinical ($p=0.01$) and endoscopic subscores ($p=0.001$) but not the histologic subscore ($p=0.1$). FC decreased significantly between the 2 time points from a median of 661 ug/g to 294 ug/g ($p=0.02$).

Likewise, both quality of life questionnaires improved significantly following antibiotic therapy: The median SIBDQ increased from 44 to 50 ($p=0.02$) and the median IBD disk score decreased from 59 to 31 ($p=0.01$). Both antibiotic regimens had comparable effects. No serious adverse events were noted.

Conclusion: We show that FC and quality of life questionnaires reflect real time changes in inflammatory pouch activity modified by therapeutic interventions.

This study validates the use of FC as biomarker sensitive to change in pouch disease activity and encourage its use when managing patients with a pouch. The data may contribute to the development of a fully validated index of pouchitis disease activity for use in clinical practice and clinical trials.

Disclosure: Nothing to disclose.

P0332

PREVALENCE OF DISEASE RELATED MALNUTRITION IN PATIENTS WITH INFLAMMATORY BOWEL DISEASE: A MULTICENTRIC CROSS-SECTIONAL STUDY

C. Vigano¹, A. Palermo¹, G. Mulinacci¹, A. Losco², G. Meucci³, F.A. Caprioli⁴, A. Amato⁵, S. Massironi¹, GSMII Study Group

¹University of Milano-Bicocca and European Reference Network on Hepatological Diseases (ERN RARE-LIVER), San Gerardo Hospital, Division of Gastroenterology and Center for Autoimmune Liver Diseases, Department of Medicine and Surgery, Monza, Italy, ²ASST Santi Paolo e Carlo, UO Gastroenterologia Presidio San Carlo, Milano, Italy, ³Ospedale San Giuseppe, Unità di Gastroenterologia ed Endoscopia Digestiva, Milano, Italy, ⁴Università degli Studi di Milano, Fondazione IRCCS Cà Granda, Ospedale Policlinico di Milano, Department of Pathophysiology and Transplantation, Unit of Gastroenterology and Endoscopy, Milano, Italy, ⁵Ospedale Valduce, Gastroenterology Unit, Como, Italy

Contact E-Mail Address: chiara.vigano@hotmail.it

Introduction: Inflammatory bowel diseases (IBD) are chronic, relapsing, inflammatory disorders of the gut. In IBD many factors might lead to malnutrition, namely decreased food intake, intestinal malabsorption, chronic faecal loss of proteins and erythrocytes, and inflammation. Disease Related Malnutrition (DRM) is a specific type of malnutrition caused by a concomitant disease¹. To date prevalence and risk factors for DRM in IBD are not well defined².

Aims & Methods: The primary aim of the study was to define the prevalence of both DRM and microelement deficiency in patients with IBD; the secondary aim was to assess variables related to DRM.

A multicentre, cross-sectional study was performed including all adult patients with IBD at 11 centers in the Lombardy District, Northern Italy, adhering to the Gruppo di Studio per le Malattie Infiammatorie Intestinali (GSMII), over an inclusion period of two weeks. Nutritional status was assessed with the Body Mass Index (BMI) and the Malnutrition Universal Screening Tool (MUST).

According to the European Society for Clinical Nutrition and Metabolism (ESPEN) guidelines³, DRM was defined as being at risk of malnutrition (MUST ≥ 1) combined with either a BMI $< 18.5 \text{ kg/m}^2$ or unintentional weight loss $> 10\%$ indefinite of time or $> 5\%$ over the last 3 months and BMI $< 20 \text{ kg/m}^2$ if < 70 years of age, or $< 22 \text{ kg/m}^2$ if ≥ 70 years of age.

Results: Among the 295 enrolled patients (148 Crohn's disease (CD), 147 Ulcerative colitis (UC)), the prevalence of DRM was of 23%, with no statistical difference between CD and UC.

In CD, DRM patients had higher median Crohn's Disease Activity Index (CDAI) than non-malnourished patients (128.5 vs 56.0, $p < 0.0001$), no difference in Disease Activity Index (DAI) was found in UC. When compared to non-malnourished IBD patients, those with DRM had higher median C-reactive protein (CRP) levels (0.3 mg/dl vs 0.24 mg/dl, $p = 0.04$) and lower albumin (3.9 g/dl vs 4.2 g/dl $p = 0.0019$), prealbumin (20 mg/dl vs 25 mg/dl, $p = 0.0082$) and haemoglobin levels (12.8 g/dl vs 13.7 g/dl, $p < 0.0001$).

At univariate logistic regression, the variables related to DRM were: current hospitalization ($p < 0.0001$, Odds Ratio [OR] 32.14, CI 3.94-262.21), hospitalization in the previous month ($p < 0.0001$, OR 17.23, CI 6.10-48.73), serum albumin ($p = 0.002$, OR 0.37, CI 0.18-0.70), BMI ($p < 0.0001$, OR 0.63, CI 0.55-0.71), CRP ($p = 0.005$, OR 1.39, CI 1.10-1.74), CDAI for CD ($p = 0.0028$, OR 1.00, CI 1.00-1.09), and male gender ($p = 0.01$, OR 0.50, CI 0.29-0.89). At the multivariate analysis, only hospitalization in the previous month was significantly associated to DRM ($p = 0.0007$, coefficient 0.5).

In 23% of IBD patients a deficiency of at least one micronutrient was present, with no difference between UC and CD. In particular vitamin B12 deficiency (level $< 197 \text{ pg/ml}$) was present in 8 CD (5.4%) and 4 UC patients (2.7%) and folate deficiency (levels $< 3.89 \text{ ng/ml}$) in 17 CD (11.5%) and 12 UC patients (8.2%); a ferritin level $< 15 \text{ mg/dl}$ was present in 20 CD (13.5%) and 22 UC patients (in 15%).

Conclusion: DRM and microelement malnutrition are highly prevalent conditions in the IBD population. DRM in IBD seems to be associated with intestinal disease activity and recent hospitalization.

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P0333

LATENT TUBERCULOSIS IN PATIENTS WITH INFLAMMATORY BOWEL DISEASE CANDIDATES TO BIOLOGICS: PREVALENCE AND EFFECTIVENESS OF CHEMOPROPHYLAXIS

M. Saladino¹, L.M. Amato¹, R. Gaudiano², L. Carrozza¹, D. Brinch¹, S. Muscarella¹, P. Melatti¹, F. Di Giorgio¹, M. Cappello¹

¹Gastroenterology and Hepatology Section, Promise, University of Palermo, Palermo, Italy, ²University of Palermo, Infectious Disease Section, Palermo, Italy

Contact E-Mail Address: saladinomarica@gmail.com

Introduction: Screening for latent tuberculosis (LTBI) is recommended before starting biologic agents in Inflammatory Bowel Disease (IBD) because of the risk of reactivation. Anti-TB prophylaxis is mandatory in those patients with a positive screening test.

Aims & Methods: The aim of this study is to assess the prevalence of LTBI in IBD-patients candidates for biological therapy, the reliability of screening tests and effectiveness of therapy. A retrospective observational study was conducted on all IBD-patients submitted to screening for treatment with biological agents between November 2019 and April 2021 in our tertiary referral center. Patient's characteristics (type of IBD, type of biologics, screening results, history of previous TB, concomitant therapy, TB prophylaxis) were analyzed in relation to outcomes.

Results: 394 IBD-patients (254 CD, 138 UC, 2 undetermined colitis, 241 males, mean age 46 yrs) were recruited. Mean age was 56,96 (SD $\pm$ 12,09) in patients with LTBI and 44,75 (SD $\pm$ 16,35) in those negative for LTBI ($p < 0,0001$), there were no other significant differences between the two groups.

All patients were screened for LTBI: 390 through quantiFERON-TB gold and 4 through TST; 361 patients (91,6%) were negative, 27 (6,85%) tested positive. 6 cases obtained a undetermined result (1,52%), most of them on steroids; 5 of them performed a repeat test (4 quanti-FERON-TB Gold and 1 TBSpot) with a negative result.

All patients with LTBI received prophylactic treatment: 19 isoniazid (INH), 5 rifampicin (RMP), 3 a combination of both. 73.68% completed INH treatment (9.21 $\pm$ 2.55 months), 26,32% stopped therapy for adverse reactions and were switched to rifampicin. Rifampicin treatment was completed by all patients without side effects. Biologics were started after one month. The majority of patients were treated with anti-TNF alfa agents (235), vedolizumab was used in 116, ustekinumab in 43. None of the patients submitted to TB prophylaxis presented a TB reactivation while on therapy, regardless of the type of biologic, and on follow-up.

Conclusion: Our results confirm that the prevalence of LTBI in our country is low but not negligible and is related to age. Quantiferon-TB-gold is confirmed as an accurate screening method for LTBI. Chemoprophylaxis either with RMP or INH proved to be highly effective in preventing reactivation, but safety is an issue especially for INH. LTBI is not a contraindication to biologics since none of the patients experienced a reactivation.

Disclosure: Nothing to disclose

P0334

TELEMONITORING IBD WITH THE APP CARE4TODAY IBD: A REAL-LIFE CASE-CONTROL STUDY

A. Costantino^{1,2}, D. Noviello³, M. Maregatti², F.S. Conforti¹, D. Stocco³, F. Cinque², M. Vecchi^{1,2}, F. Caprioli^{1,2}

¹Foundation IRCCS Ca' Granda Ospedale Maggiore Policlinico, Gastroenterology and Endoscopy, Milano Italia, Italy, ²University of Milan, Department of Pathophysiology and Transplantation, Milan, Italy, ³Politecnico di Milano, Department of Mathematics, Milan, Italy

Contact E-Mail Address: andreasconstantino@gmail.com

Introduction: Inflammatory Bowel Diseases (IBD) are chronic relapsing inflammatory diseases characterized by a progressive and disabling course which requires a strict long-term monitoring and timely optimization of treatment during a disease flare. [1, 2]

The use of telemedicine has developed quickly in recent years. In particular, mobile applications (Apps) have been developed for the remote monitoring of patients with IBD to ensure a tight control of the disease. [3-5]

During COVID-19 outbreak, we start adopting telemedicine solutions (tele-visits) and we start proposing an asynchronous digital solution to remote monitoring symptoms in IBD patients, the App Care4Today IBD (Bepatient, Paris, France), free of charge for patients as sponsored by Janssen (Beerse, Belgium).

Aims & Methods: First aim of the study was to evaluate the use and trust towards Care4today IBD App among IBD patients, and to identify possible determinants influencing patients' trust. Second aim was to evaluate differences in terms of clinical outcomes and patients' contacts with health care professionals (HCPs).

We performed a retrospective real-life observational single center case control study.

From April 2021 to May 2021, we have proposed to download Care4today IBD to consecutive IBD patients, while it was not proposed to a control group of consecutive IBD patients (June-August 2021).

Ease of use, patients' satisfaction, trust and prospective for future use were assessed through a 5 points Likert scale questionnaire adapted from the validated SUTAQ (Service User Technology Acceptability Questionnaire), a score of at least 4/5 was considered as agreement. Machine learning (ML) tools, decision tree (DT) and random forests (RF), were used to identify the determinants of patients' trust.

Demographic data and disease-related characteristics were extrapolated from patient's clinical records and collected. Clinical characteristics recorded during the activation date of Care4today IBD were considered as baseline conditions. The number of contacts with HCPs in the 6 months after the App activation were reported. Contacts were defined as outpatient accesses (visits or televisits, endoscopic and ultrasound examinations) and inpatient accesses (emergency room and hospitalization).

Results: Out of 176 enrolled patients, 120 patients used the App (68.2%), and 73 (41.5%) used it actively.

Among the patients who compiled the SUTAQ (61/173, 35.2%), 86.9% of patients trusted to use the App, 65.6% would recommend it to other patients with IBD and 59% found the App simple to use. The statements "the app can allow my HCPs to better monitor my condition" and "I believe that monitoring apps can be a useful tool for managing my disease" were agreed by 83.6%, and by 70.5%, respectively.

In contrast, disagreement (93.4% giving a score <3/5, and 86.9% giving a score ≤2/5) was expressed for the statement "Apps will replace my regular health and/or social care".

Regarding the ML analysis, the DT showed the variable that has been found to influence the most patients' trust is the conviction that the app is a tool useful for better monitoring of their disease by the HCP since it

represents the root of the tree which explains the final decision; the RF confirmed that this variable influenced the most patients' trust.

Considering contacts and clinical outcomes, no significant differences were observed among the two groups.

Conclusion: Forty percent of our patients actively used the Care4today IBD App, and approximately two-thirds of the respondents proved to be well disposed to its usage, showing a good level of confidence and trust in it.

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P0335

MUCIN MRNA ISOFORM SIGNATURES AS POTENTIAL NOVEL BIOMARKERS TO EVALUATE DISEASE STATUS IN PATIENTS WITH INFLAMMATORY BOWEL DISEASES

W. Arras¹, T. Breugelmans¹, B. Oosterlinck¹, H. Ceuleers¹, J. De Man¹, M. Somers², A. Jauregui Ameza², B. De Winter^{2,1}, A. Smet¹

¹University of Antwerp, Laboratory of Experimental Medicine and Paediatrics, Wilrijk, Belgium, ²University Hospital Antwerp, Edegem, Belgium

Contact E-Mail Address: arraswout@hotmail.com

Introduction: Inflammatory bowel diseases (IBD), such as Crohn's disease (CD) and ulcerative colitis (UC), are characterized by perpetual chronic relapsing inflammation of the intestines. Due to their large heterogeneity, it is difficult to find the right therapy for the right patient. Therefore, there is a need to find novel biomarkers for the monitoring of IBD. Mucosal barrier dysfunction and aberrant mucin expression are major hallmarks in the pathophysiology of IBD [1-2].

Furthermore, mucins are highly polymorphic which results in the occurrence of several mRNA isoforms. These mRNA isoforms could translate to proteins that exhibit functional differences. Currently, little attention has been given to the importance of mucin mRNA isoforms in IBD.

The aim of our study is to investigate IBD associated mucin mRNA isoforms and their potential as novel biomarkers for the evaluation of disease activity and the identification of IBD subtypes.

Aims & Methods: To obtain this goal, RNA was extracted from colonic and terminal ileal biopsies of IBD patients (both CD and UC) that underwent an endoscopy at the Antwerp University Hospital (UZA) for clinical reasons (i.e. acute flares or surveillance endoscopy when in remission). Additionally, patients without a history of IBD undergoing an endoscopy due to a positive faecal occult blood test (FOBT) which show no endoscopic abnormalities, were included as controls (Table 1).

Biopsies from a macroscopically inflamed (if present) and non-inflamed region from the same patient were used. The quality of the RNA samples was assessed with capillary electrophoresis and quantified using Qubit fluorometric quantitation. Library preparation was performed with the PacBio Iso-Seq multiplex protocol adapted for targeted transcriptome sequencing. Targeted capture was accomplished by using a custom-designed pool of probes, developed for the capture of MUC1, MUC2, MUC3A, MUC4, MUC5AC, MUC5B, MUC6, MUC7, MUC12, MUC13, MUC15, MUC16, MUC17, MUC19, MUC20, MUC21 and MUC22 gene transcripts.

Samples were sequenced on the PacBio Sequel platform at the University of Antwerp. The data was analysed by using the isoseq3-pipeline. The resulting high-quality isoform sequences were mapped, redundant isoforms collapsed (coverage 99% and identity 95%) and additional filtering with SQANTI3 [3] was performed.

	Colonic biopsies			Ileal biopsies		
	CD	UC	Control	CD	UC	Control
Non-inflamed	11	9	6	4	1	4
Inflamed	11	10	NA	1	1	NA

Table 1: A total of 58 samples were sequenced, comprising 47 colonic and 11 terminal ileum biopsies. The samples comprise a combination of inflamed and non-inflamed biopsies of both Crohn's disease (CD) and ulcerative colitis (UC).

Results: Throughout all samples, 77 unique isoforms with a high abundance (sum of counts >40) were identified, of which the majority originated from MUC13 (27) and MUC3A (18). The read count of some isoforms seems to suggest differential isoform expression between the different IBD subtypes.

Conclusion: Next, Illumina RNA-Seq will be used to confirm this observation. Future efforts will be directed towards quantifying the isoforms of interest and correlating their expression with disease activity and IBD subtypes.

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P0336

BIOMARKERS OF EXTRACELLULAR MATRIX TURNOVER AND NEUTROPHIL ACTIVITY PREDICT LONG-TERM RESPONSE TO VEDOLIZUMAB IN PATIENTS WITH CROHN'S DISEASE

M. Sorokina Alexdóttir¹, A.R. Bourgonje², M. Karsdal¹, M. Pehrsson¹, R. Loveikyte², H. van Dullemen², M.C. Visschedijk², E. A. M. Festen², R.K. Weersma², K.N. Faber², G. Dijkstra², J.H. Mortensen¹

¹Nordic Bioscience, Immunoscience, Herlev, Denmark, ²University Medical Center Groningen, Gastroenterology and Hepatology, Groningen, Netherlands

Contact E-Mail Address: mara@nordicbio.com

Introduction: Crohn's disease (CD) is a relapsing-remitting inflammatory disease of the gastrointestinal (GI) tract characterized by high infiltration of neutrophils and other immune cells into the intestinal tissue, resulting in increased proteolytic mediated extracellular matrix (ECM) remodeling, reflecting mucosal damage. Disease management has substantially improved with the emergence of biologics such as the $\alpha 4\beta 7$ -integrin inhibitor vedolizumab (VEDO). However, considering the high rate of primary non-response to VEDO in patients with CD, there is an unmet need for predictive serum biomarkers capable of determining response to treatment prior to its initiation.

Aims & Methods: The aim of this study was to investigate whether biomarkers of neutrophil activity, mucosal damage, and ECM remodeling could serve as non-invasive tools for predicting long-term response to VEDO in patients with CD. Serum levels of human neutrophil elastase (HNE)-derived fragments of calprotectin (CPa9-HNE [serum calprotectin]) and matrix metalloproteinase (MMP)-derived fragments of type I (C1M), III (C3M), IV (C4M), and VI (C6Ma3) collagen, type III collagen formation (PRO-C3), basement membrane turnover (PRO-C4) and T-cell activity (C4G), were measured using protein fingerprint assays in patients with CD (n=32) before VEDO therapy. Long-term response was defined as VEDO treatment of at least 12 months.

Results: CPa9-HNE was significantly increased at baseline in non-responders compared with responders ($P < 0.05$). Biomarkers C1M, C3M, C4M, C6Ma3, PRO-C3, C3M/PRO-C3, C4M/C4G and PRO-C4/C4G were significantly increased at baseline in non-responders compared with responders (all $P < 0.05$, Table 1).

Biomarker	Continued use n = 17	Discontinued use n = 15	p-value
C1M (ng/ml)	36.1 [25.02–49.80]	108.6 [57.47–148.45]	0.001
C3M (ng/ml)	10.5 [9.43–11.81]	15.2 [13.07–16.44]	0.006
C3M/PRO-C3	1.6 [1.42–1.80]	2.6 [1.98–3.13]	0.008
C4M (ng/ml)	24.5 [22.36–28.16]	36.5 [28.24–46.68]	0.010
PRO-C4 (ng/ml)	182.0 [170.48–203.68]	266.8 [207.20–308.26]	0.010
C4M/C4G	1.4 [0.81–1.77]	2.0 [1.40–2.44]	0.020
PRO-C4/C4G	8.4 [6.02–12.56]	14.5 [9.66–17.12]	0.033
C6Ma3 (ng/ml)	0.6 [0.53–0.84]	0.8 [0.68–1.02]	0.015
CPa9-HNE (ng/ml)	231.7 [195.32–302.60]	401.2 [281.36–452.00]	0.003

Table 1. Baseline serum biomarker levels stratified by response to VEDO. Values are displayed as medians with IQR.

All biomarkers were able to predict response to VEDO at baseline (AUC [95% CI]: C1M 0.85 [0.75–0.98]; C3M 0.79 [0.62–0.95]; C4M 0.77 [0.6–0.93]; C6Ma3 0.75 [0.58–0.92]; C3M/PRO-C3 0.78 [0.6–0.95]; C4M/C4G 0.74 [0.56–0.92]; PRO-C4/C4G 0.72 [0.54–0.9]; CPa9-HNE 0.81 [0.66–0.96]; all $P < 0.05$).

The proportion of long-term users of VEDO treatment was highest in the first tertile for all the biomarkers (73–91%), which decreased in a concentration-dependent manner across the second and third tertiles, indicating that patients with the lowest concentrations of these markers less frequently discontinued treatment at one year after initiation.

Conclusion: Baseline levels of serum biomarkers for neutrophil activity (CPa9-HNE [serum calprotectin]) and mucosal damage (C1M, C3M, C4M, C4G, C6Ma3, PRO-C4, and PRO-C3) could predict long-term response to VEDO in patients with CD. Therefore, these biomarkers could aid in early decision making concerning treatment with vedolizumab in patients with CD.

Disclosure: Nothing to disclose.

P0337

HEPATIC STEATOSIS BUT NOT FIBROSIS IS INDEPENDENTLY ASSOCIATED WITH A POOR OUTCOME IN PATIENTS WITH INFLAMMATORY BOWEL DISEASES

H.K. Hyun¹, H.-W. Lee², E.A. Kang², J. Park², S.J. Park², J.J. Park², T.I. Kim², J.S. Lee², B.K. Kim², J.Y. Park², D.Y. Kim², S.H. Ahn², S.U. Kim², J.H. Cheon²

¹Yonsei University College of Medicine / Yonjin Severance hospital, Department of Internal Medicine, Yonjin, Korea (Republic of),

²Yonsei University College of Medicine / Severance Hospital, Department of Internal Medicine, Seoul, Korea (Republic of)

Contact E-Mail Address: hyunhk0703@yuhs.ac

Introduction: The simultaneous increasing prevalence of nonalcoholic fatty liver disease (NAFLD) and inflammatory bowel disease (IBD) has been reported, but the effects of NAFLD on outcomes of IBD has yet to be elucidated. We investigated whether the presence of NAFLD could influence the outcomes of patients with IBD.

Aims & Methods: A total of 4,114 patients who were diagnosed as having IBD between November 2005 and November 2020 were studied. Hepatic steatosis and fibrosis was assessed using hepatic steatosis index (HSI) ≥ 30 and fibrosis-4 (FIB-4) ≥ 1.45 , respectively. Primary outcome was a clinical relapse defined as IBD-related admission, IBD-related surgery, or first use of corticosteroids, immunomodulators, or biologics agents.

Results: The prevalence of NAFLD in IBD patients was 16.7%. Patients with hepatic steatosis and advanced fibrosis were older, higher BMI and had a higher prevalence of diabetes at baseline (all $p < 0.05$).

Adjustment	By HSI ≥ 30			By FIB-4 ≥ 1.45		
	Adjusted HR	95% CI	p value	Adjusted HR	95% CI	p value
Model 1	1.510	1.161-1.964	0.002	0.705	0.504-0.986	0.041
Model 2	1.497	1.144-1.959	0.003	0.693	0.496-0.969	0.032
Model 3	1.687	1.283-2.219	<0.001	0.919	0.642-1.315	0.643
Model 4	1.697	1.291-2.230	<0.001	0.949	0.663-1.359	0.777
Model 1: age, gender, duration of inflammatory bowel disease diagnosis, and body mass index.						
Model 2: Model 1 + smoking status, hypertension, and diabetes.						
Model 3: Model 2 + white blood cell count, hemoglobin, platelet count, erythrocyte sedimentation rate, serum C-reactive protein, total bilirubin, aspartate aminotransferase, alanine aminotransferase, gamma-glutamyltransferase, and serum albumin.						
Model 4: Model 3 + ulcerative colitis disease location.						

Table 3. Adjusted HRs with 95% CIs of steatosis and significant fibrosis to predict clinical relapse in UC patients.

In our multivariable cox regression models, hepatic steatosis was independently associated with the increased risk of clinical relapse in UC (hazard ratio [HR]=1.697, 95% confidence interval [CI] 1.291–2.230; $p < 0.001$) and CD patients (HR=1.536, 95% CI 1.130–2.087; $p = 0.006$).

In contrast, Advanced liver fibrosis was not significantly associated with the risk of clinical relapse in UC and CD patients (all $p > 0.05$).

Conclusion: The hepatic steatosis was independently associated with the increased risk of clinical relapse in UC and CD patients, whereas fibrotic burden in liver was not. Further studies should investigate whether the assessment and therapeutic intervention of NAFLD improves clinical outcomes in IBD patients.

Disclosure: Nothing to disclose.

P0338

USE OF PLATELET-LYMPHOCYTE RATIO AND NEUTROPHIL-LYMPHOCYTE RATIO AS A POTENTIAL PROGNOSTIC MARKER IN IBD

O. Fagan¹, C. McGrath¹, H. Logan¹, E. Slattery¹

¹University Hospital Galway, Gastroenterology, Galway, Ireland

Contact E-Mail Address: olgafagan@gmail.com

Introduction: Platelets and Platelet-Lymphocyte Ratio (PLR) have been suggested as a non-invasive biomarker for IBD.

Aims & Methods: To assess whether neutrophil-lymphocyte ratio (NLR) and platelet-lymphocyte ratio (PLR) predict response in IBD patients with an acute severe flare.

IBD patients admitted with acute severe colitis between January-2017-December-2019 were assessed.

Results: 64-patients (88% (n=56) UC, 9% (n=6) CD, 3% (n=2) indeterminate) were included (55% male, 38-years (11-90years)). Of those with UC, 59% (n=33) had pancolitis, 39% (n=22) had left-sided colitis and 1 had proctitis. Amongst those with CD, 83% (n=5) had colonic disease and 17% (n=1) had ileal disease. Examining therapies received by the cohort prior to admission: 48% (n=21) had received biologic therapy, 32% (n=18) had received immunotherapy, and 3% (n=2) had underwent surgery previously. 33% (n=21) were on biologic therapy at admission.

36% (n=23) received rescue-treatment (95% infliximab, 5% ciclosporin). There was an association between total platelet count (Z-score 9.76, $P < 0.05$), NLR (Z-score 9.76, $p < 0.05$) and PLR (Z-score 9.76, $P < 0.05$) and risk of colectomy.

Patients with colectomy-free-survival at 1-year displayed lower NLR and PLR compared with those who did not (6.7 [1.1-33.0] vs 7.5 [1.7-21.00]; $p = 0.39$ and 242 [106-1438] vs 259 [155-1300]; $p = 0.11$).

Patients who received rescue-therapy (n=23), had lower week-8 PLR and NLR and persistence of drug at 6-months ($p < 0.05$). Lower platelet count and PLR at 8-weeks post rescue-therapy was a predictor of persistence of therapy at 6-months (262 [267-469] v 348 [373-558], $p = 0.01$ and 218 [82-521] v 256 [71-630], $p = 0.34$), conversely CRP was not (8 [1-36] v 2.9 [1-6], $p = 0.23$).

Conclusion: Higher platelet count, NLR and PLR on admission with acute severe colitis are associated with progression to colectomy. NLR and PLR should be considered an important prognostic tool in the assessment of acute severe colitis and when elevated should form part of decision making with respect to early escalation of rescue therapy. Platelet count and PLR at 8-weeks post rescue-therapy may also act as a biomarker for prolonged response to therapy.

Disclosure: Nothing to disclose.

P0339

DETECTION OF IRON RESTRICTED ERYTHROPOIESIS IN PATIENTS WITH INFLAMMATORY BOWEL DISEASE: OVERCOMING THE INFLAMMATION TANGLER

A. Aksan^{1,2}, C. Mangold³, J. Stötzel^{1,2}, K. Farrag^{1,4}, L. Tessmer^{1,4}, O. Schröder^{1,4}, J. Stein^{1,4,5}

¹Interdisciplinary Crohn-Colitis Centre Rhein-Main, Frankfurt am Main, Germany, ²Justus-Liebig University, Institute of Nutritional Science, Giessen, Germany, ³Goethe University, Faculty of Medicine, Frankfurt am Main, Germany, ⁴DGD Clinics Sachsenhausen, Department of Gastroenterology and Clinical Nutrition, Frankfurt am Main, Germany, ⁵Institute of Pharmaceutical Chemistry, Goethe University, Frankfurt am Main, Germany

Contact E-Mail Address: ayscak@gmail.com

Introduction: Serum ferritin can indirectly estimate body iron stores and is the most specific biomarker of absolute iron deficiency (AID). However, in inflammatory bowel disease (IBD) the acute-phase response can obscure AID. Patients with active IBD may also have anaemia of chronic disease (ACD), i.e., normal/increased stores but with limited iron availability for erythropoiesis (iron-restricted erythropoiesis, IRE). The European Crohn's & Colitis Organization suggests adding biomarkers to distinguish functional ID from AID in ACD.

We compared the utility of red cell indices and biochemical markers to detect IRE in IBD patients and set a decision threshold for selection of markers to discriminate AID and iron sequestration.

Aims & Methods: We aimed to compare the utility of red cell indices and biochemical markers to detect IRE in IBD patients and set a decision threshold for selection of markers to discriminate AID and iron sequestration. An observational cross-sectional study was conducted in IBD patients. Blood samples were analysed for CBC, iron status (serum ferritin, SF; transferrin saturation, TSAT; serum iron % of hypochromic red cells, %HYPO; reticulocyte haemoglobin content, CHr; soluble transferrin receptor, sTfR) and high sensitivity CRP (hs-CRP) as inflammation marker by standard methods. sTfR-F index was calculated (sTfR (mg/L)/log¹⁰ SF (µg/L)).

First, patients with SF<30µg/L were selected as controls consistent with AID to define decision thresholds for iron markers in patients with SF≥30µg/L. This decision threshold was then used to evaluate IRE in patients with SF≥30µg/L. Last, the accuracy of iron markers in the presence/absence of inflammation were assessed and a diagnostic threshold determined for each context.

Results: 312 IBD patients (159f/153m;163CD/149UC;42.7±14.5y) were enrolled; 122/312(39.1%) had inflammation. 43/312 patients with SF <30 µg/L were assigned to the AID-control group. Results in controls were: TSAT (cut-off 20%; AUC^{ROC} 0.730;sens.65%, spe.34%), %HYPO (3.5%; 0.733;42%, 93%), CHr (32pg; 0.713; 51%, 86%), sTfR (2.70mg/L; 0.775; 81%, 63%), sTfR-F (2.01; 0.914; 88%, 88%). sTfR-F was used as reference for IRE in patients with SF ≥30 µg/L.

Patient group	Value	TSAT (%)	SF (µg/L)	%HYPO	CHr (pg)	sTfR (mg/L)
All patients	AUC ^{ROC}	0.761	0.888	0.738	0.708	0.966
	Sen./Spe.%	67/71	52/79	39/96	43/92	91/87
	Cut-off	20 %	30 µg/L	3.5 %	32 pg	2.7 mg/L
Patients with inflammation	AUC ^{ROC}	0.755	0.861	0.845	0.729	0.962
	Sen./Spe.%	68/59	90/54	60/94	55/87	90/98
	Cut-off	20 %	100 µg/L	3.5 %	32 pg	3.7 mg/L
Patients without inflammation	AUC ^{ROC}	0.774	0.906	0.717	0.708	0.972
	Sen./Spe.%	67/78	56/99	32/97	38/95	97/82
	Cut-off	20 %	30 µg/L	3.5 %	32 pg	2.7 mg/L

Table 1. Accuracy of markers as detectors of IRE in patients with IBD.

Conclusion: sTfR had the best accuracy as a sole marker to detect IRE in patients with and without inflammation, with a higher cut-off in the context of inflammation. Addition of SF in patients without inflammation had additional value. The relative cost-effectiveness of the markers alone or in combination is under investigation.

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P0340

RENAL INVOLVEMENT IN A COHORT OF PAEDIATRIC PATIENTS WITH INFLAMMATORY BOWEL DISEASE

A. Kourti¹, E. Stefos¹, I. Kanavaki¹, D. Bacharakis², D. Polymeros³, P. Matsota⁴, S. Fessatou¹

¹Department of Paediatric Gastroenterology, Hepatology and Nutrition, 3rd Department of Paediatrics, Attikon University General Hospital, National and Kapodistrian University of Athens, Athens, Greece, ²Nephrology Unit, Department of Internal Medicine, Attikon University General Hospital, National and Kapodistrian University of Athens, Athens, Greece, ³Attikon University Hospital - Department of Hepatogastroenterology, 2nd Department of Internal Medicine, Athens, Greece, ⁴Second Department of Anesthesiology, Attikon University Hospital, National and Kapodistrian University of Athens, Athens, Greece

Contact E-Mail Address: sfessatou@yahoo.gr

Introduction: Inflammatory Bowel Disease (IBD) is a chronic, relapsing inflammatory disorder that predominantly affects the gastrointestinal tract. Renal involvement in IBD is rather uncommon and ranges from 4-23% in adults and 1-2% in children with IBD. It can be explained by different mechanisms – IBD activity independent, IBD activity dependent, metabolic consequences, amyloidosis and medication adverse effects. In our study we aimed to describe the spectrum of renal involvement in our IBD patients.

Aims & Methods: This is a retrospective analysis of renal function of paediatric IBD patients that are being followed in our pediatric gastroenterology department during the last three years.

Results: The study involved 75 IBD patients, aged 4-17years old. 44% were male and 56% female, 67% had Crohn's Disease (CD) and 33% Ulcerative Colitis (UC). Of these IBD patient's renal involvement was observed from urinalysis in 12 (16% - 8 with CD and 4 with UC): 7 patients had only proteinuria, 3 proteinuria and hematuria and 2 proteinuria and glycosuria. Further investigation with renal ultrasound, nephrolithiasis tests, timed 24-hour urine collection for quantitative measurement of protein excretion, serum urea, creatinine, C3/C4 and antinuclear antibody testing (ANA) was performed. The severity of IBD was recorded based upon PCDAI and PUCAI scores. Four patients underwent renal biopsy (table). Of all the 12 patients: in 4 patients renal damage was due to medication adverse effect (reversed after discontinuation of mesalazine), 2 had glomerulone-

phritis (IgA nephropathy and focal segmental glomerulonephritis), 1 had thin basement membrane disease, and another one had pyelonephritis in combination with chronic active tubulointerstitial nephritis, possible due to mesalazine. Three patients had IBD-related dependent renal involvement and 1 resulted in chronic renal failure due to amyloidosis.

Patient/ Disease	Ur / Cr	Pro	Bld	Glu	Disease activity	5-ASA	Further tests	Biopsy	Intervention
1-UC	normal	+1	-	+2	PUCAI 20	Yes	normal	No	IBD-dependent renal involvement
2-CD	normal	+1	-	-	PCDAI <10	Yes	normal	No	Recession after discontinuation of mesalazine
3-CD	normal	+2	-	-	PCDAI <10	Yes	normal	No	
4-CD	Elevated	+2	-	-	PCDAI <10	Yes	normal	No	
5-CD	Ur normal	+1	-	-	PCDAI <10	Yes	normal	No	
6-CD	Normal	+1	-	-	PCDAI <10	No	Takayasu arteritis,	Yes	Normal renal function
7-CD	normal	+3	+2	-	PCDAI <10	No	PET-scan (+) glomerulonephritis Severe Proteinuria IgA Nephropathy	Yes	
8-UC	Elevated Cr at acute episode of pyelonephritis	+2	+1	-	PUCAI 30	Yes	Urinary casts	Yes	Recession after discontinuation of mesalazine and chemoprophylaxis for urinary tract infections
9-CD	normal	+1	+2	-	PCDAI <10	No	normal	No	Thin basement membrane disease
10-CD	normal	+2	-	-	PCDAI 25	Yes	normal	No	Discontinuation of mesalazine IBD-related dependent renal involvement
11-CD	Elevated Cr	+1	-	+1	PCDAI 20	Yes	normal	No	Discontinuation of mesalazine IBD-related dependent renal involvement
12-UC	Elevated Ur, Cr	+3	-	-	PUCAI 20	Yes	Severe proteinuria	Yes	Chronic renal failure

Table: Laboratory tests, renal biopsy and diagnosis in paediatric IBD patients with renal involvement.

Conclusion: A high index of clinical suspicion is needed for the early diagnosis and prevention of IBD-related renal manifestations and complications.

Disclosure: Nothing to disclose.

P0341

A PHARMACIST-LED POST INDUCTION REVIEW CLINIC IMPROVES COMPLIANCE WITH KEY PERFORMANCE INDICATORS FOR PATIENTS NEWLY STARTED ON BIOLOGIC THERAPIES IN INFLAMMATORY BOWEL DISEASE

D. Al-Zarrad¹, A. Chana¹, L. Dyall¹, U. Meade¹, N. Arebi¹, N. Kamperidis¹

¹St Marks Hospital- London Northwest University Healthcare NHS Trust, Gastroenterology, London, United Kingdom

Contact E-Mail Address: dania.al-zarrad@nhs.net

Introduction: Biologic therapies induce and maintain long term remission in Inflammatory Bowel Disease. 30% of patients fail to respond to induction regimens.¹ Early identification of these patients avoids unnecessary drug exposure with associated costs. The IBD standards as per registry² recommends a post-induction, and a 12 monthly review for all newly initiated biologic therapy as a key performance indicator (KPI). We therefore set up a dedicated Post Induction Review (PIR) clinic to meet the KPI and evaluated its clinical effectiveness.

Aims & Methods: The PIR clinic was independently run by an IBD specialist pharmacist, following a period of training under physician supervision. Data was captured using a pro-forma documenting baseline demographics, disease status, previous and current medical therapy, and response using disease activity indices (Harvey-Bradshaw index for Crohn's disease (CD), and Partial Mayo score for Ulcerative colitis (UC)).

The primary outcome was the proportion of patients who attended a PIR, and a 12-month review, according to the summary of product characteristics (SPC) for each biologic.

Secondary outcomes were appropriate escalation of non-responders and significant adverse drug reactions to a physician and relevant documentation of disease activity indices. 50 consecutive patients, who attended the new PIR clinic between September 2020 to January 2021, were compared with 30 randomly selected biologic patients from 2019-2020 (control group).

Results: The CD and UC populations are 32(64%) CD patients in PIR clinic were compared to 17 (57%) in the control group and UC patients 18(36%) in PIR compared to 13(43%) in control group. Median time from starting biologic to PIR clinic was 10 weeks compared to 11.5 weeks in the control group.

Table 1 summarises the comparative outcomes between PIR clinic patients versus those started on biologic therapy prior to the PIR clinic. Three patients were excluded from PIR group when analysing documented disease activity scores due to prior surgeries/stomas. Prior to introduction of PIR clinic programme it was challenging to track patients newly started on biologics.

There was an overall improvement with PIR being conducted in line with the SPCs for infliximab, adalimumab, ustekinumab and vedolizumab (UC). The PIR assessment following induction with CD was slightly delayed compared to control: the reasons for this include lack of appointment slots, and administrative issues with the appointment bookings.

More importantly there was a marked improvement of escalation in therapy for non-responders within 1 month from 3% to 50%; and in 12 months follow-up arranged from 73% to 98%.

	Pre-PIR clinic (Control) N=30	PIR Clinic N=50
PIR review as per the SPC		
Infliximab (at weeks 10-12)	3 (27%)	6 (55%)
Adalimumab (at week 10)	0 (0%)	2 (40%)
Vedolizumab CD (at weeks 6-8)	1 (33%)	2 (22%)
Vedolizumab UC (at weeks 8-10)	1 (14%)	9 (90%)
Ustekinumab (at weeks 14-16)	0 (0%)	1 (7%)
Documented disease activity indices	4 (13%)	8 (16%)
Primary non-response and escalation to physician with change in therapy made within 1 month	1 (3%)	2 (50%)
12 months follow-up arranged after initiating biologic treatment	22 (73%)	49 (98%)

Table1: Comparative summary of the KPIs for biologic therapy of the PIR clinic outcomes, and prior to initiation of the PIR clinic programme

Conclusion: To our knowledge, this is the first study looking the effectiveness at a dedicated pharmacist-led PIR clinic with a general improvement in KPI. This model of care can be implemented in other similar healthcare settings and utilise skills mix of the IBD team.

Future attention will be focused on improving the PIR assessments for CD patients started on vedolizumab this is due to the fact that an additional dose can be given at week 10.

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P0342
PREDICTIVE MODEL FOR OUTCOMES IN INFLAMMATORY BOWEL DISEASE PATIENTS ON MAINTENANCE INFLIXIMAB THERAPY

R. Wong¹, P. Charilaou¹, A. Hemperly², L. Qin³, Y. Pan¹, P. Mahtani¹, R. Longman¹, B. Boland², P. Dulai², A. Holmer², D. Lukin¹, S. Singh², M. Valasek⁴, W.J. Sandborn², E. Scherl¹, N. Vande Casteele², R. Battat¹
¹Weill Cornell Medicine, Dept of Medicine, Division of Gastroenterology and Hepatology, New York, United States, ²University of California San Diego, Department of Medicine, Division of Gastroenterology, La Jolla, United States, ³Weill Cornell Medicine, Dept of Pathology, New York, United States, ⁴University of California San Diego, Department of Pathology, La Jolla, United States

Contact E-Mail Address: rew9046@nyp.org
Introduction: No data exist on predictors of outcomes for inflammatory bowel disease (IBD) patients on maintenance infliximab (IFX) therapy, or on models using validated histologic data and drug levels in maintenance.
Aims & Methods: To create a prediction model of future outcomes in IBD patients on maintenance IFX.
Adults on maintenance (≥ week14) IFX with serum trough concentration within 90 days of colonoscopy with biopsy were included. Ileostomy or ileal pouch-anal anastomosis were excluded. Patients who discontinued IFX after drug level measurement were included only if outcomes existed >90 days post baseline, were off IFX <90 days, and were not on new therapy for >90 days. Data were collected through chart review. A blinded pathologist provided histologic scoring (Robarts Histopathologic Index (RHI)). The primary composite endpoint (negative outcome) was either IBD-related surgery, hospitalization or objective inflammation (endoscopic activity simple endoscopic score-Crohn's Disease ≥3, Mayo endoscopic score ≥1 for ulcerative colitis), or if unavailable, fecal calprotectin ≥50ug/g, or C-reactive protein (CRP) ≥1.0).
Multivariable analysis included predictors of the primary outcome with p<0.1 on univariable analysis. IFX levels and RHI thresholds were determined using receiver operator characteristic curve (AUC). A clinical prediction score was created based on each variable's odd ratios on multivariable analysis. The model was trained on an internal cohort (Weill Cornell Medicine) and externally validated (University of California, San Diego).
Results: In 81 included patients (internal cohort n=48, external n=33), both cohorts had similar characteristics, RHI scores, and IFX concentrations. Baseline IFX <9.3 ug/mL (AUC 0.64, p=0.04) and RHI >12 (AUC 0.60, p=0.07) were optimal thresholds to predict negative outcomes. They were also the only variables with p<0.1 on univariable analysis (Table 1).
Other predictors were not significant, including female (OR 0.90, 95% CI 0.28-2.88, p=0.863), age (OR 1.01, 95% CI 0.98-1.05, p=0.494), Crohn's disease (OR 0.90, 95% CI 0.28-2.8, p=0.853), baseline active endoscopic disease (OR 3.26, 95% CI 0.77-13.8, p=0.109), baseline clinical remission

(OR 1.03, 95% CI 0.32-3.33, p=0.960), baseline steroid use (OR 0.79, 95% CI 0.22-2.88, p=0.725), baseline immunomodulator use (OR 0.7, 95% CI 0.18-2.76, p=0.610), baseline IBD surgery (OR 1.67, 95% CI 0.36-7.67, p=0.512), baseline IFX clearance (mL/day) (OR 0.13, 95% CI 0-35.02, p=0.472), CRP (OR 0.37, 95% CI 0.1-1.37, p=0.137), and fecal calprotectin (OR 2.17, 95% CI 0.26-17.89, p=0.473). On multivariable analysis both IFX<9.3ug/mL and RHI>12 met model inclusion criteria (Table 1).
The 2-variable clinical predictive scoring model had good discrimination for negative outcomes for training (AUC 0.71, 95% CI 0.57-0.84) and external (AUC 0.73, 95% CI 0.57-0.89) cohorts.
In the joint cohort (n=81), IFX <9.3ug/mL (OR 5.3, 95% CI 1.9-14.8, p=0.01) and RHI score >12 (OR 3.4, 95% CI 1.1-10.3, p=0.03) were significantly associated with the primary outcome. Observed scores of 0, 1 and 2 predicted risks for negative outcomes of 15% (external)-23% (internal), 46% (internal)-50% (external), and 75% (external)-100% (internal), respectively.
The model performed similarly well on the joint cohort for objective inflammation (AUC=0.71 (0.60-0.82), IFX<9.3ug/mL (OR 3.7, 95%CI 1.3-10.8, p=0.02), RHI>12 (OR 4.4, 95%CI 1.5-13.4, p=0.008). IFX drug level alone performed similarly well to the unbiased 2-variable model (internal cohort: complete model: AUC 0.70 [0.55-0.85] vs. IFX alone: AUC 0.65 [0.51-0.79], p=0.5, external cohort: complete model: AUC 0.70 [0.52-0.88] vs. IFX alone: AUC 0.71 [0.54-0.87] p=0.9).

	Univariable Analysis	Univariable Analysis	Multivariable Analysis	Multivariable Analysis
Predictor	OR [95% CI]	p-value	OR [95% CI]	p-value
IFX Drug Level <9.3 ug/mL	3.61 [1.06-12.25]	0.039	4.31 [1.16-16.03]	0.029
RHI Score >12	3.26 [0.89-14.91]	0.072	4.57 [0.907-20.97]	0.051

Scoring system (OR rounded to closest 0.5 and divided by 4.5):
IFX Drug level <9.3ug/mL = 1 point, RHI >12 = 1 point

Table 1. Multivariable Prediction Model for IBD-related Hospitalization/ Surgery or Objective Inflammation

Conclusion: In patients on maintenance IFX therapy, a model using IFX concentration and RHI score predicted patient outcomes. Maintenance IFX concentrations alone performed similarly well.
Disclosure: Nothing to disclose.

P0343
TOXIN GENE POLYMERASE CHAIN REACTION ASSAY FOR CLOSTRIDIoidES DIFFICILE CAN BE AN INDICATOR SUGGESTING THE NEED FOR RAPID ESCALATION OF TREATMENT IN PATIENTS WITH INFLAMMATORY BOWEL DISEASE
S. Kim¹, J. Jung², H.-J. Lee¹, J.P. Im¹, J.S. Kim¹, S.-J. Koh¹
¹Seoul National University College of Medicine, Internal Medicine and Liver Research Institute, Seoul, Korea (Republic of), ²Seoul National University College of Medicine, Medicine, Seoul, Korea (Republic of)

Contact E-Mail Address: seulji.k@snu.ac.kr
Introduction: Toxin gene polymerase chain reaction (PCR) assay for *Clostridioides difficile* (*C.difficile*) is the most sensitive test among the diagnostic methods for *C.difficile* infection (CDI) and thus, PCR positivity could be a true infection, but it could also simply be colonization. Although there have been several studies on the incidence rate of CDI in IBD patients and the prognosis of CDI co-occurrence with IBD, there have been no studies on the meaning of the *C. difficile* PCR test result itself in patients with IBD regardless of CDI symptoms.

Aims & Methods: This study aimed to elucidate the role of toxin gene PCR assay for *C.difficile* in predicting the course of inflammatory bowel disease (IBD). This study also investigate the potential factors associated with the PCR positivity in patients with IBD.

This is a retrospective single-center cohort study at Seoul national university hospital from 2020 to 2021. Patients with IBD who underwent stool analysis with Toxin gene PCR of *C.difficile* were retrospectively enrolled. Medical records were reviewed and data including IBD subtype, extent, severity and medications were collected. Patients were followed for 180 days after the date of PCR test to assess the clinical course of IBD.

Results: A total of 156 patients with IBD who underwent a *C.difficile* toxin PCR test were enrolled in this study, including 123 with ulcerative colitis (UC) and 33 with Crohn's disease (CD). Among them, the PCR-positive rate was 16.03%.

Further analyzing the PCR-positive patients, 76% of patients were treated for CDI and 24% of those did not receive treatment. 89% of the treated patients received oral vancomycin, and 11% of patients received metronidazole.

Although there was no significant difference in baseline IBD severity between the PCR positive group and the PCR negative group, the patients with PCR positivity had a statistically significant increase in drug escalation for IBD treatment within 180 days after PCR test (48% in PCR positive group vs 4.58% in PCR negative; $P=0.006$).

This result was maintained even after adjusting through inverse probability of treatment weighting (IPTW) based on the propensity score. In the multivariable analysis, treatment with azathioprine was the only risk factor associated with PCR positivity in patients with IBD (OR 5.19, CI 1.32-23.3, $P=0.023$).

Conclusion: *C.difficile* toxin PCR positive IBD patients showed a significantly higher rate of treatment escalation, regardless of IBD severity. Therefore, it is important to carefully monitor PCR-positive IBD patients and to intervene in treatment quickly without delay, keeping in mind that PCR-positive IBD patients are more likely to worsen symptoms. Further research is needed on the underlying mechanism between PCR positivity and the course of IBD.

Disclosure: Nothing to disclose.

P0344

HIGHER ADALIMUMAB TROUGH LEVELS ARE ASSOCIATED WITH HISTOLOGIC REMISSION AND MUCOSAL HEALING

R. Wong¹, L. Qin², Y. Pan¹, P. Mahtani¹, R. Longman¹, D. Lukin¹, E. Scherl¹, R. Battat¹

¹Weill Cornell Medicine, Dept of Medicine, Division of Gastroenterology and Hepatology, New York, United States, ²Weill Cornell Medicine, Dept of Pathology, New York, United States

Contact E-Mail Address: rew9046@nyp.org

Introduction: Therapeutic drug monitoring is a mainstay in Crohn's disease (CD) and ulcerative colitis (UC). Data demonstrate that elimination of histologic inflammation is associated with improved outcomes.^{1,2} Recent data found reduced efficacy of adalimumab (ADA) to achieve histologic remission defined using the Robarts Histopathologic Index (RHI).³

A plausible explanation for suboptimal histologic outcomes may be inadequate drug exposure. However, data on the relationship between serum adalimumab concentrations and histologic outcomes with validated indices are lacking.

Aims & Methods: Aim: To perform the first real-world study assessing the relationship between adalimumab concentrations and a validated histologic disease activity index.

Patients from a tertiary IBD center with adalimumab (ADA) trough drug concentrations measured during maintenance therapy (≥ 14 weeks), and colonoscopy with biopsy performed within 90 days from 2013-2020 were included. Chart review was performed for demographic data and disease characteristics. RHI scores were assigned to biopsies by a blinded pathologist. Rates of endoscopic (CD: absence of ulcers, UC: Mayo endoscopic score <2) and histologic (RHI = 0) remission were assessed. Mucosal healing (MH) was defined as achieving both endoscopic and histologic remission.

The primary analysis evaluated the relationship between drug concentration and histologic remission using receiver operating characteristic curve analysis. Outcome proportions were compared above and below identified optimal (youden) thresholds using Fisher's exact test. Serum ADA concentrations were measured using homogeneous mobility shift assay (Prometheus Laboratories, San Diego).

Results: Thirty-six patients were included (26 CD, 9 UC, Table 1). Median cohort age was 34 years old, and 56% were female. The median ADA drug concentration was 11.1ug/mL (IQR: 7.0-15.5ug/mL). Median time from treatment initiation to drug concentration measurement was 103 weeks (Table 1).

The area under the curve for ADA concentrations to identify histologic remission was 0.80 (95% CI 0.61-0.99). The optimal ADA concentration was ≥ 16.3 ug/mL (sensitivity 70%, specificity 90%). Patients with ADA ≥ 16.3 ug/mL had higher histologic remission rates (78%) compared to lower ADA concentrations (14%, $p=0.002$). ADA ≥ 16.3 ug/mL had higher endoscopic remission (100%) compared to lower ADA levels (57%, $p=0.04$). ADA ≥ 16.3 ug/mL also had higher MH rates (86%) compared to lower levels (12%, $p=0.001$).

	N (%)
Median Age at Drug Level (years)	34
Gender (female)	20 (0.56)
Type of IBD	
Crohn's Disease	26 (0.72)
Ulcerative Colitis	9 (0.25)
Indeterminate Colitis	1 (0.02)
Adalimumab	
Median Drug Level Concentration (ug/mL) [IQR 25-75]	11.1 [7.0-15.5]
Median Dose (mg)	40
Median Frequency (every X weeks)	2
Median Weeks of Therapy (wk)	103
Endoscopy	
CD: Presence of ulcers (lack of remission)	7/24 (0.29)
UC: Mayo Score <2 (presence of remission)	1/4 (0.25)
Histology	
RHI score = 0 (histologic remission)	10/30 (0.33)
Median RHI Score	8.5
Mucosal Healing	
Endohistologic Remission	8/24 (0.33)

Table 1. Cohort Demographics (n=36)

Conclusion: These first real-world data on the relationship between adalimumab concentrations and RHI demonstrate higher adalimumab drug concentrations are strongly associated with histologic remission and MH. A serum ADA concentration that is higher than traditional targets (≥ 16.3 ug/mL) is needed for histologic remission.

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Disclosure: Nothing to disclose.

P0345

TYPE I COLLAGEN DEGRADATION FRAGMENTS (C1M) AND HUMAN NEUTROPHIL ELASTASE-DERIVED FRAGMENTS OF CALPROTECTIN (CPA9-HNE) REFLECT BIOCHEMICAL AND ENDOSCOPIC DISEASE ACTIVITY IN PATIENTS WITH INFLAMMATORY BOWEL DISEASES

A.R. Bourgonje¹, M. Sorokina Alexdóttir², R. Loveikyte¹, M. Pehrsson², A.-C. Bay-Jensen², H.M. van Dullemen¹, M.C. Visschedijk¹, E.A.M. Festen¹, R.K. Weersma¹, M.A. Karsdal², K.N. Faber¹, J.H. Mortensen², G. Dijkstra¹

¹University Medical Center Groningen, Gastroenterology and Hepatology, Groningen, Netherlands, ²Nordic Bioscience, Biomarkers and Research, Herlev, Denmark

Contact E-Mail Address: a.r.bourgonje@umcg.nl

Introduction: Crohn's disease (CD) and ulcerative colitis (UC) are characterized by intestinal inflammation and increased extracellular matrix (ECM) remodeling, which are key pathophysiological mechanisms in patients with IBD and strongly interrelated and may culminate into mucosal damage. Alterations in intestinal ECM turnover as well as macrophage and neutrophil activity may be reflected by secreted products that are released into the circulation.

In this study, we aimed to investigate associations between serum biomarkers of neutrophil activity (serum calprotectin) and collagen degradation (mucosal damage), and biochemical and endoscopic disease activity in patients with IBD.

Aims & Methods: Serological biomarkers of collagen formation (PRO-C3, PRO-C4, PRO-C6), matrix metalloproteinase (MMP)-mediated collagen degradation (C1M, C3M, C4M, C4G, C6Ma3) and intestinal inflammation (VICM [macrophage activity], human neutrophil elastase-derived fragment of calprotectin (CPa9-HNE [serum calprotectin, neutrophil activity])) were measured using neo-epitope protein fingerprint technology in 100 patients with IBD (CD: $n=44$; UC: $n=56$). Biochemical disease activity was assessed using C-reactive protein (CRP) levels and available faecal calprotectin (FCal) levels. Endoscopic disease activity was determined using the Simple Endoscopic Score for CD (SES-CD) and Mayo endoscopic subscore for UC.

Results: C1M strongly associated with elevated CRP levels (defined as $>5\text{mg/L}$, $P<0.001$) in patients with IBD and significantly associated with faecal calprotectin levels in patients with UC (Spearman's $\rho=0.75$, $P<0.001$). In patients with CD, C1M reasonably discriminated between patients with mild and moderate-to-severe endoscopic disease activity (AUC=0.73, $P=0.01$), whereas this discrimination was more subtle in patients with UC (AUC=0.68, $P=0.08$). CPa9-HNE levels were significantly increased in patients with elevated CRP levels ($P=0.002$ for both CD and UC) and associated best with faecal calprotectin levels in patients with CD compared with UC (CD: $\rho=0.43$, $P=0.06$; UC: $\rho=0.20$, $P=0.45$).

Finally, CPa9-HNE levels were able to discriminate between mild and moderate-to-severe endoscopic disease activity in patients with CD (AUC=0.75, $P<0.01$).

Conclusion: C1M and CPa9-HNE levels associate with biochemical (CRP, FCal) and endoscopic disease activity in patients IBD, where C1M demonstrated higher accuracy in UC and CPa9-HNE appeared to be more useful

in CD. Therefore, C1M and CPa9-HNE could serve as surrogate biomarkers for the assessment of disease activity in patients with UC and CD, respectively. Our results should be validated in additional prospective, larger patient cohorts to corroborate these findings.

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P0346

THE ROLE OF TIM-4 IN THE PATHOGENESIS OF ULCERATIVE COLITIS IN MICE

Y. Xie¹, F. Wang²

¹The First Affiliated Hospital of Nanchang University, Department of Gastroenterology, Nanchang, China, ²The First Affiliated Hospital of Nanchang University, Nanchang, China

Contact E-Mail Address: xieyong_tfahoncu@163.com

Introduction: Ulcerative colitis (UC) is a type of chronic, idiopathic, and immune-mediated inflammatory bowel disease. Currently, no available therapies can control symptoms adequately in UC patients. T cell immunoglobulin and mucin domain 4 (Tim-4) is a novel immune regulatory molecule that can participate in the immune process and maintain immune homeostasis. However, the role of Tim-4 in UC is unclarified.

Aims & Methods: The present study aimed to explore the certain role of Tim-4 in the occurrence and development of UC. BALB/c mice were subjected to experimental acute dextran sodium sulphate (DSS) colitis. Mice were treated with anti-Tim-4 mAb or a control antibody.

Results: Administration of anti-Tim-4 antibody to mice attenuate colitis compared with administration of a control antibody. After blocking, TLR4/NF- κ B signaling pathway was significantly down-regulated, and Treg cells and M1/M2 tended to normalize.

Furthermore, Firmicutes were decreased and Bacteroidetes, Proteobacteria and campylobacter were increased in experimental colitis mice induced by DSS. The abundance of intestinal microorganisms in mice was increased, and the bacterial colony structure was similar to that of healthy mice.

Conclusion: High expression of Tim-4 was thought to contribute to the pathogenesis and an underlying mechanism of UC. Targeting the Tim-4/TLR4/NF- κ B axis may be a promising novel therapeutic strategy for UC.

Disclosure: The authors declare no conflict of interest.

P0347

PROTEOMIC ANALYSES DO NOT REVEAL SUBCLINICAL INFLAMMATION IN FATIGUED PATIENTS WITH QUIESCENT INFLAMMATORY BOWEL DISEASE

A.R. Bourgonje¹, S.J. Wichers¹, S. Hu^{1,2}, H.M. van Dullemen¹, M.C. Visschedijk¹, K.N. Faber¹, E.A.M. Festen¹, G. Dijkstra¹, J.N. Samsom³, R.K. Weersma¹, L.M. Spekhorst¹

¹University Medical Center Groningen, Gastroenterology and Hepatology, Groningen, Netherlands, ²University Medical Center Groningen, Genetics, Groningen, Netherlands, ³Erasmus University Medical Center, Pediatrics, Division of Gastroenterology & Nutrition, Rotterdam, Netherlands

Contact E-Mail Address: a.r.bourgonje@umcg.nl

Introduction: Fatigue is a common and clinically challenging symptom in patients with inflammatory bowel diseases (IBD). While fatigue occurs most often in patients with active disease, up to 50% of patients with quiescent disease still report significant fatigue of unknown etiology. Here, we aimed to investigate whether fatigue in patients with quiescent IBD is reflected by circulating inflammatory proteins, that in turn might reflect ongoing subclinical inflammation.

Aims & Methods: Ninety-two (92) different inflammation-related proteins were measured in plasma of 350 patients with quiescent IBD (188 Crohn's disease [CD]; 162 ulcerative colitis [UC]). Quiescent IBD was defined as clinical (Harvey-Bradshaw Index [HBI] <5 or Simple Clinical Colitis Activity Index [SCCAI] <2.5) and biochemical remission (C-reactive protein [CRP] <5 mg/L) at time of sampling. Fatigue severity was assessed on a visual analogue scale (VAS).

Results: None of the analysed plasma proteins were differentially abundant between mildly (1st quartile, Q1) or severely (4th quartile, Q4) fatigued patients under a false discovery rate of 10%. Considering nominal significance ($P < 0.05$), however, leukemia inhibitory factor receptor (LIF-R) concentrations were inversely associated with severe fatigue, also after adjustment for confounding factors ($P < 0.05$).

Although solely LIF-R showed weak ability to discriminate between mild (Q1) and severe (Q4) fatigue (area under the curve [AUC]=0.61, 95% CI: 0.53-0.69, $P < 0.05$), a combined set of the top seven (7) fatigue-associated proteins (LIF-R, vascular endothelial growth factor-A [VEGF-A], glial-derived neurotrophic factor [GDNF], interleukin-20 receptor subunit alpha [IL-20RA], Delta and Notch-like epidermal growth factor-related receptor [DNER], T-cell surface glycoprotein CD5 [CD5], and extracellular newly identified receptor for advanced glycation end-products binding protein [EN-RAGE], also known as protein S100-A12, all $P < 0.10$) was observed to have reasonable discriminative performance (AUC=0.82 [95% CI: 0.74-0.91], $P < 0.01$).

Conclusion: Fatigue in patients with IBD is not clearly reflected by distinct circulating inflammatory protein signatures, which suggests that subclinical immune activation as defined by the studied panel of inflammatory proteins could not be detected. Reduced shedding of the LIF-R protein could be related to fatigue in IBD through modification of the oncostatin-M (OSM) signaling pathway, or through induction of pro-inflammatory phenotypes of T-cells, macrophages, or neural cells. Future studies are warranted to investigate other proteomic or metabolic markers that may accurately reflect fatigue in quiescent IBD, which might represent alternative pathophysiological pathways.

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P0348

ASSOCIATION OF SERUM VITAMIN D LEVELS WITH DRUG TROUGH CONCENTRATIONS AND ANTI-DRUG ANTIBODY LEVELS DURING INFlixIMAB THERAPY IN PATIENTS WITH INFLAMMATORY BOWEL DISEASE

O. Schütte¹, L. Tessmer^{2,3}, J. Stötzel^{1,2}, O. Schröder^{2,3}, N. Awal², A. Aksan^{1,2}, J. Stein^{2,3,4}

¹Justus-Liebig University, Institute of Nutritional Science, Giessen, Germany, ²Interdisciplinary Crohn-Colitis Centre Rhein-Main, Frankfurt am Main, Germany, ³DGD Clinics Sachsenhausen, Department of Gastroenterology and Clinical Nutrition, Frankfurt am Main, Germany, ⁴Institute of Pharmaceutical Chemistry, Goethe University, Frankfurt am Main, Germany

Contact E-Mail Address: ayscak@gmail.com

Introduction: Vitamin D (vitD) status is a well-recognised risk factor implicated in inflammatory bowel disease (IBD). Genetic polymorphisms in the vitD receptor [VDR] were shown to be linked to susceptibility to IBD, while low vitD levels in patients with IBD have been associated with active inflammation, disease severity, poor quality of life, and adverse clinical outcomes.

Previous mechanistic studies have suggested that protective effects of higher vitD levels in patients with IBD are in part mediated through anti-inflammatory cytokine profiles and antimicrobial peptides.

Previous observations point to a possible effect of pre-treatment vitD levels on patient response to anti-tumour necrosis factor alpha [TNF- α] therapy.

Aims & Methods: The aim of this study was to explore potential effects of serum vitD levels on treatment response to infliximab (IFX) in patients with IBD. A cross-sectional retrospective study was conducted using medical records and routine blood samples of patients with IBD.

Blood samples were analysed for standard blood count, total 25OH vitD and inflammation parameters (high sensitivity C-reactive protein, hsCRP; and/or faecal calprotectin, fcal) were detected in blood and stool using standard methods. Serum anti-TNF- α trough concentrations (IDX-TC) and levels of anti-drug antibodies to anti-TNF- α (IFX-ADA) were detected using IDKmonitor® ELISA system, Immundiagnostik AG, Bensheim, Germany. Inflammation was characterised by enhanced levels of the inflammatory biomarkers hsCRP (≥ 5 mg/L) and/or fcal (≥ 250 µg/g).

Biochemical remission was defined by clinical remission in association with normal levels of both of these biomarkers. IFX was administered at a dose of 5-10 mg/kg every 8 weeks over an observation period of 64 weeks. A low IFX-TC was defined as <3µg/mL and a high IFX-TC as >7µg/mL. Positive IFX-ADA levels were defined as >100 AU/mL.

Results: 86 patients with IBD (42f/44m;57CD/29UC;41.3±13.9y) were enrolled. Of these, 24/86(27.9%) had inflammation and 31(36.0%) had vitamin D deficiency at the start of IFX treatment. 71/86(82.6%) patients were treatment naïve. Of the 86 patients, 68 (79.1%) received a treatment dose of 5mg/kg and 18 (20.9%) a dose of 10 mg/kg. VitD deficiency and insufficiency were detected in 31/86(36.0%) and 20/86(23.3%) patients, respectively. Patients with vitD deficiency had significantly lower IFX-TCs during follow-up, independent of the IFX dose per kg.

Moreover, the proportion of patients with positive IFX-ADA titres was found to be significantly higher in patients with VitD deficiency than without (17% vs. 4%, respectively, $p < 0.05$). Serum IFX-TCs at week 8 of treatment correlated positively with baseline vitD levels ($r = 0.374$, $p < 0.05$).

Conclusion: Our results indicate that in patients with IBD treated with IFX, serum vitD concentrations are related not only to drug trough levels but also, importantly, to the development of IFX-ADAs. Serum vitD should be screened prior to therapy and monitored throughout, with a view to maintaining levels within a normal or high-normal range.

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P0349

POTENTIAL BIOMARKER PAI-1 PROMOTES THE DISEASE ACTIVITY AND THERAPEUTIC RESPONSE IN BIOLOGICAL SAMPLES OF INFLAMMATORY BOWEL DISEASES

B. Jójárt¹, T. Molnár², D. Kata³, V. Szabó¹, A. Varga¹, T. Resál⁴, P. Bacsur⁴, K. Szántó⁴, I. Földesi³, T. Molnár⁴, J. Maléth¹, K. Farkas⁴

¹University of Szeged, Szent-Györgyi Albert Medical School, Department of Medicine, HAS-USz Momentum Epithelial Cell Signaling and Secretion Research Group, HCEMM-USz Molecular Gastroenterology Research Group, Szeged, Hungary, ²University of Szeged, Szent-Györgyi Albert Medical School, Department of Medicine, HAS-USz Momentum Epithelial Cell Signaling and Secretion Research Group, Szeged, Hungary, ³University of Szeged, Szent-Györgyi Albert Medical School, Institute of Laboratory Medicine, Szeged, Hungary, ⁴University of Szeged, Szent-Györgyi Albert Medical School, Department of Medicine, Szeged, Hungary

Contact E-Mail Address: jojart.boldizsar@gmail.com

Introduction: Inflammatory bowel diseases (IBD) are characterized by an unregulated immune response leading to intestinal inflammation. At present, accurate monitoring of intestinal inflammation depends mainly on clinical indices (symptoms and blood parameters) and endoscopy, in conjunction with histological and radiological imaging techniques. These tests are mostly invasive, time-consuming, and expensive.

Therefore, a simple, reliable, accurate, and non-invasive test, with the ability to differentiate IBD from other gastrointestinal conditions and to monitor disease activity and treatment, will have important clinical implications. It is well-established that expression of several cytokines, such as TNF- α , IL-1 β and IL-6, correlate with the inflammation and the disease activity.

Aims & Methods: Therefore, our aim was to identify cytokines with potential biomarker quality.

Blood and biopsy samples were collected from 87 active IBD patients and 35 controls without IBD. Inclusion criteria included change of therapy or initiation of new treatment for IBD patients. Organoid culture (OC) was generated from 5 clinically active IBD patients and 5 controls. Cytokine Array was used to analyse cytokine expression patterns. Total protein and mRNA were isolated from biopsies and from OCs. Protein levels were measured by ELISA and gene expression by qRT-PCR in serum, mucosa and in OCs. Immunofluorescence (IF) staining was used to observe the presence and localisation of cytokines.

Results: The cytokine array showed that plasminogen activator inhibitor 1 (PAI-1) was one of the cytokines, which was detected in most inflamed biopsy samples, but not in controls.

Furthermore, the detection number was significantly lower in samples from the non-inflamed part of the colon. Serum and mucosal PAI-1 concentrations were significantly higher in patients with endoscopically

and clinically active disease compared to inactive patients and controls. Whereas no significant difference was observed between Crohn's-disease and ulcerative colitis patients. Correlation analysis revealed that serum PAI-1 level correlates with disease activity.

In addition, IF staining of the biopsy samples revealed a significantly higher percentage of PAI-1 positive cells in the inflamed mucosa compared to the control. *Ex vivo* organoids recapitulated the findings in biopsy samples. The gene expression of PAI-1 was significantly lower in patients responding to anti-TNF- α therapy, than in the non-responder patients, whereas the protein level significantly decreased after the initiation of therapy compared to non-responders.

Conclusion: Our findings suggest that serum and mucosal PAI-1 expression correlates with the disease activity in IBD patients, suggesting that it could be utilized to monitor disease activity and possibly therapy response.

Disclosure: Nothing to disclose.

P0350

USE OF HAEMATOLOGICAL IRON PARAMETERS ALONE OR IN COMBINATION TO DETECT IRON DEFICIENCY IN INFLAMMATORY BOWEL DISEASE

C. Mangold¹, L. Tessmer^{2,3}, K. Farrag^{2,3}, O. Schröder^{2,3}, A. Aksan^{2,4}, J. Stein^{2,3,5}

¹Goethe University Frankfurt, Faculty of Medicine, Frankfurt am Main, Germany, ²Interdisciplinary Crohn-Colitis Centre Rhein-Main, Frankfurt am Main, Germany, ³GKD Clinics Sachsenhausen, Department of Gastroenterology and Clinical Nutrition, Frankfurt am Main, Germany, ⁴Justus-Liebig University, Institute of Nutritional Science, Giessen, Germany, ⁵Institute of Pharmaceutical Chemistry, Goethe University, Frankfurt am Main, Germany

Contact E-Mail Address: ayscak@gmail.com

Introduction: Iron deficiency (ID) is among the most common extraintestinal manifestations of inflammatory bowel disease (IBD). The European Crohn's and Colitis Organization (ECCO) last updated guidelines on ID diagnosis in 2015, recommending diagnosis of ID in IBD patients to be based on only one iron parameter, namely ferritin. It is likely that ID is still under-detected in IBD patients, due in particular to a lack of awareness of subtle clinical symptoms among physicians, imprecisions of laboratory tests and difficulties in interpreting these accurately.

Aims & Methods: We aimed to investigate which sole parameter or combination of parameters can best predict ID in patients with IBD. A retrospective cross-sectional study was conducted using routine blood samples from patients with IBD. Blood samples were analysed for CBC, iron status (serum ferritin, SF; transferrin saturation, TSAT; mean corpuscular volume, MCV), the inflammation parameter high sensitivity CRP (hsCRP) and soluble transferrin receptor (sTfR) by standard methods. A multiparameter index test (MCV, TSAT, SF) was performed to detect ID when at least 2 of the 3 parameters indicated ID. sTfR ferritin index (sTfR-F) was calculated (sTfR (mg/L)/log¹⁰ SF (μ g/L)). Cut-off values for TSAT (<20%) and SF (<30 μ g/L or <100 μ g/L) were defined according to ECCO guidelines and for MCV (80fL) according to the literature. Criteria taken to indicate absolute ID (AID) were hsCRP <5mg/L, SF 30 μ g/L and TSAT <20%, while functional ID (FID) was denoted by hsCRP $\geq$ 5mg/L, SF <100 μ g/L and TSAT <20%.

Results: 240 IBD patients (120f/120m;120CD/120UC;42.9 $\pm$ 14.6y) were enrolled. Of these, 71/240(29.6%) had inflammation. 47/240 patients had ID, of whom 25/47 had FID and 22/47 had AID. ROC analysis was performed to compare different parameters as detectors of ID and to summarise the performance of each respective parameter (Table 1).

In the absence of inflammation, a combination of the common markers TSAT and SF <30µg/L is sufficient to detect a large majority of cases of ID. In patients with inflammation, TSAT and SF <100µg/L in combination still detect the majority of ID cases. However, addition of MCV, which showed high specificity regardless of inflammation, was found to add additional value to the diagnosis, especially in the context of inflammation ($p<0.001$).

Patient group	Outcome	MCV	TSAT	SF	sTfR	sTfR-F
All patients	AUC ^{ROC}	0.810	0.985	0.850	0.820	0.878
	Sens./Spe. %	25.0/98.7	100.0/89.2	53.3/94.3	47.5/94.7	65.0/88.8
Patients with inflammation	AUC ^{ROC}	0.729	1.000	0.806	0.755	0.866
	Sens./Spe. %	20.0/96.3	100.0/86.3	96.0/55.6	34.8/96.2	43.5/96.2
Patients without inflammation	AUC ^{ROC}	0.843	0.991	0.970	0.948	0.987
	Sens./Spe. %	31.6/99.0	100.0/95.6	89.5/96.2	76.5/92.9	100.0/88.9

Table 1. Analytical performance of iron status parameters to detect ID in patients with IBD with/without co-presence of inflammation.

Conclusion: Of those parameters studied, none was suitable to diagnose ID in patients with IBD when taken alone. Independent of whether there was active inflammation, TSAT and SF seemed to adequately define ID; however, in both cases the addition of MCV had additional value, and particularly so when inflammation was present.

The additional value of sTfR (or sTfR-F) is questionable due its high cost and limited availability. However, prospective large-scale studies are needed to evaluate whether determination of sTfR and sTfR-F could be worthwhile.

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P0351 LATENT CROHN'S DISEASE SUBGROUPS ARE IDENTIFIED BY FAECAL CALPROTECTIN PROFILES: A RETROSPECTIVE ANALYSIS OF THE LOTHIAN CROHN'S DISEASE INCEPTION COHORT

N. Constantine-Cooke^{1,2}, K. Monterrubio-Gómez¹, N. Plevris^{2,3}, L. Derikx⁴, B. Gros³, G.-R. Jones⁵, R. Marioni², C. Lees^{2,3}, C. Vallejos^{1,6}
¹University of Edinburgh, MRC Human Genetics Unit, Edinburgh, United Kingdom, ²University of Edinburgh, Centre for Genomic and Experimental Medicine, Edinburgh, United Kingdom, ³University of Edinburgh, Edinburgh IBD Unit, Edinburgh, United Kingdom, ⁴Radboud University Medical Centre, Gastroenterology and Hepatology, Nijmegen, Netherlands, ⁵University of Edinburgh, Centre for Inflammation Research, Edinburgh, United Kingdom, ⁶The Alan Turing Institute, London, United Kingdom

Contact E-Mail Address: nathan.constantine-cooke@ed.ac.uk
Introduction: Faecal calprotectin (FCAL) is a neutrophil degranulation product associated with mucosal inflammation in Crohn's disease (CD). Escalation with an anti-TNF therapy on the basis of clinical symptoms combined with biomarkers in patients with early CD results in better clinical and endoscopic outcomes than symptom-driven decisions alone¹. Indeed, normalisation of FCAL (<250 µg/g) within one year of diagnosis is associated with better long-term outcomes².
Aims & Methods: We aimed to:
1. Determine if five-year FCAL profiling could identify "classes" of CD patients associated with Montreal disease progression, hospitalisation, and surgery.
2. Assess if membership of these classes was associated with factors at diagnosis (e.g. treatment and disease phenotype).
Demographic, clinical, follow-up data and FCAL results were extracted from the Lothian IBD registry, a rigorously phenotyped database of all IBD patients receiving secondary care from NHS Lothian³. All CD patients diagnosed between 2005 and 2017 with FCAL >250 (µg/g) at diagnosis, a followup FCAL within one year, and an additional FCAL within five years of diagnosis were included.
Latent class mixed models, an extension of linear mixed effects models with class-specific fixed effects, were used to model and group FCAL trajectories. Fixed and random effects of this model were modelled using natural cubic splines: permitting flexible models.
Akaike information criterion, Bayesian information criterion, alluvial plots, and plots of mean class trajectories were used to decide the optimal number of classes. Log-rank tests of Kaplan-Meier estimators were used to test for associations between class membership and poor disease outcomes. Chi-squared tests, Fisher's exact test and ANOVA were used to find possible associations between class membership and variables available at diagnosis and treatments prescribed within one year of diagnosis.
Results: Of 1390 incident CD cases, 356 subjects met the study inclusion criteria, who had 2856 FCAL measurements (median 7 per subject) within five years of diagnosis. Four latent classes were found to be the most appropriate.
Class 1 and 3 were both characterised by decreasing trajectories. Class 1 decreased almost immediately, whilst class 3 decreased at one year after diagnosis.
Class 4 demonstrated a remitting, relapsing trajectory whilst class 2 demonstrated consistently FCAL. Class membership was significantly associated with hospitalisation, Montreal disease progression, and a composite endpoint but not surgery.
Of variables typically available at diagnosis, smoking status and the presence of upper gastrointestinal inflammation were all found to be significantly associated with class membership.

Significant associations between class membership and both biologic and thioprine prescriptions were found with less biologic and thioprine treatments being prescribed for class 2.

Conclusion: Latent class mixed models are highly effective for identifying latent classes within the CD population from FCAL profiles and have potential for being deployed as a risk prediction tool.

This approach also allows common trajectories to be generated in a data driven approach. In the future, these models should be applied to a larger cohort including ulcerative colitis patients in addition to a validation cohort.

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P0352

COMPARISON OF CLINICAL IMPROVEMENT AS MEASURED BY TWO QUALITY-OF-LIFE INDEXES: A POOLED ANALYSIS OF VEDOLIZUMAB RANDOMIZED CLINICAL TRIALS IN INFLAMMATORY BOWEL DISEASE

E. Louis¹, P. Kamble², D. Lindner³, C. Agboton⁴

¹CHU Liège and Liège University, Gastroenterology, Liège, Belgium, ²Takeda Pharmaceuticals Inc., Global Evidence and Outcomes-Gastroenterology, Marlborough, United States, ³Takeda Pharmaceuticals, Zurich, Switzerland, ⁴Takeda Pharmaceuticals, Dept. of Medical Affairs, Zurich, Switzerland

Contact E-Mail Address: christian.agboton@takeda.com

Introduction: Improvement in Quality of life (QoL) is an ultimate therapeutic goal for disease management in ulcerative colitis (UC) and Crohn's disease (CD) as recommended by STRIDE II and SPIRIT initiatives.^{1,2}

The aim of this analysis was to better understand the capacity of the 32-item inflammatory bowel disease questionnaire (IBDQ) and its 10-item short version (SIBDQ) in evaluating response to treatment. IBDQ improvement is generally defined as a change of the total score by >16 points (>9 for SIBDQ) and remission is defined as IBDQ score of ≥170 or more (≥60 for SIBDQ).

Aims & Methods: This was a post-hoc analysis, pooling data across six Phase 3 studies of vedolizumab IV or SC in UC (3 studies) and CD (3 studies), five of which were randomized controlled trials (RCTs), and one single-arm study in CD.³⁻⁵ The pooled dataset included VARSITY⁶, the only study in UC with an active control arm (adalimumab). In the five RCTs, patients were

randomized at Week 6, except in VARSITY where a treat-through design was used. The 3 time points studied include Week 0 (baseline), Week 26 or 30, and Week 52. Comparisons of the IBDQ and SIBDQ were based on observed data.

Results: The pooled dataset included 1458 patients with UC and 974 patients with CD for whom IBDQ data was reported at least once. Of these, 892 patients with UC were in the vedolizumab group, 384 in the active control group, and 182 in the placebo arm. In CD patients, 808 received vedolizumab and 166 placebo.

Across all studies, the IBDQ showed that in UC and CD together, 75.5% of vedolizumab-treated patients reported an improvement at Week 52, and 63.7% were in IBDQ remission at Week 52 compared with 68.7% (IBDQ improvement) and 46.0% (IBDQ remission) for patients receiving placebo. In UC, IBDQ improvement was generally higher for vedolizumab-treated patients (71.8%) than for patients in the placebo (61.7%) or active control groups (50.8%).

In CD, the difference between vedolizumab and the control group was less visible, with 81.3% showing improvement at Week 52 on vedolizumab vs. 75.0% for control group.

In vedolizumab patients, SIBDQ-based remission was observed less frequently than IBDQ-based remission at Week 52, with proportions of 50.3% (UC) and 37.7% (CD) for SIBDQ, compared with 65.4% (UC) and 60.9% (CD) for IBDQ-based remission.

A similar pattern was observed in placebo control patients with proportions of 24.5% (UC) and 27.9% (CD) for SIBDQ-based remission compared with 40.4% (UC) and 51.0% (CD) for IBDQ. Both scales showed good concordance, with SIBDQ-based remission matching IBDQ-based remission in 84.4% of patients (22.5% Yes/Yes and 61.9% No/No), and SIBDQ-based improvement matching IBDQ-based improvement in 89.9% of cases (70.0% Yes/Yes and 19.9% No/No) [Table].

All patients, all visits, UC+CD		IBDQ-based remission (n=5712)	
		Yes	No
SIBDQ-based remission	Yes	22.5%	0.0%
	No	15.6%	61.9%
		IBDQ-based improvement (n=3219)	
		Yes	No
SIBDQ-based improvement	Yes	70.0%	0.4%
	No	9.8%	19.9%

Bold text denotes concordance

Table. Concordance between IBDQ and SIBDQ.

Conclusion: This first analysis showed a slightly different dynamic for the SIBDQ and IBDQ, especially in CD. The 2 scales served their purpose of monitoring the QoL of patients; however concordance between the two scales for remission was lower than for improvement.

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Pravin Kamble: Employee of the study sponsor, Takeda and holds Takeda stock or stock options.

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P0353

USE OF FAECAL CALPROTECTIN AS A PROGNOSTIC MARKER OF RESPONSE TO TREATMENT WITH FILGOTINIB: POST HOC ANALYSIS FROM THE SELECTION STUDY

E. Louis¹, B. Feagan^{2,3}, T. Hisamatsu⁴, V. Taliadouros⁵, R. Jongen⁶, A. Oortwijn⁵, C. Van der Donckt⁶, L. Peyrin-Biroulet⁷

¹CHU Liège University Hospital, Department of

Gastroenterology, Liège, Belgium, ²Alimentiv, London, Canada,

³Western University, Division of Gastroenterology, London Health

Sciences Centre, London, Canada, ⁴Kyorin University School of

Medicine, Department of Gastroenterology and Hepatology,

Tokyo, Japan, ⁵Galapagos NV, Leiden, Netherlands, ⁶Galapagos

NV, Mechelen, Belgium, ⁷University Hospital of Nancy, University

of Lorraine, Department of Gastroenterology, Vandoeuvre-lès-

Nancy, France

Contact E-Mail Address: Alessandra.Oortwijn@glpg.com

Introduction: Filgotinib (FIL) is a once-daily, oral, preferential JAK1 inhibitor approved for the treatment of ulcerative colitis (UC). In SELECTION, FIL 200 mg (FIL200) was efficacious in inducing and maintaining clinical remission vs placebo (PBO) in patients with moderately to severely active UC.¹

Increased faecal calprotectin (FC) has been associated with the risk of relapse and is broadly used as a non-invasive monitoring tool in patients with UC. We assessed the operating properties of FC as a prognostic marker of the response to treatment with FIL200.

Aims & Methods: SELECTION was a phase 2b/3, double-blind, randomized, PBO-controlled trial (NCT02914522) comprising two induction studies and one maintenance study.¹

Using Mann-Whitney U tests and receiver operating characteristic (ROC) curves with comparison of areas under the curve (AUC), these *post hoc* analyses evaluated the ability of median FC concentration and FC concentration thresholds vs histological and endoscopic assessments to discriminate Mayo Clinic Score (MCS) response, endoscopic response and endoscopic remission after induction (week 10), and clinical remission after maintenance (week 58) treatment with FIL200.

Results: FC concentration at baseline was not a strong prognostic factor for MCS response at week 10 (median [interquartile range (IQR)] µg/g, yes: 1450 [561–3056] vs no: 1211 [455–2734], $p=0.0938$), whereas FC concentration at week 10 was associated with MCS response (median [IQR] µg/g, yes: 209 [68–720] vs no: 1133 [347–2101], $p<0.0001$), endoscopic response (yes: 102 [41–301] vs no: 756 [211–1741], $p<0.0001$) and endoscopic remission (yes: 59 [29–186] vs no: 527 [148–1598], $p<0.0001$) at week 10.

Using a cut-off of 250 µg/g to create a binary outcome, FC <250 µg/g (FC250) at week 10 was associated with a MCS response at week 10 (yes: $n=340$ [positive predictive value (PPV): 75.9%]; no: $n=454$ [negative predictive value (NPV): 61.5%]).

Combining FC250 with symptomatic outcomes (partial MCS [pMCS] remission) improved both the PPV (79.8%) and NPV (73.5%) for MCS response at week 10. FC250 was associated with an endoscopic response at week 10 (PPV: 42.2%; NPV: 90.4%; ROC curve AUC: 0.724 [95% confidence interval: 0.693–0.754]). The combination of FC250 with pMCS remission at week 10

was prognostic for clinical remission at week 58 with a higher AUC than that of either endoscopic response, Geboes histological remission, FC250 or pMCS remission alone (Table 1).

		ROC curve				Logistic regression	
		Yes	No	PPV	NPV	AUC (95% CI)	Odds ratio (95% CI) p value ^a
FC250	Yes	51 (47.2%)	57 (52.8%)	47.2%	–	0.606	2.440
	No	22 (26.8%)	60 (73.2%)	–	73.2%	(0.536–0.676)	(1.316–4.525)
pMCS remission	Yes	61 (42.1%)	84 (57.9%)	42.1%	–	0.576	2.290
	No	13 (24.1%)	41 (75.9%)	–	75.9%	(0.516–0.636)	(1.131–4.638)
Endoscopic response	Yes	37 (50.7%)	36 (49.3%)	50.7%	–	0.606	2.472
	No	37 (29.4%)	89 (70.6%)	–	70.6%	(0.536–0.676)	(1.359–4.495)
Geboes histological remission	Yes	32 (45.1%)	39 (54.9%)	45.1%	–	0.559	1.661
	No	42 (33.1%)	85 (66.9%)	–	66.9%	(0.489–0.629)	(0.915–3.014)
FC <250 µg/g and Geboes histological remission	Yes	27 (50.0%)	27 (50.0%)	50.0%	–	0.570	1.957
	No	46 (33.8%)	90 (66.2%)	–	66.2%	(0.502–0.637)	(1.031–3.714)
FC <250 µg/g and Geboes histological remission and endoscopic response	Yes	20 (60.6%)	13 (39.4%)	60.6%	–	0.581	3.018
	No	53 (33.8%)	104 (66.2%)	–	66.2%	(0.523–0.640)	(1.394–6.536)
FC <250 µg/g and pMCS remission	Yes	45 (51.7%)	42 (48.3%)	51.7%	–	0.629	2.870
	No	28 (27.2%)	75 (72.8%)	–	72.8%	(0.558–0.700)	(1.568–5.252)

Clinical remission = endoscopic subscore of ≤1, rectal bleeding subscore of 0 and a reduction of ≥1 point in stool frequency subscore from induction baseline to achieve a subscore of ≤1.

pMCS = sum of rectal bleeding, stool frequency and physician's global assessment subscores.

pMCS remission = pMCS of ≤1.

Endoscopic response = endoscopic subscore of ≤1.

Geboes histological remission = grade 0 of ≤0.3, grade 1 of ≤1.1, grade 2A of ≤2A.3, grade 2B of 2B.0, grade 3 of 3.0, grade 4 of 4.0, and grade 5 of 5.0.

^aAll p values are nominal.

AUC, area under the ROC curve; CI, confidence interval; FC, faecal calprotectin; FC250, FC <250 µg/g; FIL200, filgotinib 200 mg; NPV, negative predictive value; pMCS, partial Mayo Clinic Score; PPV, positive predictive value; ROC, receiver operating characteristic.

Table 1. Prognostic value of FC concentration and invasive and non-invasive assessments at week 10 for clinical remission at week 58 in patients receiving FIL200.

Conclusion: FC concentration following induction with FIL200 is associated with a short-term response. The combination of FC250 and pMCS remission at week 10 may be a good, non-invasive prognostic marker of clinical remission at week 58. These findings raise the possibility that some patients could avoid undergoing endoscopy at early time points with the use of close biomarker and symptom monitoring.

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P0354

MEASURING ADALIMUMAB AND INFLIXIMAB TROUGH LEVELS FROM FINGER PRICK BLOOD WITH A RAPID POINT-OF-CARE ASSAY

L. Brosi¹, C. Reinhard¹, J. Afonso¹, T. Schuster¹, C.-B. Gerhold¹, B. Ricken¹

¹BÜHLMANN Laboratories AG, Schönenbuch, Switzerland

Contact E-Mail Address: jpa@buhlmannlabs.ch

Introduction: Several studies demonstrated a positive correlation between anti-TNFα drug trough levels and the therapeutic outcome of inflammatory bowel disease (IBD) patients. Commercially available rapid assays support laboratories in the fast and easy detection of adalimumab (ADL) and infliximab (IFX) concentrations.

A hindrance for true point-of-care (POC) use is the assay's dependency on serum as analyte matrix, because serum preparation from whole blood requires laboratory equipment and is time-intensive. Therefore, in this work ADL and IFX lateral flow assays that can process capillary blood and venous whole blood are presented.

Included in the assay kits are all components that are needed to generate a measurement without further sample preparation steps or additional laboratory equipment. The assays can be run on an easy-to-use desktop lateral flow reader.

Aims & Methods: We designed a lateral flow assay kit for the analysis of ADL and IFX in capillary blood and (EDTA) whole blood specimen, respectively. The POC kits consist of disposable capillaries for blood collection from finger prick blood or venous whole blood and transfer to dropper bottles that are prefilled with chase buffer. Sample and chase buffer are mixed by gently flipping the tube, before the mixture is applied on the lateral flow test cassette. For matrix agreement studies EDTA whole blood, whole blood without anticoagulant and capillary blood were spiked with ADL and IFX and partially used for plasma and serum preparation.

Serum and plasma samples were analysed with the Quantum Blue® Adalimumab and Infliximab assays, while the corresponding whole blood and EDTA whole blood, as well as spiked capillary blood samples were analysed with the newly developed POC sample preparation system.

Additionally, linearity, within-run precision and robustness experiments were performed with the POC ADL and IFX assays to demonstrate suitability for routine use.

Results: Good comparability between all tested matrices including capillary blood to serum was demonstrated. Both POC assays revealed a bias of less than 15 % at the clinical decision points for ADL (5 µg/mL and 12 µg/mL) and IFX (3 µg/mL and 7 µg/mL). Linearity for POC ADL and POC IFX rapid assays is given over a measuring range of 1.3 – 35 µg/mL and 0.4 – 20 µg/mL, respectively. Within-run precision determined with spiked EDTA whole blood samples was between 6 – 18 % and 6 – 20 % for the POC ADL and POC IFX rapid assays, respectively. Robustness experiments revealed that capillary and EDTA whole blood samples can be used within 20 minutes after dilution with chase buffer. This also allows a certain flexibility at the clinician's site.

Conclusion: Two POC assays for the determination of ADL and IFX in capillary or venous whole blood samples were successfully developed. Both assays can be used by non-laboratory professionals with time to results of only 15 minutes and without the need for additional laboratory equipment. The excellent agreement to serum trough levels shows that the here presented POC assays are ideal for ADL and IFX therapeutic drug monitoring analysis in a clinician's office or an infusion site.

Disclosure: BÜHLMANN Laboratories AG; Employee.

P0355

REAL-TIME CLASSIFICATION OF CROHN'S DISEASE CLINICAL REMISSION BY HEALTH-RELATED QUALITY OF LIFE (HRQOL) QUESTIONNAIRES IN COMBINATION WITH BIOMARKERS: DATA FROM A REAL-WORLD PROSPECTIVE INCEPTION COHORT

T. Sharar Fischler^{1,2}, I. Goren^{1,2}, J. Ollech^{1,2}, R. Barkan^{1,2}, T. Pfeffer Gik^{1,2}, B. Raykhel^{1,2}, Y. Kutukov^{1,2}, A. Friedenberg^{1,2}, M.H. Pauker^{1,2}, Y. Broitman^{1,2}, Y. Snir^{1,2}, H. Bana^{1,2}, I. Avni-Biron^{1,2}, I. Dotan^{1,2}, H. Yanai^{1,2}

¹Rabin Medical Center, Division of Gastroenterology, Petah Tikva, Israel, ²Tel Aviv University, Sackler Faculty of Medicine, Tel Aviv, Israel

Contact E-Mail Address: talifis@yahoo.com

Introduction: Patient centered outcomes assessment is required by global regulatory authorities in Crohn's disease (CD) trials. However, the optimal instrument, outcome(s) and their utility in practice are not yet defined. Here we aimed to evaluate the contribution of two health-related quality of life (HRQoL) questionnaires in the classification of clinical remission (CR) compared to active disease (non-remission) in a prospective cohort of patients with CD.

Aims & Methods: This was a cross-sectional analysis of HRQoL questionnaires of patients with newly diagnosed CD from a prospective inception cohort (2018-2020). Analysis was done on comprehensive data collected from this cohort who is followed and cared by a multidisciplinary team (including IBD-oriented gastroenterologist determining treatment plans, an IBD nurse, and a dietitian). All patients in the cohort are scheduled for semi-annual study visits for additional assessment and data collection. After 1-year from diagnosis these patients were assessed for CR that was defined by a composite of: Crohn's disease activity index (CDAI) < 150, no active perianal disease, steroid-free, no treatment escalation and no hospitalizations > 3 months. In parallel, biomarkers (C-reactive protein [CRP] and fecal calprotectin [FC]) and HRQoL measures were captured. HRQoL was evaluated by two questionnaires: the short IBD questionnaire (SIBDQ) and patient reported outcome 2 (PRO2). These scores were individually assessed as a diagnostic test for CR by logistic regression models and receiver operating characteristic (ROC) curve analysis.

Results: Out of 120 enrollees, 85 completed 1-year follow-up: female 50.6%, median age 27 years (IQR 22-39), active smokers 16.5%, median BMI 21.7 kg/m² (IQR 20.1-25.2). At diagnosis: inflammatory phenotype (B1) 72.9%, complex perianal disease 11.8%, extra-intestinal manifestation 29.4%, all patients with active disease of whom 55.3% with moderate-severe CD (CDAI>220).

During the first year after diagnosis 62.3% were treated with a biologic therapy and 7% required surgery. After 1-year from diagnosis 61.1% attained CR. Biomarkers were lower among patients who were in CR vs those with active disease (FC- 49.5 [IQR:13.5-141.7] vs 230 [IQR: 84-440], $p=0.002$, CRP- 0.17 [IQR: 0.06-0.6] vs 0.46 [IQR: 0.12-1.53], $p=0.005$, respectively). Similarly, SIBDQ and PRO2 scores were significantly favorable among those patients who attained CR (59 [IQR: 53-64] vs. 43 [IQR:34-58.2], and 1.42 [IQR:0-4.7] vs 7.7 [IQR: 3.1-15], respectively, both $p<0.001$). Modeling individual HRQoL scores with and without specific biomarkers revealed that the optimal predictor for our stringent definition of CR was a combination of PRO2 score and FC levels. The model yields a ROC with an area under the curve (AUC) of 0.871 (95% CI 0.796-0.946) and with a discrimination slope of 39%. If electing a specificity of 97% and sensitivity of 82% the usage of the model may result in a 43% drop in routine physician visits with only 3.4% (1/29 patients) probability to make a mistake and wrongly assess a patient as a remitter (false negative).

Conclusion: Combination of PRO2 and FC had a high discriminatory ability between patients in CR vs active disease in a real-world inception cohort of patients with newly diagnosed CD. Application of this model in clinical practice may contribute to decision making based on specific thresholds for improved patient allocation (i.e. remote / IBD-nurse) rather than intense routine physician visits. Thus, utilization of this model may impact health policy and monitoring plans for patients with CD.

Disclosure: Nothing to disclose.

P0356

CRP TO ALBUMIN RATIO AND NEUTROPHIL TO LYMPHOCYTIC RATIO AS A PREDICTOR OF MUCOSAL HEALING IN EGYPTIAN PATIENTS WITH ULCERATIVE COLITIS TREATED WITH BIOLOGICAL THERAPY

M. Eltabbakh¹, Y. Abd El Razek¹, S. Abdelrahman¹, A. Al Breedy¹

¹Ain Shams University, Tropical Medicine, Hepatology and Gastroenterology Department, Cairo, Egypt

Contact E-Mail Address: dr_tabbo84@yahoo.com

Introduction: There is some evidence of a possible role of some serum biomarkers in the ulcerative colitis setting, in particular concerning disease severity. Many patients experience loss of response to biological therapy during the first year of therapy. An early predictor of clinical remission and mucosal healing is needed.

Aims & Methods: Objectives: To evaluate the role of non-invasive biomarkers as an early predictor of mucosal healing in ulcerative colitis patients treated with biological therapy.

Methods: This was a prospective cohort study starting from January 2020 till January 2021. We included ulcerative colitis cases started biological therapy at our IBD unit at tropical medicine department, Ain Shams University, Egypt. We excluded patients on corticosteroids more than 20 mg/day. Mayo score and Mayo endoscopic score were used to assess the severity of the disease. Each patient was followed up at week 12 and week 24 from starting therapy to assess response to treatment. Ileocolonoscopy examination was repeated at week 24 to assess mucosal healing. Endoscopic mucosal healing was measured by Mayo endoscopic sub score (0 or 1 points). The following indices were calculated at starting treatment: Neutrophil-Lymphocytic ratio(N/L), platelet lymphocytic ratio(P/L), CRP/Albumin ratio and platelet monocyte ratio(P/M).

Results: Twenty patients with ulcerative colitis were included in our study. The mean age of the studied cases was 33.75±9.6. Most of our cases were females (60%). Most of our cases (65%) had clinical response at 6 months follow up. Mucosal healing achieved in seven cases only after six months follow up.

There was a significant decrease in median N/L ratio in 6 months follow up (Median baseline was 2.62 with IQR (1.87 – 6.5), at 3 months was 2.26 (1.54 – 4.06) while at 6 months was 1.85 (1.28 – 2.8)($P=0.044$). Median PLT/L ratio significantly decreased at 6 months (142.37 (115.81 – 212.11) in comparison to 3 months and baseline (239.17 (122.77 – 326.25) and 263.75 (146.95 – 432.64) respectively ($P=0.019$)). Median PLT/M ratio was 823.33 (516.7 – 1760.65) at starting treatment while it decreased significantly 787.5 (550.17 – 1560) and 541.93 (396.32 – 748.03) at 3 months and 6 months respectively ($P=0.035$).

Also, Median CRP/albumin ratio decreased significantly at 6 months 2.56 (0.81 – 3.59) and 3 months 2.32 (1.2 – 3.88) while it was 4.57 (1.48 – 18.29) at starting treatment with biological treatment ($P=0.026$). In relation to mucosal healing at 6 months; Baseline median N/L ratio was significantly associated with mucosal healing (1.84) while it was (5.57) in cases who did not achieve mucosal healing ($P=0.016$). Also, Baseline median CRP/albumin ratio was significantly associated with mucosal healing (1.67) in comparison to (14.29) in patients who did not achieve mucosal healing ($P=0.036$).

		Mucosal healing		Test value	P- value	Sig.
		No (13)	Yes (7)			
N/L ratio	Median (IQR)	5.57 (2.2 – 9.17)	1.84 (1.5 – 2.53)	-2.417#	0.016	S
	Range	0.74 – 11.19	0.86 – 2.86			
PLT/L ratio	Median (IQR)	257.5 (141.79–388.89)	298.42 (152.11–476.39)	-0.674#	0.501	NS
	Range	106.21 – 576.67	103.79 – 594.29			
PLT/M ratio	Median (IQR)	605.41 (466.25 – 1730)	1040 (602 – 1845)	-0.991#	0.322	NS
	Range	356.67 – 5070	412.86 – 1890			
CRP/ Albumin	Median (IQR)	14.29 (1.62 – 20.36)	1.67 (1.35 – 3.33)	-2.100#	0.036	S
	Range	1.34 – 33.13	0.86 – 5.81			

S:Significant NS: Non-Significant

#:Mann-Whitney test

Table.

Conclusion: CRP/albumin ratio and N/L ratio at starting treatment with biological treatment in patients with ulcerative colitis may be considered as a useful non invasive markers for prediction of mucosal healing at six months follow up.

Disclosure: Nothing to disclose.

P0357

ARTIFICIAL INTELLIGENCE IN HISTOPATHOLOGICAL DIAGNOSIS OF IBD – A PILOT STUDY

P. Čačić¹, A. Demirovic^{2,3}, M. Subašić⁴, L. Žužak⁴, S. Pelajić¹, A. Biščanin^{1,2}, V. Tomasić¹, Z. Dorosulić¹, D. Kralj¹, D. Ogresta¹, F. Babić¹, B. Krušlin^{2,3}, D. Hrabar^{2,1}

¹Sestre Milosrdnice University Hospital Center, Department of Gastroenterology and Hepatology, Zagreb, Croatia, ²University of Zagreb, School of Medicine, Zagreb, Croatia, ³Sestre Milosrdnice University Hospital Center, Ljudevit Jurak Clinical Department of Pathology and Cytology, Zagreb, Croatia, ⁴University of Zagreb, Faculty of Electrical Engineering and Computing, Zagreb, Croatia

Contact E-Mail Address: petra.cacic@gmail.com

Introduction: Diagnosis of IBD is made upon a combination of clinical, endoscopic, histological, biochemical and radiographic features. The lack of the gold standard and inter-observer variability, especially in endoscopic and histological analysis, makes it even more challenging. Moreover, according to studies, 10-15% of IBD cases remain unclassified (IBDU). According to the results of an International Workshop on the initial histopathologic diagnosis of colitis, expert gastrointestinal pathologists correctly identified 64% of cases with CD and 74% of cases with UC, with even lower rate among non-expert gastrointestinal pathologists. Therefore, we aimed to develop a convolutional neural network (CNN)-based system for histopathological automatic distinction between CD and UC.

Aims & Methods: Single tertiary center retrospective study was performed. A total of 2255 histology images (200x magnification) of 27 colon biopsies from 23 patients, collected between 2010 and 2020 were analysed. Minimum duration of follow up was 26 months. Diagnosis at the end of follow up was presumed as definitive and patients with IBDU at the end of follow up were excluded from analysis. At the moment of sampling 11 patients were classified as UC, 10 as CD and 2 were unclassified. At the end, one patient with UC was reclassified to CD, and in IBDU group both patients were reclassified to UC.

Histology slides were digitalized using microscope digital camera Olympus UC 90 and Olympus cellSens Dimension Software package. A 46 layer convolutional neural network for image classification was used. Image dataset was split for 3-fold cross validation. Every fold had constitution of training (75%, 70% and 80%) and validation datasets (25%, 30% and 20%). The performance of the model was measured by calculating the area under the receiving operating characteristic curve (AUC), sensitivity, specificity, positive and negative predictive values (PPV and NPV).

Results: Mean AUC was 72.3%. The best model was able to automatically distinct CD from UC with an accuracy of 76.1%; sensitivity of 70%; specificity of 89%; PPV 93.4%; NPV 57.7%. The time it takes to classify one histology image is approximately 0.135 seconds.

Conclusion: Although the performance of our model was similar to pathologists, it should be interpreted with great caution due to small sample size. Application of AI methods in histopathology of inflammatory disease is still very limited because of complexity, variations in the stainability of individual cases, small but significant variations in slides preparation technique between centers etc. However, deep learning technologies are rapidly progressing, and AI models may become a useful tool in the pathology of IBD.

Disclosure: Nothing to disclose.

P0358

THERAPEUTIC DRUG MONITORING: STANDARDIZATION OF PROMONITOR QUICK IFX AND PROMONITOR QUICK ADL POINT OF CARE TESTS WITH WHO INTERNATIONAL STANDARDS FOR THE QUANTIFICATION OF INFLIXIMAB AND ADALIMUMAB IN WHOLE BLOOD AND SERUM

A. Ametzazurra¹, J. Pascual¹, L. Del Río¹, A. Urigoitia¹, D. Nagore¹, M.B. Ruiz-Argüello¹

¹Progenika Biopharma, Grifols, R&D, Derio, Spain

Contact E-Mail Address: amagoia.ametzazurra@progenika.grifols.com

Introduction: Promonitor Quick IFX and Promonitor Quick ADL are rapid point of care lateral flow tests (LFT) based on a sandwich immunoassay for the quantification of infliximab (IFX) and adalimumab (ADL), respectively, in human whole blood (finger prick or venous) or serum.

These tests are to be used as an aid in Therapeutic Drug Monitoring (TDM) of inflammatory bowel disease (IBD) and rheumatic patients under anti-TNFα therapy. The international standards (IS) developed by World Health Organization (WHO) for IFX and ADL allow harmonization and comparability among different assays.

Aims & Methods: Objectives: The aim of this study, was to show that Promonitor Quick IFX and Promonitor Quick ADL can measure either reference or biosimilar drugs, as well as to evaluate the agreement of Promonitor Quick IFX and Promonitor Quick ADL tests and the WHO IS.

Methods: Clinical and Laboratory Standards Institute EP10-A3 guidelines were followed to estimate the bias of Promonitor Quick assays when used to quantify IFX or ADL in samples containing the reference drugs, biosimilars or the WHO IS. Briefly, whole blood was spiked with four known concentrations of IFX or ADL, including current clinical decision levels. Ten replicates were measured of each level along two days.

Promonitor Quick IFX was evaluated using the reference drug, SB2 and CT-P13 biosimilars, and the WHO IS (NIBSC 16/170).

Promonitor Quick ADL was evaluated using the reference drug, ABP501 and SB5 biosimilars, and the WHO IS (NIBSC 17/236).

Results were obtained in combination with the automated portable reader PQreader.

Results: Bias was estimated by comparing the observed concentration of drug spiked whole blood samples. Each biosimilar was compared to the reference at the different drug levels tested. Results showed that Promonitor Quick IFX and Promonitor Quick ADL are able to measure equivalently any molecule (see Table below).

The accuracy or closeness of the agreement between the result provided by Promonitor Quick IFX and Promonitor Quick ADL and the true value of the measurand was assessed by measuring the IS developed by the WHO (see Table). Similar results were obtained when serum matrix was used.

Promonitor Quick IFX bias results					Promonitor Quick ADL bias results			
IFX concentration (µg/mL)	Bias (%)				ADL concentration (µg/mL)	Bias (%)		
	CT-P13	SB2	GP1111	WHO IS		ABP501	SB5	WHO IS
3	14%	3%	4%	8%	3	17%	2%	3%
7	9%	0%	5%	15%	5	13%	3%	12%
10	1%	5%	6%	8%	8	2%	2%	7%
					10	5%	17%	10%

Table. Bias results in whole blood samples.

Each molecule was compared to the reference drug.

Conclusion: Promonitor Quick IFX and Promonitor Quick ADL allow monitoring of patients treated with IFX and ADL, respectively, with just a finger prick sample. Both tests can quantify reference and biosimilar drugs with

equivalent results. Moreover, comparable results were obtained with the WHO IS, and thus, demonstrate that Promonitor Quick tests are suited to accurately determine drug levels at the clinical decision points in both whole blood and serum, proving to be an effective and valuable tool in TDM and immediate decision making in the doctor office or hospitals.

Disclosure: The authors are Progenika Biopharma - Grifols employee.

P0359

CORRELATION OF THE PROMONITOR QUICK ADL LATERAL FLOW-BASED POINT OF CARE TEST TO QUANTIFY ADALIMUMAB IN A FINGER PRICK OR SERUM SAMPLES WITH THE REFERENCE ELISA TECHNIQUE

A. Ametzazurra¹, J. Pascual¹, L. Del Río¹, C. Balo Farto², C. Fernández³, A. Mera², F.J. De Toro³, D. Nagore¹, M.B. Ruiz-Argüello¹

¹Progenika Biopharma, Grifols, R&D, Derio, Spain, ²Hospital Clínico Universitario de Santiago, Servicio Reumatología, Santiago de Compostela, Spain, ³Complejo Hospitalario Universitario A Coruña, Servicio Reumatología, A Coruña, Spain

Contact E-Mail Address: amagoia.ametzazurra@progenika.grifols.com

Introduction: The goal of this study was to validate the use of capillary blood in a real point-of-care (POC) setting for patients under adalimumab treatment by using Promonitor Quick ADL lateral flow test. Results were compared to the Promonitor ELISA reference technique in serum samples used by centralised laboratories. In addition, the use of serum samples with Promonitor Quick ADL test in comparison with Promonitor-ADL ELISA was validated.

Aims & Methods: A prospective, observational study was designed to evaluate the performance of a rapid test (Promonitor Quick ADL, Progenika, Spain). 137 adalimumab treated rheumatology consecutive patients (167 samples) were recruited in two hospitals in Galicia, Spain. Prior to the injection, a finger prick and a serum sample were obtained and analysed. Results were read with the automated portable PQreader instrument. Additionally, the same serum sample was subsequently analysed with the ELISA test for comparative purposes.

Qualitative (positive (PPA) and negative (NPA) agreements) and quantitative (Pearson correlation and bias) performance of the Promonitor Quick ADL test was compared to ELISA, as well as between different specimens following CLSI EP09-A3.

Results: Overall agreement between Promonitor Quick ADL finger prick and ELISA test was 95% (94% PPA; 100% NPA). The quantitative comparison showed a good correlation (Pearson correlation coefficient: 0.7 and observed bias: 17%) (Table 1).

Similar results were also observed when serum was used with either the Promonitor Quick ADL or the ELISA tests (98% overall agreement, 0.8 correlation coefficient; 2% bias) (Table 1).

Qualitative Comparison				
	N*	PPA	NPA	overall
POC finger prick vs ELISA	160	94%	100%	95%
POC serum vs ELISA	166	97%	100%	98%
Quantitative Comparison				
	N*	Pearson correlation	Bias	
POC finger prick vs ELISA	78	0.7	17%	
POC serum vs ELISA	87	0.8	2%	

*Only samples in the common measurement range for both methods considered.

Table 1. Performance results. ADALIMUMAB DRUG

Conclusion: Promonitor Quick ADL can be used to reliably quantify adalimumab in capillary blood or serum samples and results are comparable to those obtained with the reference ELISA technique. The use of the rapid POC test with finger prick will allow clinicians to monitor their patients in a fully decentralized mode to aid in the decision-making process.

Disclosure: A. Ametzazurra, J. Pascual, L. Del Río, D. Nagore and MB. Ruiz-Argüello are Progenika Biopharma - Grifols employee.

P0360

THE IMPACT OF DRUG LEVELS TO ANTI-TNF AND ANTI-INTEGRIN AGENTS ON COVID-19 VACCINE RESPONSE IN PATIENTS WITH IBD

J. Doherty¹, R. Stack², N. O'Morain², M. Tosetto³, R. Inzitari⁴, D.J. Daghfal⁵, P. Doran⁴, C. O'Morain⁶, G.A. Doherty⁷
¹St Vincent's Hospital, Dublin, Ireland, ²St. Vincent's University Hospital, Gastroenterology, Dublin, Ireland, ³St. Vincent's University Hospital, Dublin, Ireland, ⁴University College Dublin, Dublin, Ireland, ⁵Abbott Laboratories, Lake Forest, IL, United States, ⁶Trinity College Dublin - Faculty of Health Sciences, Trinity College Dublin; Dublin/IE, Faculty of Health Sciences, Dublin, Ireland, ⁷University College Dublin, Gastroenterology, Dublin, Ireland

Contact E-Mail Address: jaynedohertie@hotmail.com

Introduction: Patients with IBD receiving biologic agents, especially anti-TNF agents have reduced response rates to COVID-19 vaccination [1]. The reason for this is unclear and whether a patient's drug levels at the time of vaccination impacts vaccine response is unknown.

Aims & Methods: To determine if a patients drug level to biologic agents at the time of COVID-19 vaccination impacts antibody response.

IBD patients and healthy controls (HC) were recruited prospectively from five centres and quantitative antibody responses and drug levels assessed following COVID-19 vaccination.

Results: 270 IBD patients and 116 HCs were recruited. Median age was 39.5 years. 145 patients were treated with anti-TNF therapy. Median anti-spike protein (SP) immunoglobulin (Ig)G levels post-complete vaccination in our IBD cohort was significantly lower than HC (2,613 AU/mL versus 6,871 AU/mL, $p < 0.001$). IBD patients receiving anti-TNF therapy had significantly lower anti-SP IgG levels (2,445AU/mL) than those not receiving TNF-inhibitors (3868AU/mL) ($p < 0.001$). 99 patient's treated with infliximab, 24 with adalimumab and 12 with vedolizumab had drug levels at the time of vaccination.

	IBD Cohort (n=270)	Adequate drug levels	Low Drug Levels	p value
Median age (IQR)	39.5			
Male gender	160 (59.3%)			
Crohn's Disease	155 (55.5%)			
Anti-TNF therapy	145 (53.7%)			
Median Infliximab levels	8.9 µg/ml			
Median Adalimumab levels	12.2 µg/ml			
Median Vedolizumab levels	11.5 µg/ml			
Median Spike Protein Ab levels post vaccination (AU/mL)	2613	3018	2235	0.16

Table.

We found no significant correlation between SP IgG levels post-vaccination against COVID-19 and IFX levels (correlation co-efficient -0.17, $p = 0.09$), adalimumab levels (correlation co-efficient -0.28, $p = 0.24$), vedolizumab levels (correlation co-efficient -0.11, $p = 0.74$) or positive antibodies to inf-

liximab (correlation co-efficient -0.15, $p = 0.6$). Although a slight numerical difference, low drug levels to biologic agents did not impact subsequent SP IgG levels. Median SP IgG levels in patients with low drug levels were 3081AU/mL versus 2235AU/mL in those with adequate levels ($p = 0.16$).

Conclusion: Although IBD patients receiving anti-TNF agents have reduced antibody response to vaccination against COVID-19 a patients drug levels at the time of vaccination does not appear to impact antibody response for those receiving anti-TNF or anti-integrin agents. We are currently exploring other mechanisms of action for the reduced response seen in IBD patients.

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P0361

ANORECTAL DISORDERS AMONG IBD PATIENTS IN REMISSION, WITH FECAL INCONTINENCE AND TREATED WITH BIOLOGICS – PILOT STUDY FROM A TERTIARY REFERRAL CENTER

M. Jelakovic¹, K. Grubelic Ravic¹, A. Ladic¹, N. Turk¹, A. Barišić¹, D. Anzulović Grgic¹, S. Cukovic-Cavka^{1,2}, M. Brinar^{1,2}, Z. Krznaric^{1,2}

¹UHC Zagreb, Gastroenterology and Hepatology, Zagreb, Croatia,

²University of Zagreb, School of Medicine, Zagreb, Croatia

Contact E-Mail Address: mislavjelakovic@gmail.com

Introduction: Anorectal disorders and fecal incontinence (FI) are highly prevalent in inflammatory bowel disease (IBD) patients with reports in literature ranging from 20-80%. However, there is limited data on anorectal disorders among IBD patients with FI who are in remission and treated with biologics.

Aims & Methods: In this cross-sectional observational study we have included IBD patients, treated with biologics through our out-patient clinic. Demographics and medical data were collected from electronic medical charts, while patients were screened for FI using the St. Mark's incontinence score (SMIS). Significant FI was characterized as SMIS ≥ 6 . High resolution anorectal manometry (HRAM) following London protocol and classification was used for detection of anorectal disorders (AD). Descriptive and analytical statistical analysis was used.

Results: We included 100 patients (43 female/57 male) in clinical remission treated with biologics, median age 41 years (range 18-70), 41 patients had ulcerative colitis (UC) and 59 had Crohn's disease (CD). Median disease duration was 7 years (range 1-32). Significant FI was identified in 53 patients (53%) out of which 92.45% were in biochemical and 35.85% in endoscopic remission. FI was more prevalent among CD patients (64.1%) compared to UC (33.9%), but the difference did not reach statistical significance. There was no significant correlation between FI and gender, type or number of biologics or disease duration.

There was a significant positive correlation with age ($r=0.2457$, $p<0.05$), especially for patients older than 50 years of age who also had significantly higher average SMIS scores compared to younger patients (13.6 ± 5.4 vs 11.5 ± 2.9 ; $t=2.1$; $p<0.05$). HRAM was conducted in seven patients with significant FI (SMIS 10.6 ± 2.3), out of which 3 had dyssynergia with anal hypotension, 3 had isolated dyssynergia and one had isolated rectal hypersensitivity.

Conclusion: Based on our findings we can conclude that FI is highly prevalent among IBD patients in clinical, but also in endoscopic remission with increased risk with older age. Among these patients AD are common, especially anal hypotension and dyssynergia. Further studies are needed to better understand the prevalence and treatment options of AD in this population.

Disclosure: Nothing to disclose.

P0362

DECREASED MUSCLE MASS AND STRENGTH IN INFLAMMATORY BOWEL DISEASE PATIENTS

I. Ergenc¹, C. Ismail Basa², A. Üzümlü², Ş. Şahin³, H.T. Kani⁴, R. Aslan¹, A. Tufan Çiçin⁵, Ö. Kasımay Çakır⁶, O. Atug¹, Y. Özen Alahdab¹

¹Marmara University, Gastroenterology, Istanbul, Turkey, ²Marmara University School of Medicine, Istanbul, Turkey, ³Marmara University, Istanbul, Turkey, ⁴Marmara University, School of Medicine, Gastroenterology, Istanbul, Turkey, ⁵Marmara University School of Medicine, Geriatrics, Istanbul, Turkey, ⁶Marmara University, Physiology, Istanbul, Turkey

Contact E-Mail Address: ergencilkay@gmail.com

Introduction: Sarcopenia is a progressive and generalised reduction in skeletal muscle mass and strength and it is associated with increased adverse outcomes. Age-related sarcopenia is termed primary sarcopenia. Muscle loss secondary to inactivity, systemic diseases (inflammatory, neoplastic or organ failure) or malnutrition is termed secondary sarcopenia. In the course of Inflammatory Bowel Disease (IBD), the risk of sarcopenia is increased due to increased systemic inflammation and malabsorption.

Aims & Methods: This study aims to investigate the risk, prevalence, severity and associated factors of sarcopenia in IBD patients. Consecutive IBD patients meeting the ECCO (European Crohn's and Colitis Organisation) diagnosis criteria under the follow-up of the outpatient gastroenterology clinic of our tertiary center were invited. Patients with physical disability, pregnancy, osteoporosis and active malignancy were excluded. Healthy subjects without any immune or chronic inflammatory disorders were enrolled as a control group. The risk of sarcopenia was assessed via SARC-F (Strength, assistance with walking, rising from a chair, climbing stairs, and falls) questionnaire. Muscle strength was assessed by measurement of handgrip strength with the Jamar hydraulic hand dynamometer. Body composition including lean muscle mass was assessed with bioimpedance analysis (BIA). Physical performance was assessed by a 4-meter usual gait speed (UGS) test. European Working Group on Sarcopenia in Older People (EWGSOP) algorithm is applied to diagnose sarcopenia and determine the severity.

Results: A total of 121 patients with IBD, and 50 healthy controls were included. Patient and control groups had similar age and sex distribution. In IBD group 56 patients were diagnosed with Crohn's Disease (CD), and 64 patients were diagnosed with ulcerative colitis (UC). The Median SARC-F questionnaire score of IBD patients was higher than health controls (1 vs 0 $p=0.000$). IBD patients displayed a significant reduction in mean appendicular skeletal muscle mass (ASM: 25.5 ± 6.0 vs 28.2 ± 5.2 ; $p=0.006$), and appendicular skeletal muscle mass/height² (ASM/Height²: 9.4 ± 2.1 vs 9.9 ± 0.9 ; $p=0.033$). Gait Speed Test performance was significantly lower in IBD patients [1.06 (0.95-1.21) vs 3.51 (2.86-3.91) $p=0.000$]. According to EWGSOP cut-offs, 13 (10.7%) patients had clinical suspicion of sarcopenia, 19 (15.7%) had probable sarcopenia, and two (2%) had definite sarcopenia. Sarcopenia prevalence was not found to be correlated with disease activity, disease type, steroid use within the last year, and biological treatment.

	Crohn's Disease (n=45)	Ulcerative Colitis (n=56)	Healthy controls (n=50)
Appendicular skeletal muscle mass	26.0± 5.4	25.0± 6.5	28.1± 5.26
Muscle strength	31.8 ± 11.8	30.3 ± 11.6	33.1±10.8
Body mass index (Mean±SD)	25.1 ± 4.6	27.3 ± 4.7	24.9 ± 3.4
L1 ileal	20 (%37.0)	-	-
L2 colonic	2 (%3.7)	-	-
L3 ileocolonic	32 (%57.3)	-	-
E1 proctitis	-	3 (%5.6)	-
E2 left colitis	-	36 (%66.7)	-
E3 extensive colitis	-	18 (27.1)	-

Table 1: Disease localisation, muscle mass and strength of patients

Conclusion: Appendicular skeletal muscle mass, handgrip strength, and gait speed were significantly lower in patients with IBD compared to healthy controls. Although clinical suspicion of sarcopenia was detected in more than 15% of IBD patients, only two of them were eventually diagnosed with sarcopenia. For further assessment of the relation between appendicular skeletal muscle mass and the factors related to IBD, a larger sample size is required.

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Disclosure: Nothing to disclose.

P0363

COMPARATIVE FREQUENCY OF STRUCTURAL CHANGES IN THE PANCREAS IN CHRONIC PANCREATITIS AND INFLAMMATORY BOWEL DISEASES BY ENDOSONOGRAPHY

E. Lomakina¹, A. Budzinskay², E. Belousova¹

¹Moscow Regional Research and Clinical Institute (MONIKI), Department of Gastroenterology, Moscow, Russian Federation,

²Moscow Regional Research and Clinical Institute (MONIKI), Department of Endoscopy, Moscow, Russian Federation

Contact E-Mail Address: kate-den@bk.ru

Introduction: Some data confirm that risk of pancreatic damage in inflammatory bowel disease (IBD) is higher than in general population. The changes of pancreatic structure can be described by certain criteria in endosonographic examination (EUS).

Aims & Methods: To compare and assess the structural pancreatic alterations by Rosemont EUS criteria in chronic pancreatitis (CP) and IBD.

56 CP patients and 24 IBD patients without significant clinical pancreatic signs were examined (UC-15 persons and CD-9 persons). All patients underwent EUS with an assessment of parenchymatic and ductal structures of pancreas according to Rosemont EUS classification.

Results: In IBD patients hyperechoic bands in the pancreatic parenchyma, dilated lateral branches of main pancreatic duct (MPD), hyperechoic contour of pancreas, and areas of adjacent lobular structures were more often detected. In accordance with the Rosemont classification "definitive" CP was established in 25% of IBD cases, "suspected" CP in 25% of cases, "possible" CP in 33.3% and no EUS signs of CP were found in 16.7%. All changes were expressed in pancreatic head and body only. The normal EUS picture of the pancreatic tail was preserved in most of the examined patients.

In CP patients pseudocysts of pancreatic tail and body, MPD dilatation, intraductal calcifications and calcifications in lateral branches were observed. In total EUS-signs such as "definitive" CP were detected in 46% of CP patients, 26% - "suspected" CP, 28% - "possible" CP.

Disease	Definitive CP Abs (%)	Suspected CP Abs (%)	Possible CP Abs (%)	No SP symptoms Abs (%)
CP	25 (46%)	14 (26%)	15 (28%)	0
IBD	6 (25%)	6 (25%)	8 (33.3%)	4 (16.7%)

Table. Frequency of pancreatic EUS damages (Rosemont classification) in IBD and CP patients

Totally, different pancreatic damages of various severity was found in 83.3% of IBD patients. In this group Rosemont pancreatic parenchyma signs were detected in 59% of cases and ductal changes in 41% of cases. While in CP the parenchyma was affected in 36% of cases and the ducts in 64% of cases.

Conclusion: EUS data demonstrate different pancreatic structural changes in CP patients (mainly ducts) and in IBD patients (mainly parenchyma). Thus, EUS confirms the high frequency of predominantly parenchymal structural changes in IBD patients who didn't demonstrate clinical pancreatic manifestations. We believe that EUS can identify latent pancreatic alteration in IBD.

Disclosure: Nothing to disclose.

P0364

ADAPTATION OF QUESTIONNAIRES USED IN THE TRANS-IBD RANDOMISED CLINICAL TRIAL

D. Dohos^{1,2}, A. Erőss¹, N. Farkas², A. Váradi², P. Hegyi^{2,3,4}, P. Sarlós⁵

¹Heim Pál National Children Hospital, Budapest, Hungary,

²Institute for Translational Medicine, University of Pécs, Medical School, Department of Medicine, Pécs, Hungary, ³Semmelweis University, Centre for Translational Medicine, Budapest, Hungary,

⁴Semmelweis University, Division of Pancreatic Diseases, Heart and Vascular Center, Budapest, Hungary, ⁵University of Pécs, Medical School, First Department of Internal Medicine, Division of Gastroenterology, Pécs, Hungary

¹Heim Pál National Children Hospital, Budapest, Hungary, ²Institute for Translational Medicine, University of Pécs, Medical School, Department of Medicine, Pécs, Hungary, ³Semmelweis University, Centre for Translational Medicine, Budapest, Hungary, ⁴Semmelweis University, Division of Pancreatic Diseases, Heart and Vascular Center, Budapest, Hungary, ⁵University of Pécs, Medical School, First Department of Internal Medicine, Division of Gastroenterology, Pécs, Hungary

Contact E-Mail Address: dohos.dora@gmail.com

Introduction: The TRANS-IBD RCT is designed to provide strong evidence of the impact of transitional care on quality of life and patient management, increasing physician-patient satisfaction, and ongoing education. The primary outcome is measured with the IMPACT-III questionnaire, that is already adapted in Hungary.

Secondary outcomes include measurement of drug adherence (MARS), self-efficacy (IBDSES-A), transition readiness (TRAQ and STARx-A, STARx-P), patient satisfaction (CACHE), and not lost to follow-up, disease activity.

Aims & Methods: Our aim was to perform a cross-cultural adaptation of the questionnaires used in the TRANS-IBD RCT. As a step in the adaptation process based on international guidelines, an English-Hungarian and then a Hungarian-English translation was made, with the correction of linguistic and cultural dissonances. In the final step, ten randomly selected adolescents assessed the comprehensibility.

The Hungarian version of the questionnaires was tested among adolescents with inflammatory bowel disease in a pre-defined age group from nine Hungarian gastroenterology centres. R statistic program was used in the statistical analysis (R version 4.1.0, R Core Team, Vienna, Austria, 2021).

Internal consistency was determined by Cronbach's alpha coefficients. To assess if the model fits the original model, confirmatory factor analysis (CFA) was conducted, root Mean Square Error of Approximation (RMSEA), Comparative Fit Index (CFI), and Tucker-Lewis Index (TLI) were used.

Results: A total of 122 adolescents completed the questionnaires (47% male, mean age 17.12 [min-max: 14-19]). Linguistic translation and semantic evaluation of the questionnaires were not a problem during the adaptation process.

During the cultural evaluation, an item related to health insurance was modified in the TRAQ questionnaire and items related to appointment keeping were deleted in STARx questionnaires. During the comprehensibility interviews, some misunderstandings were identified and corrected accordingly. The final versions of the questionnaires were comprehensible to our population in terms of both content and language.

During the statistical analyses modification was made in IBD-SES due to an error in the CFA analyses. In the MARS, IBD-SES and TRAQ questionnaire, Cronbach's α scores were found good (0.864; 0.729; 0.865, respectively), while in the CACHE questionnaire the score was rated as excellent (0.906). The internal consistency was unacceptable in STARx-A, and questionable in STARx-P (0.415 and 0.693, respectively). The test-retest reliabilities were satisfactory in MARS, IBD-SES, CACHE and in the STARx questionnaires ($r=0.814$; $r=0.819$; $r=0.892$; $r=0.787$; $r=0.788$, respectively), while it remained under the acceptable level in TRAQ ($r=0.034$). Except in the STARx questionnaires, the confirmatory factor analyses show statistically acceptable results.

Conclusion: Adaptation of questionnaires is essential to conduct a clinical trial that provides high scientific evidence. The Hungarian MARS, IBD-SES, TRAQ, and CACHE questionnaires are feasible, reliable, reproducible, and comparable with the original validated versions.

The adaption of the STARx tools was not successfully accomplished, thus the future evaluations with the translated STARx surveys are not comparable with any international results.

Disclosure: Nothing to disclose.

P0365

INFLAMMATORY BOWEL DISEASE WITH CONCOMITANT ENDOMETRIOSIS: FREQUENCY AND CHARACTERIZATION IN A CASE-CONTROL PROSPECTIVE STUDY

B. Neri¹, C. Russo², M. Mossa¹, R. Mancone¹, F. Pizzi¹, A. Selntigia², E. Calabrese¹, C. Exacoustos², L. Biancone¹

¹Università degli Studi di Roma Tor Vergata, Medicina dei Sistemi, Unità di Gastroenterologia, Rome, Italy, ²Università degli Studi di Roma Tor Vergata, Scienze Chirurgiche, Unità di Ginecologia, Rome, Italy

Contact E-Mail Address: benedettoneri@gmail.com

Introduction: Inflammatory bowel disease (IBD) and endometriosis are immuno-mediated chronic inflammatory diseases observed in young women, sharing some of the clinical manifestations (i.e. abdominal pain). The possible association between endometriosis and IBD is undefined.

Aims & Methods: In a multidisciplinary approach, we aimed to assess, in prospective matched-control study, the frequency of endometriosis in IBD patients (pts) with compatible symptoms. Secondary end point was to assess differences in terms of characteristics of endometriosis and -related symptoms in pts with vs without IBD.

All female IBD pts in childbearing age referring symptoms compatible with endometriosis were enrolled and referred to dedicated gynecologists for transvaginal ultrasonography. Each IBD pt with endometriosis (Case) was retrospectively matched for age (± 5 yrs) and body mass index (BMI) (± 1) with 3 Controls with endometriosis but no-IBD.

Inclusion criteria for Cases were:

1. Female gender;
2. Age ≥ 18 and ≤ 55 years;
3. Well-defined diagnosis of IBD;
4. Regular follow-up;
5. Symptoms compatible with endometriosis;
6. Consent.

Inclusion criteria for Controls were:

1. Female gender;
2. Age ≥ 18 and ≤ 55 years;
3. Well defined diagnosis of endometriosis.

Exclusion criteria for Cases and Controls were:

- 1) Pregnancy;
- 2) Menopause.

Characteristics of IBD, endometriosis and adenomyosis were classified according to standard criteria. The study was approved by the Ethic Committee. Data were expressed as median [range]. The Student-t Test and χ^2 test were used for comparisons.

Results: Endometriosis was diagnosed in 19 (57.9%) out of 28 IBD pts with compatible symptoms. Overall, 76 pts with endometriosis were assessed (age, yrs: 38 [24-53]; BMI 21.5 [17.3-41.6]), including 19 pts with IBD and 57 with no-IBD. These 19 IBD pts included 10 (52.6%) Crohn's Disease (CD), 9 (47.4%) Ulcerative Colitis (UC) (IBD duration: 14[1-35] yrs).

CD extent included: ileum in 3 (30%), colon in 1 (10%), ileum-colon in 6 (60%) pts. CD behavior was non-stricturing non-penetrating in 5 (50%), stricturing in 3 (30%), penetrating in 2 (20%) pts, with perianal disease in 3 (30%). UC extent included proctitis in 2 (22.2%), left-sided in 3 (33.3%), pancolitis in 4 (44.4%)pts.

Cases and Controls were comparable in terms of age (38 [25-53] vs 38 [24-48] yrs; $p=0.42$), BMI (21.6 [17.3-41.6] vs 21.2 [18.3-41.4]; $p=0.58$), frequency of dysmenorrhea (16 [84.2%] vs 45 [78.9%]; $p=0.86$), dyschezia (7 [36.8%] vs 12 [21.1%]; $p=0.28$), dysuria (3 [15.8%] vs 3 [5.3%]; $p=0.32$). Dyspareunia was significantly more frequent in Cases vs Controls (14 [73.7%] vs 26 [45.6%], $p=0.03$).

At transvaginal ultrasonography, deep infiltrating endometriosis was significantly more frequent in Cases vs Controls, being observed in all the 19 [100%] IBD pts and in 44 [77.2%] non-IBD controls ($p=0.02$). The high frequency of rectal endometriosis observed in IBD pts (7 [36.8%]), did not differ from Controls (12 [24.6%]; $p=0.1$). Adenomyosis was observed in 13 (68.4%) Cases and in 25 (43.8%) Controls ($p=0.06$).

Conclusion: In the tested IBD population, half of IBD pts with compatible symptoms showed endometriosis with a high rate of rectal endometriosis. A higher frequency of dyspareunia and deep infiltrating endometriosis (observed in all Cases) was observed in IBD vs non-IBD controls. Endometriosis should be searched in IBD pts with compatible symptoms, often mimicking IBD activity.

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Disclosure: Nothing to disclose.

P0366

PREDICTIVE FACTORS OF MALNUTRITION IN PATIENTS WITH INFLAMMATORY BOWEL DISEASES

O. Chatti¹, W. Dahmani¹, N. Elleuch¹, W. Ben Ameer¹, A. Hammami¹, A. Ben Slama¹, A. Braham Ep Krifa¹, S. Ajmi¹, M. Ksaa¹, H. Jaziri¹, A. Jmaa¹

¹Sahloul University Hospital, Gastroenterology, Sousse, Tunisia

Contact E-Mail Address: oumaimachatti93@gmail.com

Introduction: Malnutrition is a very common and underappreciated complication in patients with inflammatory bowel diseases (IBD), which represent a high-risk population for malnutrition, even in patients in remission. However, little statistical information is available on the predictors of malnutrition.

Aims & Methods: The aim of this study is to assess nutritional status in a cohort of IBD patients and to determine predictive factors of malnutrition. This is a cross-sectional study conducted in the hepato-gastroenterology department of the Sahloul University Hospital over a period of one year. This study included 105 patients followed for IBD diagnosed on clinical, endoscopic and/or histological criteria at least 6 months before the start date of the study. We evaluated associations between demographic and clinical characteristics and risk of malnutrition assessed by the Malnutrition Universal Screening Tool (MUST-score). This tool includes body mass index (BMI), recent weight loss, and whether the patient will have no nutritional intake for more than 5 days.

Results: Our study included 105 patients, of whom 77 patients (73.3%) had Crohn's disease and 28 patients had ulcerative colitis (26.7%). The mean age at data collection was 38.6 ± 15.8 years. Our population was divided into 48 males (45.7%) and 57 females (54.3%), 52 non-smokers, 23 smokers and 30 ex-smokers. Only 15 patients (14.3%) were in an acute phase of their disease, including 10 patients with anorexia in the last 5 days. Thirty seven patients (35.2%) were overweight, 47 patients (44.8%) had a normal BMI and 21 patients (20%) were considered underweight. Using the MUST score, 43 (41%) patients were classified as low risk of malnutrition and 62 (59%) were classified as medium or high risk. In univariate analysis: Crohn's disease, disease activity, and use of immunomodulators and steroids were significantly associated with an increased risk of malnutrition (respectively $p=0.001$; $p=0.006$; $p=0.001$; $p=0.021$).

Conclusion: The MUST score is an easy tool to assess the risk of malnutrition in IBD patients.

Crohn's disease, disease activity, and use of immunomodulators and steroids are significant predictors of under nutrition risk. Therefore, assessment and screening for malnutrition should be routinely included in IBD clinical practice.

Disclosure: Nothing to disclose.

P0367

PARAMETERS AFFECTING FISTULA TREATMENT RESPONSE IN PERIANAL FISTULIZING CROHN'S DISEASE UNDER BIOLOGICAL THERAPY: A MACHINE LEARNING MODEL STUDY

H. Salva¹, H.T. Kani², E. Isik Polat³, I. Ergenç², O.F. Simitcioglu⁴, H. Coban¹, G. Polat³, Y. Özen Alahdab², C. Cimsit⁴, O. Atug²

¹Marmara University, School Of Medicine, Department of Internal Medicine, Internal Medicine, Istanbul, Turkey, ²Marmara University, School Of Medicine, Department of Gastroenterology, Gastroenterology, Istanbul, Turkey, ³Middle East Technical University, Graduate School of Informatics, Ankara, Turkey, ⁴Marmara University, School Of Medicine, Department of Radiology, Istanbul, Turkey

Contact E-Mail Address: hazalsalva@gmail.com

Introduction: Monitoring the disease activity with a non-invasive and accurate scale was still challenging in Perianal Fistulizing Crohn's Disease (PFCD). Machine learning-based prediction models have been increasing in number for evaluation of disease activity in inflammatory bowel disease (IBD). Magnetic resonance imaging (MRI) is still the gold standard technique in the diagnosis and assessment the disease activity in PFCD.

Aims & Methods: This study aims to describe the clinical characteristics and radiological scores of PFCD patients and generate a data-driven machine learning predictive model for radiological healing.

Primary endpoints for response were MAGNIFI-CD ≤ 6 and a decrease in Van Assche Index (VAI) radiologic scores after Anti-TNF treatment.

Secondary endpoints were the need for intraabdominal surgery and clinical fistula response. The PFCD patients who were followed-up in our IBD-specific out-patient clinic with a perianal MRI before and after the Anti-TNF treatment were included in the study. MAGNIFI-CD Score and VAI were calculated before and after the treatment.

Demographic and clinical data including smoking habits, Montreal Classification, Parks Fistula Classification, seton history, proctitis/rectitis history, stenosis history, history of abscess, Harvey-Bradshaw Index (HBI) and Perianal Disease Activity Index (PDAI) clinical were collected. A predictive machine learning model was generated by using ElasticNet Regression which utilizes both Lasso (L1 norm) and Ridge (L2 norm) regularizations.

Results: A total of 47 PFCD patients were enrolled in the study. The median age was 40 years (19 – 74) and 20 (42.6%) were female. The median time between the first and last perianal MRI was 19 months (4 – 98).

Seventeen patients had simple fistulas and 26 patients had complex fistulas. According to the Park classification, 28 patients had intersphincteric, 7 patients had transsphincteric, 11 patients had intersphincteric and transsphincteric fistulas. Thirty-one patients' VAI scores was decreased following the treatment and 16 patients' scores stayed the same or increased. According to the MAGNIFI CD score, 29 (61.7%) of patients were in remission following the treatment. Nine patients had intra-abdominal surgery during follow-up. The need for intraabdominal surgery was higher in the group with a history of an abscess ($p=0.008$). The clinical remission rate according to the HBI was significantly higher in patients with clinical fistula response ($p=0.044$).

According to our novel machine learning model, MAGNIFI-CD score prior to the treatment, rectal involvement and hyperintensity values of VAI, age at diagnosis, Parks fistula type, seton history, post-fistula antibiotic treatment and hypoalbuminemia were significant in predicting radiological progression and intraabdominal surgery requirement.

The mean squared error obtained by the model in the training data was 3.97, the variance in the score predicted by the model was 66%. The mean squared error obtained by the model in the test data is 8.23, the variance in the target variable can be explained 54%.

Conclusion: Our novel machine learning model performed promising prediction of fistula healing in PFCD by using radiological variables including pre-treatment total MAGNIFI-CD score, rectal involvement and hyperintensity values of pre-treatment VAI. Clinical scores and these parameters might be used together to predict prognosis during follow-up.

Disclosure: Nothing to disclose.

P0368

SARS-COV-2 INFECTION DOES NOT WORSEN THE CLINICAL COURSE OF INFLAMMATORY BOWEL DISEASE: A 1-YEAR PROSPECTIVE CASE-CONTROL STUDY

B. Neri¹, G. D'Agostini¹, S. Salvatori¹, M. Mossa¹, F. Bettin¹, L. Montesano¹, I. Marafini¹, E. Lolli¹, E. Calabrese¹, G. Monteleone¹, L. Biancone¹

¹Università degli studi di Roma Tor Vergata, Medicina dei sistemi, Unità di Gastroenterologia, Rome, Italy

Contact E-Mail Address: benedettoneri@gmail.com

Introduction: Whether SARS-CoV-2 infection may worsen the long-term outcome of Inflammatory bowel disease (IBD) is currently undefined.

Aims & Methods: In a prospective single center, case-control study, we aimed to investigate the possible role of SARS-CoV-2 infection as a risk factor for a worse clinical outcome of IBD at 1-year (yr).

From March to April 2021, all IBD pts with recent (<2 months) SARS-CoV-2 infection (Cases) were enrolled. Each Case was matched with 4 IBD Controls with no history of SARS-CoV-2 infection (Controls). All pts were followed-up for 1 yr. Inclusion criteria for Cases were: 1) age ≥18-≤85 yrs; 2) well-defined diagnosis of IBD; 3) SARS-CoV-2 infection <2 months; 4) written consent. Exclusion criteria was pregnancy.

Inclusion criteria for Controls were:

1. Age ≥18-≤85 yrs;
2. Well-defined diagnosis of IBD;
3. Written consent.

Exclusion criteria were:

1. Pregnancy;
2. History of SARS-CoV-2 infection.

IBD characteristics and activity were assessed at baseline and at 1 yr, according to standard criteria. Data were expressed as median [range]. The Student-t Test and χ^2 test were used for comparisons and univariate logistic regression model for assessing risk factors for IBD relapse (OR [95%CI]).

Results: The analysis included 122 IBD pts: 29 (23.7%) Cases and 93 (76.3%) Controls (150 enrolled IBD pts: 22 did not met the inclusion criteria, 6 lost at follow-up). Clinical characteristics were comparable between the 2 groups: age (43 [30-69] vs 52 [20-82] yrs; $p=0.08$), gender (F) (16 [55%] vs 62 [67%]; $p=0.36$), IBD duration (14 [2-38] vs 14 [1-45]; $p=0.99$), smoker status (5 [17.2] vs 16 [17.2]; $p=0.78$), IBD type (UC 12 [41%] vs 47 [51%]; $p=0.51$), UC extent (proctitis 5 [17%] vs 12 [13%]; $p=0.45$), left-sided (2 [7%] vs 15 [16%]; $p=0.49$), pancolitis 5 [17%] vs 15 [16%]; $p=0.76$), CD site (ileum 7 [24%] vs 25 [27%]; $p=0.51$); colon 2 [7%] vs 5 [5%]; $p=0.72$), ileum-colon 6 [21%] vs 13 [14%]; $p=0.81$), upper GI (2 [7%] vs 2 [2%]; $p=0.62$), CD behavior (non-stricturing non-penetrating 3 [10%] vs 11 [12%]; $p=0.84$); stricturing (10 [34%] vs 19 [20%]; $p=0.34$); penetrating (4 [14%] vs 13 [14%]; $p=0.95$); ongoing thiopurines in 11 (38%) vs 29 (31%); $p=0.65$), ongoing biologics in 11 (38%) vs 36 (39%); $p=0.88$) pts.

At baseline, IBD was active in 9 (31%) Cases vs 18 (19%) Controls ($p=0.28$). During 1-yr, the frequency of clinical relapse was comparable between Cases vs Controls (7 [24%] vs 16 [17%]; $p=0.57$), also when subgrouping symptoms (diarrhea, rectal bleeding, abdominal pain, fever; $p=0.57$). The same finding was observed for steroids use ($p=0.51$), biologics

withdrawal ($p=0.96$), IBD-related hospitalizations ($p=0.96$). At univariate analysis, risk factors for clinically active IBD during 1-yr included activity at baseline (3.7 [1.3-9.8]; $p=0.008$) and female gender (4.5 [1.7-11.8]; $p=0.02$), but not SARS-CoV-2 infection (1.6 [0.59-4.46]; $p=0.34$). Ongoing biologic therapy was a protective factor against IBD activity during 1-yr (0.28 [0.09-0.9]; $p=0.03$).

Conclusion: In a prospective case-control study, SARS-CoV-2 infection did not increase the risk of IBD relapse within 1-yr vs IBD control pts with no history of infection.

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P0369

SCREENING FOR SARCOPENIA IN CROHN'S DISEASE, SHOULD IT BE A MUST?

M. Mtir¹, M. Ayari¹, A. Chehaider¹, W. Khemiri¹, Y. Ben Hamadi¹, I. Abdelaali¹, T. Jomni¹, M.H. Douggui¹

¹Internal Security Forces Hospital of Tunis, Gastroenterology Department, Tunis, Tunisia

Contact E-Mail Address: mtirmaha@gmail.com

Introduction: Despite considerable therapeutic advances in the management of Crohn's disease (CD) over the past two decades, its course and complications remain unpredictable. Indeed, CD is associated with significant nutritional deficiencies and metabolic disturbances, including sarcopenia, defined as a loss of muscle strength and quantity, which represents a major health burden by reducing substantially the quality of life.

Aims & Methods: The aim of this study was to assess the prevalence and to determine the associated factors of sarcopenia during CD.

We conducted a retrospective single-center study, including patients followed for CD over a 7-year period [2014 - 2021]. Clinico-biological data, disease severity, and long-term outcomes (surgery and disease course) were collected.

Measurement of the psoas muscle area has been applied to estimate lean muscle mass as a surrogate marker of sarcopenia, these measurements were performed on computed tomography (CT) by calculating the total psoas area at the third lumbar vertebra level. Then, the total psoas area index (TPAI) was calculated using the equation: $TPAI (mm^2/m^2) = (Left Psoas Area (mm^2) + Right Psoas Area (mm^2)) / Height (m^2)$. Sarcopenia was defined by a TPAI less than 385 mm^2/m^2 for female patients and 545 mm^2/m^2 for male patients.

Results: In total, 50 patients were enrolled with a mean age of 44.3 years [20-82], a median disease duration of 106 months and a sex ratio M/F of 3.16. Sarcopenia was observed in 14 patients (28%) with a mean TPAI of 612 mm^2/m^2 [1763 - 206].

Compared with patients without sarcopenia, sarcopenic patients are more likely to have a severe malnutrition ($p=0.026$), they had a significantly lower BMI ($p=0.039$); lower ferritin levels ($p=0.026$); lower hemoglobin levels ($p=0.036$); hyponatremia ($p=0.028$) and a lower creatinine level ($p<0.0001$).

Sarcopenia was independent of disease location and extent. Regarding CD phenotype, we found that a structuring behaviour in the CD was significantly associated with the sarcopenia ($p=0.046$).

Moderate to severe CD activity, as assessed by the Crohn's Disease Activity Index (CDAI) and the Harvey Bradshaw Index (HBI), was associated with sarcopenia with a p -value of 0.03 and 0.05 respectively for both indices. When analysing, the AUROC of CDAI and HBI in predicting the presence of sarcopenia in CD was 0.634 and 0.676 respectively, with a cutoff of 183 for CDAI and 5 for HBI.

During the follow up, more patients with sarcopenia required biotherapy ($p=0.01$). Patients who underwent surgery was not in a higher risk of sarcopenia, however sarcopenia was identified as a predictive factor of the occurrence of postoperative complication with p -value = 0.05.

Conclusion: In our study, almost third of CD patients were sarcopenic. Our results suggest that sarcopenia was associated with the activity of the disease, structuring phenotype, increasing biological treatment need and major risk of postoperative complications. Systematic screening and treatment in this context should be recommended to improve the course of the disease. New potential therapeutic approach that can regulate the gut-muscle axis in inflammatory bowel disease should be investigated.

Disclosure: Nothing to disclose

P0370

SUPERB MICRO-VASCULAR IMAGING FOR PREDICTING THE ACTIVITY OF TERMINAL ILEUM LESIONS IN PATIENTS WITH CROHN'S DISEASE

H. Shimazaki¹, M. Nasuno¹, T. Hamada¹, H. Nagasawa¹, K. Sugiyama^{2,1}, M. Miyakawa¹, H. Tanaka¹

¹Sapporo IBD Clinic, Sapporo, Japan, ²Sapporo Central Hospital, Department of Gastroenterology, Sapporo, Japan

Contact E-Mail Address: shimazaki@sapicl.com

Introduction: Assessing blood flow in the bowel wall using the coloured Doppler technique for gastrointestinal ultrasonography is useful for evaluating intestinal activity in patients with Crohn's disease (CD). However, the major limitation of this technique is its sensitivity to low blood flow velocities and small vessels. Superb micro-vascular imaging (SMI) is a technique for assessing slow and micro-vascular blood flow. Currently, very few studies have evaluated intestinal activity in patients with CD using the SMI techniques.

Aims & Methods: This study aimed to compare ultrasound images obtained by SMI with endoscopic findings obtained by endoscopy, specifically in the terminal ileum of patients with CD. We retrospectively collected the data of patients with CD who underwent ultrasonography between September 2020 and December 2021 at our clinic and whose terminal ileum could be evaluated through ileocolonoscopy within 3 months before or after ultrasonography. Patients with a history of small bowel resection were excluded from this study.

Lesions in the terminal ileum were classified into four groups according to endoscopic findings (1: no ulcers, 2: aphthous ulcers [<5 mm], 3: small ulcers [5–20 mm] and 4: large ulcers [>20 mm]). Ultrasonography was performed using Aplio a550 (Canon Medical Systems Corp., Tochigi, Japan). Scanning of the small bowel was initiated by defining the terminal ileum laying ventrally on the psoas muscle and then following its course in the proximal direction to the maximum extent possible.

Blood flow signals in the intestinal wall of the terminal ileum were evaluated using SMI. The scan of SMI was initially performed using a 5-MHz convex probe, following which a more detailed scan of the affected area was performed using a 9.2-MHz linear probe. The parameter settings of SMI were as follows: colour velocity of 1.2 cm/s and colour frequency of 4 MHz. We used a simple unique score, categorised into four grades (grade 0:

no blood flow signals, grade 1: short signals, grade 2: longer signals and grade 3: longer signals reaching the mesentery), to evaluate SMI signals. Endoscopic findings and SMI grades were compared to investigate SMI signals predicting lesions in the terminal ileum.

Results: This study included 140 patients (median age, 28.5 years; median disease duration, 5.6 years), of which 32 were women. At the time of CD diagnosis, 10 patients had ileitis, 103 had ileocolitis and 27 had colitis. The median Harvey–Bradshaw index value was 2.0. Endoscopic findings of no ulcers, aphthous ulcers, small ulcers and large ulcers were revealed in 66, 40, 21 and 13 patients, respectively. SMI grades 0, 1, 2 and 3 were observed in 104, 19, 6 and 11 patients, respectively. Intestinal lesions on endoscopic findings, including aphthous, small or large ulcers, were observed in 42%, 74%, 83% and 100% of the patients with SMI grades 0, 1, 2 and 3, respectively.

Furthermore, small or large ulcers were observed in 10%, 58%, 67% and 82% of the patients with SMI grades 0, 1, 2 and 3, respectively. Small or large ulcers were observed in 67% of the patients with SMI grade 1 or above. The sensitivity and specificity of SMI grade 1 or above for predicting small or large ulcers were 70.6% and 88.7%, respectively.

Conclusion: The activity of lesions in the terminal ileum in patients with CD increased as the SMI grade increased. All patients with SMI grade 3 had some intestinal lesions. Only 10% of the patients with SMI grade 0 had small or large ulcers. This study showed that SMI grade 1 or above indicated small or large ulcers with 88.7% specificity.

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P0371

RADIOMICS COULD PREDICT SURGERY AT 10 YEARS IN CROHN'S DISEASE

L. Laterza¹, L. Boldrini², H.E. Tran², C. Votta², L. Larosa², L.M. Minordi², R. Maresca¹, D. Pugliese¹, M.A. Zocco¹, M.E. Ainora¹, L.R. Lopetuso¹, A. Papa¹, A. Armuzzi³, A. Gasbarrini^{1,4}, F. Scaldaferri^{1,4}

¹Fondazione Policlinico Universitario "A. Gemelli" IRCCS, Università Cattolica del Sacro Cuore, IBD Unit- UOS Malattie Infiammatorie Croniche Intestinali, CEMAD, Digestive Diseases Center, Rome, Italy, ²Fondazione Policlinico Universitario "A. Gemelli" IRCCS, Department of Diagnostic Imaging, Oncological Radiotherapy, and Hematology, Rome, Italy, ³Humanitas Clinical and Research Center - IRCCS, IBD Center, Rozzano, Italy, ⁴Università Cattolica del Sacro Cuore, Dipartimento di Medicina e Chirurgia Traslationale, Rome, Italy

Contact E-Mail Address: laterza.lucrezia@gmail.com

Introduction: Predicting clinical outcomes represents a major challenge in Crohn's disease (CD). Radiomics provides a method to extract quantitative features from medical images and may successfully predict clinical course, however its application in CD is still scarce.

Aims & Methods: The aim of this study is to evaluate the use of radiomics to predict the need for surgery at 10 years in a cohort of CD patients.

We retrospectively selected a cohort of CD patients with available CT scan enterographies and a 10-year follow up. Typical lesions of CD were segmented in each CT scan. An open-source R library (Moddicom) was used to extract radiomic features from each segmented lesion.

A logistic regression model based on selected radiomic features was developed to predict 10-year surgery. The model was evaluated by computing the area under the curve (AUC) of the receiver operating characteristic curve, sensitivity, specificity, positive and negative predictive values (PPV, NPV).

Results: We enrolled 30 patients, with 44 CT scans and 93 lesions. We extracted 217 radiomic features from each lesion.

The developed model was based on two radiomic features (intensity variance and normalized grey-level non-uniformity from the grey-level run length matrix) and presented an AUC (95% CI) of 0.83 (0.73-0.91) in predicting 10-year surgery. Sensitivity, specificity, PPV and NPV of the radiomic model were equal to 0.72, 0.90, 0.79, 0.86, respectively.

Conclusion: Radiomics could be a helpful tool to identify patients with high risk for surgery and needing a stricter monitoring or therapy intensification.

Disclosure: Nothing to disclose.

P0372

MAGNETIC RESONANCE TEXTURE ANALYSIS IS SUPERIOR TO MAGNETIZATION TRANSFER IMAGING FOR LONGITUDINAL ASSESSMENT OF FIBROSIS IN EXPERIMENTAL COLITIS

S. Bos¹, I. de Kock¹, L. Delrue², S. van Welden¹, P. Bunyard³, P. Hindryckx², M. De Vos¹, G. Villeirs², D. Laukens¹

¹Ghent University, Ghent, Belgium, ²Ghent University Hospital, Ghent, Belgium, ³Redx Pharma PLC, Macclesfield, United Kingdom

Contact E-Mail Address: simon.bos@ugent.be

Introduction: Differentiation between inflammatory and fibrotic bowel strictures remains a holy grail in Crohn's disease (CD) management, primarily because of the therapeutic implications. Stricture characterisation in CD patients is further hampered by the co-occurrence of inflammation and fibrosis in various degrees.

Currently, there are no validated imaging tools to differentiate fibrotic from inflammatory or mixed strictures, but several new techniques, such as magnetization transfer magnetic resonance imaging (MT-MRI) and magnetic resonance texture analysis (MR-TA), seem promising.

Aims & Methods: To investigate these possible new imaging techniques for stricture management, we assessed the performance of magnetization transfer (MT) magnetic resonance imaging (MRI) and texture analysis (TA) of T2-weighted images. Temporal MT and T2-weighted magnetic resonance (MR) images were correlated with histology as the gold standard in a model of gut fibrosis resulting from chronic colitis induced in C57BL/6J mice by cyclic administration of dextran sulfate sodium.

The performance of MT-MRI and TA was validated in the same model with an antifibrotic therapy administered to one group of mice. To check the translatability of the results, MR enterography images of patients with CD who underwent bowel surgery were retrospectively analyzed and matched with histopathology.

Results: The MT-MRI and TA entropy correlated with fibrosis on the histopathology ($r=.85$ and $.81$, respectively). However, TA entropy was superior to the MT-MRI for quantifying the progression of fibrosis (linear regression $R^2=.93$) because the MT-MRI signal was severely biased due to coexisting inflammation. The effect of the successful antifibrotic therapy was efficiently captured using TA entropy. Finally, TA entropy was a valid parameter to detect and grade intestinal fibrosis in axial T2-weighted MR images of patients with CD.

Conclusion: Based on the applied model of relapsing-remitting colitis, which allowed the study of coexisting inflammation and progressive fibrosis, we demonstrated that although MT-MRI and TA entropy are highly promising surrogate markers of intestinal fibrosis, TA entropy performed better in monitoring and quantifying fibrotic lesions in the presence of concomitant inflammation.

Disclosure: P. Bunyard is an employee of Redx Pharma Plc.

P0373

USEFULNESS AND LIMITATIONS OF COMPUTER-AIDED DETECTION (CADE) SYSTEM IN SURVEILLANCE COLONOSCOPY IN PATIENTS WITH ULCERATIVE COLITIS

Y. Maeda¹, S.-e. Kudo¹, N. Ogata¹, T. Kuroki¹, Y. Ogawa¹, S. Matsudaira¹, H. Nakamura¹, Y. Mori², T. Kudo¹, T. Hisayuki¹, T. Hayashi¹, K. Wakamura¹, H. Miyachi¹, T. Baba¹, F. Ishida¹, K. Ohtsuka³, M. Misawa¹

¹Showa University Northern Yokohama Hospital, Digestive Disease Center, Kanagawa Yokohamashi, Japan, ²University of Oslo / Showa University, Clinical Effectiveness Research Group / Digestive Disease Center, Oslo, Norway, ³Tokyo Medical and Dental University Hospital, Department of Endoscopy,, Tokyo, Japan

Contact E-Mail Address: yasuharumaeda610@hotmail.com

Introduction: With the recent progress in endoscopic interventions and the establishment of the Surveillance for Colorectal Endoscopic Neoplasia Detection and Management in Inflammatory Bowel Disease Patients: International Consensus Recommendations (SCENIC) consensus, endoscopic resection is gaining acceptance as a treatment option in patients with ulcerative colitis (UC). Therefore, the importance of detection of neoplasia in the early stage is increasing. However, lesion detection in patients with UC is difficult because of the effect of inflammation, it may be characterized by a distinct "bottom-up" growth pattern, and even expert endoscopists have relatively little experience with such cases.

Nowadays, some computer-aided detection (CADE) Systems during colonoscopy have been introduced into clinical practice for non-UC patients. The systems have been reported to raise the adenoma detection ratio.

Aims & Methods: The aim of this study is to assess the usefulness and limitations of the computer-aided detection (CADE) system in surveillance colonoscopy in patients with UC. This single-center retrospective pilot study included 180 consecutive patients with UC who underwent colonoscopy between April 20, 2021.

All colonoscopies were performed using high-definition endoscopes. In this study, the artificial intelligence (AI) algorithm of CADE has used the modified algorithm of EndoBRAIN-EYE (Cybernet system corp.), which is already on the market for targeting non-UC patients: all training images of (AI) algorithm were obtained from non-UC patients.

The overall white light endoscopy (WLE) images of eligible patients were collected and analyzed for the presence of neoplasia by the CADE system. The golden standard of the presence of neoplasia was defined as the lesion with pathologists diagnosed as neoplasia.

Results: The 180 cases analyzed included 33 lesions (4 UC-associated neoplasia, 22 sporadic neoplasia, and 7 sessile serrated lesions), lesions indicated for treatment that was detected by the endoscopist and confirmed by pathology. The macroscopic types based on the SENIC consensus were sessile in 8 cases, Superficial elevated in 22 cases, flat in 1 case, and depressed in 2 cases.

A total of 5078 images were analyzed (with lesions: 105 images, without lesions: 4973 images). The diagnostic accuracies of CADE were sensitivity 87.6%, specificity 84.8%, accuracy 84.8%, positive predictive value 10.8%, and negative predictive value 99.7%. The positive predictive value was significantly low because CADE specifically recognized mucosa with high inflammatory activity and inflammatory polyps as target lesions.

Conclusion: The CADE system specifically designed for surveillance colonoscopy of patients with UC needs to be developed.

Disclosure: Shin-ei Kudo, Yuichi Mori, and Masashi Misawa received consultant and speaker fees from Olympus Corp.

P0374

FACTORS ASSOCIATED WITH CUMULATIVE BOWEL DAMAGE USING LEMANN INDEX IN CROHN'S DISEASE – A TERTIARY CENTER EXPERIENCE

V. Domislovic¹, K. Hrabric Sonje², M. Brinar^{1,3}, S. Cukovic-Cavka^{3,1}, N. Turk¹, D. Anzulović Grgić¹, M. Jelaković¹, M. Prutki^{2,3}, Z. Krznaric^{3,1}

¹University Hospital Centre Zagreb, Department of Gastroenterology and Hepatology, Zagreb, Croatia, ²University Hospital Centre Zagreb, Clinical Department of Diagnostic and Interventional Radiology, Zagreb, Croatia, ³University of Zagreb, School of Medicine, Zagreb, Croatia

Contact E-Mail Address: viktor.domislovic@gmail.com

Introduction: The Lémann index (LI) is a unique tool that measures cumulative bowel damage in Crohn's disease (CD) and is composed of surgical procedures and severity and extent of bowel lesions according to endoscopy and MR enterography. (1) Aim of this study is to investigate factors associated with cumulative bowel damage using Lemann index in adult population with CD.

Aims & Methods: Aim of this study is to investigate factors associated with cumulative bowel damage using Lemann index in adult population with CD.

In this cross-sectional study on 178 CD patients LI was calculated evaluating 20 small bowel, 7 large bowel and 3 upper GI segments. For each segment bowel resections, inflammatory, stricturing or penetrating lesions were taken into account. Global MaRIA (gMaRIA) index was calculated using following parameters on 6 bowel segments on MR enterography: bowel wall thickness, ulcers, edema and relative contrast enhancement.

Longstanding disease was defined as ≥10 year disease duration. Disease activity was defined as CRP>5 or HBI≥5. Extent and disease behaviour was assessed using Montreal classification.

Results: This study included 320 CD patients [age 35 (25-47), 55.3% males, disease duration 7 (1-14) years, BMI 21.7 (17.6-24.9) kg/m²]. There were 103 (40%) surgically naïve and 112 (44.6%) patients with longstanding disease. Multivariate analysis on total population, adjusted for age, gender, BMI, smoking status, CRP, disease behaviour and extension, biological therapy, gMaRIA score, and HBI revealed independent predictors of elevated LI which were BMI ($\beta=-0.257$, $p<0.018$), disease duration ($\beta=0.113$, $p=0.045$) and prior surgery ($\beta=5.370$, $p<0.001$). Due to expected influence of prior surgery on cumulative bowel damage, separate analysis was performed on surgically naïve patients.

Multivariate analysis adjusted for aforementioned variables revealed following independent positive predictors; current smoking ($\beta=1.135$, $p=0.009$), perianal disease ($\beta=1.436$, $p=0.016$) and gMaRIA score ($\beta=0.087$, $p<0.001$).

Conclusion: Cumulative bowel damage is one of major concerns for both patients and clinicians. Using validated Lémann index and adjusting for multiple important confounding factors, we have revealed longer disease duration, prior surgery and lower BMI as important risk factors for cumulative bowel damage. Since surgical procedures contribute significantly to the LI, it is important to determine risk factors of cumulative bowel damage in surgically naïve patients, which were smoking status, perianal disease and higher gMaRIA score, i.e. radiological disease activity. This risk factors in CD could stratify patients at high risk for complicated course of disease.

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P0375

MAGNIFI-CD INDEX IS A STRONG PROGNOSTIC FACTOR IN PATIENTS WITH PERIANAL FISTULIZING CROHN'S DISEASE

N. Richard^{1,2}, A. Derinck³, V. Bridoux⁴, C. Savoye-Collet^{3,5}, G. Savoye^{2,1}

¹Rouen University Hospital, Department of Gastroenterology, Rouen, France, ²University of Rouen, INSERM UMR 1073, Rouen, France, ³Rouen University Hospital, Department of Radiology, Rouen, France, ⁴Rouen University Hospital, Department of Digestive Surgery, Rouen, France, ⁵University of Rouen, QUANTIF-LITIS EA 4108, Rouen, France

Contact E-Mail Address: nicolas.richard26@gmail.com

Introduction: Clinical and magnetic resonance imaging (MRI) features associated with perianal fistula closure in Crohn's disease (CD) are controversial and recently degree of fibrosis along with disease activity (MAGNIFI-CD index) have been suggested to be predictive of long-term clinical outcome.

Aims & Methods: This study aimed to analyze clinical and MRI features associated with positive long-term outcome. Positive long-term outcome was defined as the absence of surgery or hospitalization requested by perianal fistulizing CD during follow-up. CD patients with perianal disease performing MRI between 2016 and 2019 in a tertiary center were kept for

analysis. One senior and one junior radiologist performed retrospectively a blind-review of disease activity (MAGNIFI-CD index and modified Van Assche index) and degree of fibrosis. Clinical features were collected retrospectively.

Results: Fifty-two patients were analyzed: 33 female, median age 36 years $\pm$ 1,81, median follow-up duration 37,75 months $\pm$ 1,94. Positive clinical outcome was observed in 36 patients (69,23%). Median MAGNIFI-CD index was lower in patients with positive long-term clinical outcome compared to patients with negative outcome (10,75 vs. 16,50, $p < 0,01$). Similarly, a lower modified Van Assche index was found in patient with positive clinical outcome ($p < 0,05$).

In addition, patients with positive long-term outcome presented more frequently improvement in T2-weighted images ($p < 0,01$) and lower C-reactive protein (CRP) level compared with patients with negative clinical long-term outcome (5,60 vs. 34,60 mg/L, $p < 0,05$). Last, degree of fibrosis failed to predict long-term clinical outcome in this study.

Conclusion: In this study, disease activity (MAGNIFI-CD index and modified Van Assche index) but not degree of fibrosis was predictive of long-term clinical outcome along with CRP levels.

Disclosure: Nothing to disclose.

P0376

RELATIONSHIP BETWEEN DISEASE ACTIVITY AS ASSESSED BY THE MAYO SCORE AND WORK PRODUCTIVITY IN PATIENTS WITH ULCERATIVE COLITIS IN THE TOFACITINIB OCTAVE PHASE 3 INDUCTION AND MAINTENANCE STUDIES

L. Targownik¹, M.C. Dubinsky², F. Steinwurz³, A.G. Bushmakina⁴, J.C. Cappelleri⁴, E. Tai⁵, S. Gardiner⁶, P. Hur⁶, J. Panés⁷
¹Division of Gastroenterology and Hepatology, Mount Sinai Hospital, University of Toronto, Toronto, Canada, ²Icahn School of Medicine at Mount Sinai, New York, United States, ³Unit of Inflammatory Bowel Disease, Hospital Israelita Albert Einstein, São Paulo, Brazil, ⁴Pfizer Inc, Groton, United States, ⁵Pfizer Canada, Kirkland, Canada, ⁶Pfizer Inc, New York, United States, ⁷Hospital Clínic de Barcelona, IDIBAPS, CIBERehd, Formerly Department of Gastroenterology, Barcelona, Spain

Contact E-Mail Address: julian.panes@gmail.com

Introduction: Tofacitinib is an oral small molecule Janus kinase inhibitor for the treatment of ulcerative colitis (UC). Tofacitinib induction treatment has been shown to improve work productivity in patients with UC. However, the relationship between disease activity and work productivity in the tofacitinib OCTAVE clinical programme has not been described.

Aims & Methods: We aimed to evaluate the relationship between Mayo score and Work Productivity and Activity Impairment-Ulcerative Colitis (WPAI-UC) score among patients in the Phase 3 studies evaluating tofacitinib as induction or maintenance therapy for UC (OCTAVE Induction 1&2 [NCT01465763, NCT01458951]; OCTAVE Sustain [NCT01458574]). Relationships between Mayo score (total and subscores) and WPAI-UC components (absenteeism, presenteeism, productivity loss and activity impairment) were estimated using a repeated measures longitudinal model in which Mayo score/subscore was a continuous anchor and WPAI-UC was the outcome (ie a linear relationship was imposed between the outcome and anchor). In sensitivity analyses, Mayo score was used as a categorical anchor to assess the linearity assumption (which did not impose any functional relationship between outcome and anchor). Productivity loss encapsulates absenteeism and presenteeism and thus is the most comprehensive WPAI-UC component. Analyses used all available pooled data from patients receiving tofacitinib or placebo.

Results: Relationships between total Mayo score and WPAI-UC

components were very similar when using the Mayo score as a continuous anchor, compared with a categorical anchor, supporting the linearity assumption. The relationship between total Mayo score and productivity loss was robust, with total Mayo scores of 0 and 12 corresponding to productivity loss scores of 12.7% (95% CI 9.9, 15.5) and 67.1% (64.5, 69.6), respectively (Table).

For every 1- or 3-point decrease in disease activity measured by total Mayo score (0–12), productivity loss (0–100%) improved by 4.5% (4.2, 4.9) and 13.6% (12.5, 14.7), respectively. Similar trends were observed between total Mayo score and activity impairment and presenteeism; the relationship with absenteeism was weak. Similar relationships were observed between individual Mayo subscores and WPAI-UC components.

	Productivity loss, least squares mean, % (95% CI)
Total Mayo score	
0	12.7 (9.9, 15.5)
1	17.2 (14.7, 19.7)
2	21.7 (19.5, 23.9)
3	26.3 (24.4, 28.2)
4	30.8 (29.1, 32.5)
5	35.3 (33.8, 36.8)
6	39.9 (38.5, 41.3)
7	44.4 (43.0, 45.8)
8	48.9 (47.4, 50.5)
9	53.5 (51.8, 55.2)
10	58.0 (56.0, 60.0)
11	62.5 (60.3, 64.8)
12	67.1 (64.5, 69.6)
Point increase in total Mayo score	
1	4.5 (4.2, 4.9)
2	9.1 (8.3, 9.8)
3	13.6 (12.5, 14.7)

The WPAI-UC is a self-administered six-item survey that generates four metrics: absenteeism (work time missed), presenteeism (impairment whilst working), productivity loss (overall work impairment from the combination of absenteeism and presenteeism) and activity impairment (non-work activity impairment). WPAI component scores are expressed as percentages, with a higher percentage indicating greater impairment and less productivity.

The Mayo score measures disease activity by assessing stool frequency, rectal bleeding, endoscopy and Physician Global Assessment. Total Mayo score ranges from 0 to 12 points (each subscore ranges from 0 to 3), with higher scores indicating more severe disease activity. CI, confidence interval; UC, ulcerative colitis; WPAI-UC, Work Productivity and Activity Impairment-Ulcerative Colitis.

Table. Percentage of productivity loss at each total Mayo score in patients with UC in OCTAVE Phase 3 induction and maintenance studies (main model with total Mayo score as a continuous anchor)

Conclusion: In patients with UC in the induction and maintenance studies, robust relationships between Mayo score (total and subscores) and productivity loss were observed. These post hoc clinical trial data may not be fully generalisable to clinical practice.

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M.C. Dubinsky has received consultancy fees from AbbVie, Bristol Myers Squibb, Celgene, Eli Lilly, Galapagos, Gilead Sciences, Janssen Pharmaceuticals, Pfizer Inc, Prometheus Laboratories, Takeda and UCB; and is a shareholder of Trellus Health.

F. Steinwurz has received advisory board fees from Pfizer Inc; and has received consultancy and speaker fees from AbbVie, Amgen, Celltrion, Eurofarma, Ferring Pharmaceuticals, Janssen Pharmaceuticals, Sandoz, Takeda and UCB.

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P0377

RELATIONSHIP BETWEEN HEALTH-RELATED QUALITY OF LIFE AND WORK PRODUCTIVITY IN PATIENTS WITH ULCERATIVE COLITIS IN THE TOFACITINIB OCTAVE PHASE 3 INDUCTION AND MAINTENANCE STUDIES

L. Targownik¹, M.C. Dubinsky², F. Steinwurz³, A.G. Bushmakina⁴, J.C. Cappelleri⁴, E. Tai⁵, S. Gardiner⁶, P. Hur⁶, **J. Panés**⁷
¹*Division of Gastroenterology and Hepatology, Mount Sinai Hospital, University of Toronto, Toronto, Canada,* ²*Icahn School of Medicine at Mount Sinai, New York, United States,* ³*Unit of Inflammatory Bowel Disease, Hospital Israelita Albert Einstein, São Paulo, Brazil,* ⁴*Pfizer Inc, Groton, United States,* ⁵*Pfizer Canada, Kirkland, Canada,* ⁶*Pfizer Inc, New York, United States,* ⁷*Hospital Clínic de Barcelona, IDIBAPS, CIBERehd, Formerly Department of Gastroenterology, Barcelona, Spain*

Contact E-Mail Address: julian.panes@gmail.com

Introduction: Tofacitinib is an oral small molecule Janus kinase inhibitor for the treatment of ulcerative colitis (UC). Tofacitinib induction treatment has been shown to improve work productivity in patients with UC. However, the relationship between health-related quality of life (HRQoL) and work productivity in the tofacitinib OCTAVE clinical programme has not been described.

Aims & Methods: We aimed to evaluate the relationship between Inflammatory Bowel Disease Questionnaire (IBDQ) domains and Work Productivity and Activity Impairment-Ulcerative Colitis (WPAI-UC) components among patients in the Phase 3 studies evaluating tofacitinib as induction or maintenance therapy for UC (OCTAVE Induction 1&2 [NCT01465763, NCT01458951]; OCTAVE Sustain [NCT01458574]).

Relationships between IBDQ (total and domain scores) and WPAI-UC components (absenteeism, presenteeism, productivity loss and activity impairment) were estimated using a repeated measures longitudinal model in which IBDQ domain score was a continuous anchor and WPAI-UC component score was the outcome (ie a linear relationship was imposed between the outcome and anchor).

In sensitivity analyses, IBDQ domain score was used as a categorical anchor to assess the linearity assumption (which did not impose any functional relationship between outcome and anchor). Productivity loss includes absenteeism and presenteeism and thus is the most comprehensive WPAI-UC component. Analyses used all available pooled data from patients receiving tofacitinib or placebo.

Results: Relationships between IBDQ total score and WPAI-UC components were very similar when using the IBDQ total score as a continuous anchor, compared with a categorical anchor, supporting the linearity assumption. The relationship between IBDQ total score and productivity loss was robust, with IBDQ total scores of 224 and 32 (higher score = better HRQoL) corresponding to a 5.6% (95% CI 3.4, 7.8) and 100.7% (97.3, 104.1) impact, respectively (Table).

For every 16-point increase in IBDQ total score, productivity loss (0–100%) improved by 7.9% (7.5, 8.4) (Table). Similar trends were observed between IBDQ total score and activity impairment and presenteeism; the relationship with absenteeism was weak. Similar relationships were observed between IBDQ domains and WPAI-UC components.

	Productivity loss, least squares mean, % (95% CI)
IBDQ total score	
32	100.7 (97.3, 104.1)
40	96.8 (93.6, 99.9)
60	86.9 (84.2, 89.5)
80	76.9 (74.7, 79.2)
100	67.0 (65.3, 68.8)
120	57.1 (55.7, 58.5)
140	47.2 (46.1, 48.4)
160	37.3 (36.2, 38.4)
180	27.4 (26.1, 28.8)
200	17.5 (15.8, 19.2)
220	7.6 (5.5, 9.7)
224	5.6 (3.4, 7.8)
Point decrease in IBDQ total score	
1	0.5 (0.5, 0.5)
16	7.9 (7.5, 8.4)

The WPAI-UC is a self-administered six-item survey that generates four metrics: absenteeism (work time missed), presenteeism (impairment whilst working), productivity loss (overall work impairment from the combination of absenteeism and presenteeism) and activity impairment (non-work activity impairment). WPAI component scores are expressed as percentages, with a higher percentage indicating greater impairment and less productivity.

The IBDQ evaluates disease-related quality of life by 32 items over four domains: bowel (total domain score ranges from 10 to 70), emotional (total domain score ranges from 12 to 84), social (total domain score ranges from 5 to 35) and systemic (total domain score ranges from 5 to 35). For the total score (ranges from 32 to 224) and each domain, a higher score indicates a better quality of life.

CI, confidence interval; IBDQ, Inflammatory Bowel Disease Questionnaire; UC, ulcerative colitis; WPAI-UC, Work Productivity and Activity Impairment-Ulcerative Colitis

Table. Percentage of productivity loss at IBDQ total scores in patients with UC in OCTAVE Phase 3 induction and maintenance studies (main model with IBDQ total score as a continuous anchor)

Conclusion: In the induction and maintenance studies, robust relationships between IBDQ (total and domain scores) and productivity loss were observed. These post hoc clinical trial data may not be fully generalisable to clinical practice.

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J.C. Cappelleri, E. Tai, S. Gardiner and P. Hur are employees and shareholders of Pfizer Inc. J. Panés has received personal fees from AbbVie, Arena, Athos, Boehringer Ingelheim, Celgene, Celltrion, Ferring Pharmaceuticals, Galapagos, Genentech/Roche, GSK, Immunic, Janssen Pharmaceuticals, Mirum, Morphic, Nestlé, Origo, Pandion Therapeutics, Pfizer Inc, Progenity, Takeda, Theravance Biopharma and Wassermann; and grant support from AbbVie and Pfizer Inc.

P0378

PRESENCE OF RISK FACTORS ASSOCIATED WITH COLECTOMY AMONG PATIENTS WITH COLECTOMY IN THE TOFACITINIB OCTAVE ULCERATIVE COLITIS CLINICAL PROGRAMME

D.T. Rubin¹, L. Salese², P.G. Kotze³, J.C. Woolcott², C. Su², R. Mundayat⁴, J. Paulissen⁴, J. Torres⁵, M. Long⁶

¹University of Chicago Medicine Inflammatory Bowel Disease Center, Chicago, United States, ²Pfizer Inc, Collegeville, United States, ³IBD Outpatient Clinics, Colorectal Surgery Unit, Catholic University of Paraná, Curitiba, Brazil, ⁴Pfizer Inc, New York, United States, ⁵Gastroenterology Division, Hospital Beatriz Ângelo, Loures, Portugal, ⁶University of North Carolina, Center for Gastrointestinal Biology and Disease, Chapel Hill, United States

Contact E-Mail Address: joanatorres00@gmail.com

Introduction: Tofacitinib is an oral small molecule Janus kinase inhibitor for the treatment of ulcerative colitis (UC). Avoidance of colectomy remains an important goal of UC therapy, and there are known factors associated with increased risk of colectomy.¹

Aims & Methods: This post hoc analysis assessed baseline characteristics and presence of risk factors for colectomy among patients who underwent colectomy in the tofacitinib OCTAVE clinical programme (NCT01465763; NCT01458951; NCT01458574; NCT01470612). Incidence rates (IRs; unique patients with events per 100 patient-years [PY] of exposure) were assessed in 3 cohorts: Induction (placebo [PBO] or tofacitinib 10 mg twice daily [BID]), Maintenance (PBO, tofacitinib 5 or 10 mg BID) and Overall (patients who received ≥ 1 dose of tofacitinib 5 or 10 mg BID in the Phase 3 or open-label, long-term extension [OLE] studies). Risk factors assessed were: age < 40 years at diagnosis, extensive colitis, severe endoscopic disease (Mayo endoscopic subscore of 3), hospitalisation for colitis within 12 months, C-reactive protein > 3 mg/L and serum albumin < 3.5 g/dL.¹

Results: In total, 14 patients underwent colectomy: 3/1139 in the induction studies (tofacitinib 10 mg BID: n=2; PBO: n=1), 3/593 in the maintenance study (PBO: n=3) and 8/944 in the OLE study (tofacitinib 10 mg BID: n=8; per protocol patients were not in remission at baseline). IRs per 100 PY (95% confidence intervals; exposure) were: Induction: PBO, 2.47 (0.06, 13.74; 40.55 PY) and tofacitinib 10 mg BID, 1.26 (0.15, 4.55; 158.72 PY); Maintenance: PBO, 2.90 (0.60, 8.47; 103.48 PY), tofacitinib 5 mg BID, 0.00 (0.00, 2.48; 148.77 PY) and tofacitinib 10 mg BID, 0.00 (0.00, 2.35; 157.31 PY); Overall: tofacitinib all, 0.34 (0.16, 0.63; 2915.95 PY). Baseline characteristics of patients who underwent colectomy, including treatment duration and risk factors for colectomy, are summarised (Table); all had ≥ 1 risk factor and prior tumour necrosis factor inhibitor (TNFi) exposure.

Conclusion: Colectomies were infrequent in the OCTAVE clinical programme, all were in patients with prior TNFi exposure and most patients had multiple risk factors. For induction responders, the fact that colectomies only occurred in patients who received PBO and not tofacitinib in the maintenance study supports the importance of continued active therapy in patients with moderate to severe UC. This analysis was limited by the low number of colectomies and potential underestimation due to case report form identification without adjudication.

References: 1. Rubin DT et al. Am J Gastroenterol 2019;114:384–413.

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L. Salese, J.C. Woolcott, C. Su and R. Mundayat are employees and shareholders of Pfizer Inc. P.G. Kotze has received consultancy and speaker fees from AbbVie, Janssen Pharmaceuticals, Pfizer Inc and Takeda; and grant support from Pfizer Inc and Takeda.

Treatment group at time of colectomy	Sex, Age at diagnosis (years), Disease duration (years) ^a	Disease extent	Mayo endoscopic subscore at baseline	Hospitalisation for colitis within 12 months	Baseline CRP, mg/L	Baseline albumin, g/dL	Days of treatment prior to colectomy	Total Mayo score at last visit prior to colectomy	Risk factors present ^{b,c}
OCTAVE Induction 1 and 2									
Tofacitinib 10 mg BID	Male, 26, ≥ 6	Left-sided colitis	3	No	53.53	4.0	21	11	3
Tofacitinib 10 mg BID	Male, 41, < 6	Left-sided colitis	3	No	1.90	4.3	38	11	1
Placebo	Female, 14, < 6	Extensive/pancolitis	2	No	4.36	3.6	58	9	3
OCTAVE Sustain									
Placebo	Female, 52, ≥ 6	Extensive/pancolitis	3	Yes	4.65	4.0	126	6	4
Placebo	Female, 67, < 6	Left-sided colitis	3	Yes	19.59	3.9	143	10	3
Placebo	Female, 23, ≥ 6	Left-sided colitis	3	No	1.08	4.5	63	4	2
OCTAVE Open									
Tofacitinib 10 mg BID	Female, 35, ≥ 6	Extensive/pancolitis	3	No	13.42	4.1	62	12	4
Tofacitinib 10 mg BID	Female, 22, ≥ 6	Extensive/pancolitis	3	No	4.02	4.2	132	6	4
Tofacitinib 10 mg BID	Male, 44, < 6	Proctosigmoiditis	3	No	4.50	3.7	44	11	2
Tofacitinib 10 mg BID	Female, 20, ≥ 6	Extensive/pancolitis	3	No	36.80	4.2	92	4	4
Tofacitinib 10 mg BID	Male, 31, < 6	Extensive/pancolitis	3	Yes	1.71	4.3	56	8	4
Tofacitinib 10 mg BID	Male, 45, ≥ 6	Extensive/pancolitis	3	Yes	40.53	3.2	375	11	5
Tofacitinib 10 mg BID	Female, 31, ≥ 6	Left-sided colitis	3	Yes	4.34	4.1	47	11	4
Tofacitinib 10 mg BID	Female, 29, < 6	Extensive/pancolitis	3	Yes	7.50	4.0	174	6	5

Patients with UC in OCTAVE Induction 1&2 (8 weeks [NCT01465763; NCT01458951]), OCTAVE Sustain (52 weeks [NCT01458574]) and

OCTAVE Open (OLE study [NCT01470612]) were evaluated. All patients had prior TNFi exposure

^aData were taken from baseline of the respective studies in which the colectomy occurred

^bData were taken from baseline of OCTAVE Induction 1&2

^cRisk factors for colectomy included: age < 40 years at diagnosis, extensive colitis, severe endoscopic disease (Mayo endoscopic subscore of 3), hospitalisation for colitis within 12 months, CRP > 3 mg/L and serum albumin < 3.5 g/dL

BID, twice daily; CRP, C-reactive protein; OLE, open-label, long-term extension; TNFi, tumour necrosis factor inhibitor; UC, ulcerative colitis

P0378 Table. Baseline demographics and clinical characteristics of patients who underwent colectomy in the OCTAVE clinical programme.

J. Paulissen is an employee of Syneos Health, which was a paid contractor to Pfizer. J. Torres has received advisory board fees from Arena, Galapagos, Janssen Pharmaceuticals and Pfizer Inc; lecture fees from Galapagos and Janssen Pharmaceuticals; and research support from AbbVie and Janssen Pharmaceuticals.

M. Long has received consultancy fees from AbbVie, Bristol Myers Squibb, Calibr, Eli Lilly, Genentech/Roche, Janssen Pharmaceuticals, Pfizer Inc, Prometheus, Salix, Takeda, Target PharmaSolutions, Theravance Biopharma and Valeant; and research support from Pfizer Inc and Takeda.

P0379

A MULTI-CENTRE STUDY OF BEHAVIOURS, ATTITUDES AND BARRIERS TO EXERCISE IN INFLAMMATORY BOWEL DISEASE, A SURVEY FROM THE PATIENT'S PERSPECTIVE

N. McGettigan¹, K. Allen¹, C. Foley², S. Bennett¹, C. Lardner¹, T. Lukose¹, M. Forry¹, M. O'Reilly², O. Kelly², A. O'Toole¹, K. Boland¹
¹Beaumont Hospital, Gastroenterology, Dublin, Ireland, ²Connolly Hospital, Gastroenterology, Dublin, Ireland, ³Beaumont Hospital, Infusion Unit, Dublin, Ireland

Contact E-Mail Address: neasamcgettigan@hotmail.com

Introduction: Physical exercise has many potential benefits in IBD including an improvement in quality of life, favourable body composition changes, anti-inflammatory effects, and improved psychological health. The WHO recommends 150–300 minutes of moderate-intensity or 75–150 minutes of vigorous-intensity aerobic physical activity per week for adults aged 18–65 years.

Patients with IBD have a significant decrease in exercise tolerance compared with healthy individuals. Exercise as an adjuvant treatment modality in IBD is underutilised and data are required in patients with active IBD.

Aims & Methods: Aim:

1. To assess physical activity levels, attitudes, and barriers to exercise in patients with IBD.
2. To assess the willingness of IBD patients to engage in an exercise programme.
3. To assess the frequency of body image issues in our IBD patients.

Method: Anonymous patient surveys were completed at Beaumont and Connolly Hospitals Dublin, Ireland.

Surveys were distributed in the outpatient clinics, infusion suites and inpatient wards between October and December 2021. Descriptive statistics, χ^2 testing and Pearson's correlations was completed using Minitab17. $P < 0.05$ denoted statistical significance.

Results: Data were analysed for 203 patients of which 62% ($n=126$) had an underlying diagnosis of Crohn's disease. Over half of respondents were male ($n=115$) with mean self-reported weight of 83kg. Mean weight among females was 76 kg ($n=88$). Reportedly 71% exercise regularly, for an average of 3.2 days/week and 59 mins/day of exercise.

Men exercise for longer than women on exercise days (60 minutes, $n=108$ versus 40 minutes, $n=82$, Mann-Whitney U test= 0.0005) and UC participants exercise for longer than CD participants (60 minutes, $n=61$ versus 45 minutes, $n=105$, Mann-Whitney U test= 0.044).

The most common activity was walking (74%). A post-diagnosis change in exercise behaviour was found in 66% with three-quarters exercising less. Principal barriers to exercise included lack of energy (54%), IBD symptoms (33%), toilet access concerns (31%), joint pains (31%) and time constraints (31%). Body image issues were common (62%) and associated with female gender ($p=0.007$) and age < 45 years ($p=0.02$).

Mean importance of exercise was 4, Std. dev. 0.97 (scale 0-5, 5 very important) and importance correlated with number of exercise days ($r=0.394$, $p<0.001$).

Exercise variable	Result N (%)
Regular exercise (N, %)	
Yes	148 (73%)
No	55 (27%)
No. of days of exercise/week	
Total Responses	148/148 (100%)
Mean, Std. dev.	4, 1.42
No. of minutes exercising/day	
Total Responses	140/148 (95%)
Median, IQR	60, 41.25-60
Rating of exercise importance (0-5)	
Total Responses	197/203 (97%)
Mean, Std. Dev.	4, 0.97
Benefits of exercise (N, %)	
Feel physically better	181/196 (92%)
Improved energy	165/196 (84%)
Improved mood	182/196 (93%)
Relief of anxiety	165/190 (87%)
Preferred location of exercise (more than one answer allowed)	
Total responses	201/203 (99%)
Outdoors	141/201 (70%)
At home	40/201 (20%)
At the Gym	49/201 (24%)
Difficulty adhering to exercise programmes	
Total Responses	198/203 (98%)
Yes	133/198 (67%)
Adherence difficulty due to IBD diagnosis	
Total Responses	131/133 (99%)
Yes	83/131 (63%)
Change in exercise pattern post dx	
Total Responses	188/203 (93%)
Yes	124/188 (66%)
If yes, did you exercise more/less:	
Total Responses	124/124 (100%)
Less	93/124 (75%)

Std. dev.- standard deviation, IBD- inflammatory bowel disease, dx- diagnosis

Table 1. Results of Exercise Behaviour

Conclusion: The majority of patients meet the WHO physical activity guidelines. Body image issues are common and associated with gender and younger age. IBD patients have exercise adherence issues and exercise less because of their disease. Fatigue is a significant barrier to exercise. These data demonstrate an impact of IBD on patient-reported ability to exercise. A pilot programme of physician-supervised exercise in addition to standard care in patients with active IBD is underway to determine impact on patient attitudes, disease-related outcomes and body composition (NCT05174754).

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P0380

PREDICTOR OF THROMBOEMBOLIC COMPLICATIONS IN PATIENTS WITH SEVERE ULCERATIVE COLITIS AND MEASURES FOR THEIR PREVENTION

O. Knyazev^{1,2,3}, A. Lishchinskaya¹, A. Kagramanova¹, T. Shkurko^{2,3}, M. Zvyaglova¹, K. Noskova¹, G. Dudina¹, I. Li¹

¹Moscow Clinical Scientific Center named after A.S. Loginov, IBD, Moscow, Russian Federation, ²State Scientific Centre of Coloproctology named after A.N. Ryzhyh, IBD, Moscow, Russian Federation, ³Research Institute of Health Organization and Medical Management, Moscow, Russian Federation

Contact E-Mail Address: lalbina@inbox.ru

Introduction: Patients with inflammatory bowel diseases (IBD) could develop thromboembolic complications (TEC) more frequently, compared with the general population.

Aims & Methods: The objective was to determine the value of the D-dimer concentration and to evaluate the role of heparin prophylaxis on the risks of clinically significant TEC in patients with severe attack of total ulcerative colitis (UC).

Materials and methods: The study included patients with severe total ulcerative colitis (UC) who were hospitalized from April 2019 to May 2020 in the department of treatment of IBD of the State Medical Institution of the Moscow Clinical Scientific Center named after A.S. Loginov. During 2019-2020, 217 patients with severe total UC were examined: in 2019 – 98 patients, in 2020 – 119 patients. The concentration of D-dimer [N=0.0-0.50 mcg/ml] was determined in all patients at the time of hospitalization by micro-latex agglutination. Clinically significant TEC were visualized by Ultrasound and CT.

In 2020, according to research plan, all patients with a severe attack of total UC were treated with low-molecular-weight heparins, regardless of the presence or absence of proven high-risk factors for TEC. A regression analysis of TEC risks was carried out depending on the D-dimer concentration.

Results: TEC during the follow-up period occurred in 18 patients (8.3%); no lethal outcomes were documented. The level of D-dimer in the group of patients with TEC ranged from 1.0 to 3.8 mcg/ml, in the group of patients without a TEC ranged from 0.1 to 1.8 mcg/ml. The risk of TEC is higher in the group of patients with D-dimer concentration more than 0.50 mcg/ml (RR - 0.062; 95% CI 0.113 - 0.034; χ^2 - 105.292; $p < 0.001$). A strong correlation was established between the D-dimer level and the TEC risk ($r=0.88$; $p < 0.001$).

In 2019, clinically significant TEC were determined in 14 (14.3%) patients. In 2020, the clinically significant TEC were determined in 4 (3.4%) patients. (RR - 4.250; 95% CI 1.445 - 12.497; χ^2 - 8.431; $p = 0.004$).

Conclusion: In hospitalized patients with UC, D-dimer values had a strong correlation with the risk of a TEC. Prevention with low-molecular-weight heparins significantly reduces the risks of TEC in patients with severe total UC.

Disclosure: Nothing to disclose.

P0381

VENLAFAXINE AS AN ADJUVANT THERAPY FOR INFLAMMATORY BOWEL DISEASE PATIENTS WITH ANXIOUS AND DEPRESSIVE SYMPTOMS: A RANDOMIZED CONTROLLED TRIAL

C. Liang¹, P. Chen¹, Y. Tang¹, C. Zhang², N. Lei¹, Y. Luo¹, S. Duan¹, Y. Zhang¹

¹West China Hospital of Sichuan University, Department of Gastroenterology, Chengdu, China, ²Institute for Interdisciplinary Information Science, Tsinghua University, Beijing, China

Contact E-Mail Address: changliang0916@126.com

Introduction: The effect of antidepressant therapy on Inflammatory Bowel Disease (IBD) remains controversial. This trial aimed to assess whether adding venlafaxine to standard therapy for IBD improved the quality of life (QoL), mental health and disease activity in IBD patients with anxious and depressive symptoms.

Aims & Methods: A prospective, randomized, double-blind, placebo-controlled clinical trial was conducted. Participants diagnosed with IBD with symptoms of anxiety/depression were randomly assigned to receive either venlafaxine 150 mg daily or equivalent placebo and followed for 6 months. Inflammatory Bowel Disease Questionnaire (IBDQ), Mayo score, Crohn's disease activity index (CDAI), Hospital Anxiety and Depression Scale (HADS) and blood examination were completed before the enrollment, during and after the follow-up. Mixed linear models and univariate analyses were used to compare groups.

Results: Forty-five IBD patients were included, of whom 25 were randomized to receive venlafaxine. The mean age was 39.76 (SD=11.30) years old. 25 (55.6%) was male. Venlafaxine showed a significant improvement on QoL ($p < 0.001$) and disease course ($p = 0.035$), a greater reduction in HADS (anxiety: $p < 0.001$, depression: $p < 0.001$), Mayo scores ($p < 0.001$) and CDAI ($p = 0.006$) 6 months. Venlafaxine had no effect on IL-10 expression, endoscopic scores, relapse rate and use rate of biologics and corticosteroids, but did reduce serum level of ESR ($p = 0.003$), CRP ($p < 0.001$) and TNF- α (0.009).

Conclusion: Venlafaxine has a significantly beneficial effect on QoL, IBD activity and mental health in IBD patients with comorbid anxious or depressive symptoms. (Chinese Clinical Trial Registry, ID: ChiCTR1900021496.)

Disclosure: Nothing to disclose.

P0382

REDUCED HUMORAL RESPONSE TO TWO DOSES OF COVID-19 VACCINE IN PATIENTS WITH INFLAMMATORY BOWEL DISEASE: DATA FROM ESCAPE-IBD, AN IG-IBD STUDY

F.S. Macaluso¹, M.R.D. Principi², F. Facciotti³, A. Contaldo⁴, A. Todeschini⁵, S. Saibeni⁶, C. Bezzio⁵, F. Castiglione⁶, O.M. Nardone⁶, R. Spagnuolo⁷, P. Doldo⁷, M.C. Fantini⁸, S. Paba⁸, G. Riguccio⁹, F.S. Conforti¹⁰, C. Viganò¹¹, M. Ascolani¹², G. Fiorino¹³, C. Correale¹⁴, G. Bodini¹⁵, M. Milla¹⁶, G. Scardino¹⁷, M. Venero¹⁸, F. Desideri¹⁹, F. Caprioli^{20,10}, M. Mannino¹, G. Rizzo¹, A. Orlando¹, Italian Group for the Study of Inflammatory Bowel Disease (IG-IBD)

¹Villa Sofia-Cervello Hospital, IBD Unit, Palermo, Italy, ²Aldo Moro University, Gastroenterology, Bari, Italy, ³IEO, Experimental Oncology, Milano, Italy, ⁴S. De Bellis, Gastroenterology 2 Unit, IRCCS, Castellana Grotte, Italy, ⁵ASST Rhodense, Gastroenterology Unit, Rho, Italy, ⁶Federico II University, Naples, Italy, ⁷Università Magna Graecia, U.O. Gastroenterologia ed Endoscopia Digestiva, A.O.U. Mater Domini, Dip. di Medicina Sperimentale e Clinica, Catanzaro, Italy, ⁸University of Cagliari, System Medicine - Gastroenterology, Monserrato, Italy, ⁹UOSD Malattie Infiammatorie Croniche Intestinali, Ospedale Santa Maria del Prato, Feltre, Italy, ¹⁰Gastroenterology and Endoscopy Unit, Fondazione IRCCS Cà Granda, Ospedale Maggiore Policlinico, Milano, Italy, ¹¹University of Milano-Bicocca, Division of Gastroenterology and Center of Autoimmune Liver Diseases, Dep. of Medicine and Surgery, Monza, Italy, ¹²UOC Gastroenterologia, Ospedale Ca' Foncello, Treviso, Italy, ¹³IRCCS Ospedale San Raffaele e Università Vita-Salute San Raffaele, Dip. di Gastroenterologia ed Endoscopia Digestiva, Milano, Italy, ¹⁴Humanitas Clinical and Research Center - IRCCS, Rozzano, Italy, ¹⁵Policlinico San Martino, Internal Medicine, Genova, Italy, ¹⁶Azienda Ospedaliero Universitaria Careggi, Firenze, Italy, ¹⁷Ospedale Valduce, Gastroenterologia, Como, Italy, ¹⁸IRCCS Policlinico San Matteo, Università degli Studi di Pavia, Clinica Medica 1, Pavia, Italy, ¹⁹San Maurizio Hospital, Gastroenterology, Bolzano, Italy, ²⁰University of Milan, Fisiopatologia Medico-Chirurgica e dei Trapianti, Milano, Italy

Contact E-Mail Address: fsmacaluso@gmail.com

Introduction: Patients on immunosuppressive drugs have been excluded from COVID-19 vaccines trials, creating concerns regarding their efficacy in this setting.

Aims & Methods: Effectiveness and Safety of COVID-19 Vaccine in Patients with Inflammatory Bowel Disease (IBD) Treated with Immunosuppressive or Biological Drugs (ESCAPE-IBD) is a prospective, multicentre study promoted by the Italian Group for the study of Inflammatory Bowel Disease.

We present data on serological response eight weeks after the second dose of COVID-19 vaccination in IBD patients and healthy controls (HCs).

Results: 1076 patients with IBD and 1126 HCs were analyzed. Seropositivity for anti-SARS-CoV-2 IgG was reported for most IBD patients, even if with a lesser rate compared with HCs (92.1% vs. 97.9%; $p < 0.001$). HCs had higher antibody concentrations (median OD 8.72 [IQR 5.2-14.2]) compared to the whole cohort of IBD patients (median OD 1.54 [IQR 0.8-3.6]; $p < 0.001$) and the subgroup of IBD patients ($n = 280$) without any treatment or on aminosalicylates only (median OD 1.72 [IQR 1.0-4.1]; $p < 0.001$). IBD patients treated with anti-TNFs showed significantly lower median anti-SARS-CoV-2 IgG levels compared with those without any treatment or on aminosalicylates only (OD 1.30 [IQR 0.7-3.0] vs. 1.72 [IQR 1.0-4.1]; $p < 0.001$), those treated with Vedolizumab (OD 1.78 [IQR 1.1-4.1]; $p = 0.001$), and Ustekinumab (OD 1.71 [IQR 0.9-4.9]; $p = 0.03$).

Conclusion: Although most IBD patients showed seropositivity after two doses of COVID-19 vaccines, the magnitude of the humoral response was significantly lower than in HCs.

Differently from other studies, these findings seem to be mostly unrelated to the use of immune-modifying treatments. Regarding COVID-19 vaccination, patients with IBD should be regarded as a whole as a "frail" category, therefore requiring booster/additional doses of COVID-19 vaccine. (ClinicalTrials.govID:NCT04769258).

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CB received lecture fees from Takeda, MSD, AbbVie and Janssen. FC received lecture fees from or served as a consultant or advisory board member for Abbvie, Janssen, Pfizer, Takeda Pharmaceuticals.

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P0383

EFFICACY, PERSISTENCE AND OPTIMIZATION OF USTEKINUMAB IN ULCERATIVE COLITIS: CLINICAL DATA

I. Latras Cortés¹, S. Díez Ruiz¹, R. González Núñez¹, L. Alcoba Vega¹, L. Vaquero Ayala¹, P. Suárez Álvarez¹, M. García Prada¹, N. Cano Sanz¹, F. Jorquera Plaza¹, M. Sierra Ausín¹

¹University Hospital of León, Department of Gastroenterology, León, Spain

Contact E-Mail Address: irenelatrascortes@gmail.com

Introduction: Ustekinumab (UST) is a p40 inhibitor of interleukin 12/23 approved to treat moderately to severely active ulcerative colitis (UC).

Aims & Methods: Retrospective and descriptive study of patients with ulcerative colitis treated with ustekinumab ($N = 16$) from July 2018 to September 2021 in the Inflammatory Bowel Disease Unit of our Hospital.

The primary objective was to analyze the efficacy: clinical remission (CR) and biological remission (BR), persistence with the drug and need for dose optimization.

The secondary objective was to determine the efficacy of UST in articular manifestations in ulcerative colitis.

Results: Basal characteristics of patients and disease are summarized in Table 1.

The mean duration of treatment with UST is 17.81 months (SD 12.57). 81.30% of patients were started on UST without concomitant use of corticosteroids.

Clinical remission (partial Mayo score <2 and no subscore >1) was achieved in 25% in Week 4 (4 out of 16 subjects), 50% in Week 8 (8/16), 69.2% in Week 16 (9/13), 54.5% in Week 24, 90% in Month 12 (9/10) and 87.5% in Month 18.

Rectal bleeding, present in 81.30% of patients in the beginning, disappeared in half of them in Week 4.

Partial Mayo score decreased during the follow-up ($p < 0.001$). The median level of fecal calprotectin (FC) at the index visit was 1214.63 mg/kg (SD 954.67), and had a tendency towards normalization ($p = 0.064$). Biological remission (FC <150 mg/kg) was achieved in 56.25% of subjects at the end of follow-up. Fecal calprotectin decrease principally occurred from Week 16. In 11 patients (68.75%), the dose was optimized every 4 weeks, because of secondary non-response or partial response. Clinical remission and biological remission (FC <150 mg/kg) was accomplished in 86.6% and 45.45% of them respectively.

87.50% of subjects who had been started on UST continue treatment at the end of follow-up.

6 patients (37.5%) suffered from articular manifestations (5 peripheral arthritis, 1 ankylosing spondylitis), that improved in 83.3% after initiation of UST.

No significant adverse events were detected.

Age (years)	49.74 (SD 17.04)
Duration of the disease (years)	11.96 (SD 9.87)
Basal partial Mayo score	5.75 (SD 2.08)
Gender	
Male	9 (56.30%)
Female	7 (43.80%)
Extension of ulcerative colitis	
Proctitis	3 (18.80%)
Left colitis	11 (66.80%)
Extended colitis	2 (12.50%)
Extra-intestinal manifestations	
Yes	6 (37.50%)
No	10 (62.50%)
Basal Mayo endoscopic score	
1	1 (10.00%)
2	4 (40.00%)
3	5 (50.00%)
Previous biological therapy	
≥2 biological drugs :	8 (50.00%)
≥2 anti-TNF + VDZ :	5 (31.25%)
≥2 anti-TNF + VDZ + TOFA:	2 (12.50%)
1 biological drug	6 (37.50%)
Naïve	2 (12.50%)
Maintenance dose	
90 mg sc every 4 weeks	6 (37.50%)
130 mg iv every 4 weeks	5 (31.25%)
90 mg sc every 8 weeks	3 (18.75%)
90 mg sc every 12 weeks	2 (12.50%)
VDZ: vedolizumab. TOFA: tofacitinib	

Table 1. Characteristics of patients and disease

Conclusion: - UST is an effective treatment to achieve and maintain long-term clinical and biological remission in patients with ulcerative colitis.

- Biological remission is accomplished in half of the patients and FC decreases mainly after Week 16.

- Treatment optimization because of secondary non-response or partial response is effective in achieving clinical remission, but not so effective in achieving biological remission.

- UST may be useful in the treatment of articular manifestations, especially in peripheral arthritis, although further research is needed.

Disclosure: Nothing to disclose.

P0384

THE RISK OF SERIOUS INFECTIONS BEFORE AND AFTER ANTI-TNF THERAPY IN INFLAMMATORY BOWEL DISEASE – A RETROSPECTIVE COHORT STUDY

J. Holmgren¹, A. Fröberg², I. Visuri³, J. Halfvarson⁴, H. Hjortswang⁵, P. Karling⁶, P. Myrelid⁷, O. Olén⁸, J.F. Ludvigsson⁹, O. Grip¹⁰

¹Lund University / Section of Medicine, Department of Gastroenterology, Skane University Hospital, Malmö, Sweden,

²Lund University, Department of Ear, Nose and Throat

Diseases, Karlskrona Hospital, Karlskrona, Sweden, ³Faculty

of Medicine and Health, Örebro University, Department

of Gastroenterology, Örebro, Sweden, ⁴Örebro University,

Department of Gastroenterology, Faculty of Medicine and Health,

Örebro, Sweden, ⁵Linköping University Hospital, Department of

Gastroenterology and Hepatology, Linköping, Sweden, ⁶Umeå

University, Department of Public Health and Clinical Medicine,

Umeå, Sweden, ⁷Linköping University Hospital, Department

of Surgery, Linköping, Sweden, ⁸Karolinska Institutet, Clinical

Epidemiology Unit, Department of Medicine, Solna, Stockholm,

Sweden, ⁹Karolinska Institutet, Medical Epidemiology and

Biostatistics, Stockholm, Sweden, ¹⁰Skane University Hospital,

Gastroenterology, Malmö, Sweden

Contact E-Mail Address: johanna.holmgren@skane.se

Introduction: Serious infections have been observed in patients with inflammatory bowel disease (IBD) on anti-TNF use, but to what extent these infections are due to anti-TNF or the disease activity per se is hard to disentangle. Earlier studies on the risk of infections related to anti-TNF use have shown varying results and data from randomised controlled trials (RCTs) and observational studies are conflicting. While RCTs have rarely demonstrated any excess risks of infections, such risk increases have been reported in observational studies¹⁻⁵.

One of the reasons for the contrasting results may be that the untreated placebo group used in RCTs has a higher proportion of patients with active disease. The enrichment of severely sick (untreated) comparators makes it harder to demonstrate an increased risk of infection among treated patients.

Observational studies more often have a longer follow-up and thereby greater statistical power to detect small differences and rare events. There are several other challenges in appropriately determining the risk of serious infection. In addition to anti-TNF and immunomodulating agents (azathioprine, 6-mercaptopurine and methotrexate), disease activity, corticosteroid use, opioids, malnutrition, co-morbidity and age are all potential confounders potentially predisposing to infections⁶.

Aims & Methods: We aimed to describe how the rates of serious infections change before and after anti-TNF initiation in flaring IBD and thereby shed light on the role of anti-TNF (as opposed to that of disease activity) for the risk of infection. IBD patients naïve to anti-TNF treatment were identified at five centers participating in the Swedish IBD Quality Register, and their medical records examined in detail. Serious infections, defined as infections requiring in-patient care, the year before and after the start of anti-TNF treatment were evaluated.

Results: Among 980 patients who started their first anti-TNF therapy between 1999 and 2016, the incidence rate of serious infections was 2.19 [95% CI: 1.43-3.36] per 100 person-years the year before and 2.11 [95% CI: 1.33-3.34] per 100 person-years one year after treatment start. This corresponded to an incidence rate ratio one year after anti-TNF treatment of 0.97 [95% CI: 0.51-1.84]. Compared to before anti-TNF therapy, the incidence of serious infection was significantly decreased more than one year after treatment (Incidence rate ratio 0.56 [95% CI: 0.33-0.95], $p = 0.03$).

Time (years)	Incidence rate per 100 person years	95% Confidence interval
-1- <0	2.19	1.43-3.36
0- <1	2.11	1.33-3.34
1- <2	0.89	0.51-1.57
2- <3	0.32	0.13-0.76
3- <4	0.34	0.16-0.76
4- <5	0.36	0.16-0.79
5- <6	0.48	0.24-0.96
6- <7	0.13	0.03-0.52
>7	0.13	0.03-0.53

Table 1 The annual incidence rate of serious infections among IBD patients the year before start of anti-TNF treatment (-1- <0) and during anti-TNF treatment (0- <1, 1- <2 etc.).

Conclusion: In conclusion, in this real-world study from five Swedish centers caring for both urban and rural areas, the rate of serious infections in IBD patients was equally high the year before and the year after start of anti-TNF treatment and significantly lower beyond the first year of anti-TNF treatment. Healing the mucosa may outweigh the adverse immunosuppressive effect on the risk for infection and emphasizes the importance of treating the underlying disease. The findings are applicable when assessing the risk and benefits of therapies together with the patient.

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OO: Karolinska Institutet has received financial support from Janssen, Ferring, Takeda, and Pfizer for research led by OO and for lectures held by OO regarding subjects not related to the present study.

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P0385

ASSOCIATION OF ANTIBIOTIC USE WITH DURABILITY OF BIOLOGIC AGENTS IN INFLAMMATORY BOWEL DISEASE: A REPORT FROM THE EPI-IIRN

Y. Gorelik¹, I. Ghersin¹, D. Shlon¹, C. Friss², G. Focht², Y. Loewenberg Weisband³, S. Greenfeld⁴, R. Kariv⁵, N. Ledderman⁶, E. Matz⁷, I. Dotan⁸, H. Bar-Yoseph¹, Y. Chowers¹, D. Turner², Israeli IBD Research Nucleus
¹Rambam Health Care Campus, Gastroenterology, Haifa, Israel,
²Shaare Zedek Medical Center, Juliet Keidan Institute of Pediatric Gastroenterology Hepatology and Nutrition, Jerusalem, Israel,
³Clalit Research Institute, Tel Aviv, Israel, ⁴Maccabi Health Services, Tel Aviv, Israel, ⁵Tel Aviv Sourasky Medical Center, Gastroenterology, Tel Aviv, Israel, ⁶Meuhedet Health Services, Tel Aviv, Israel, ⁷Leumit Health Services, Tel Aviv, Israel, ⁸Rabin Medical Center, Director, Division of Gastroenterology, Petah Tikva, Israel

Contact E-Mail Address: yurigorelik@gmail.com

Introduction: The composition of the gut microbiome is associated with disease course and response to therapy in inflammatory bowel diseases (IBD).[1,2] Different effects of various antibiotic classes on immunogenicity towards anti-TNF agents were recently demonstrated.[3] We aimed to assess the association between antibiotic treatment and persistence of biologics therapy.

Aims & Methods: Data from the epidemiology group of the Israeli IBD research nucleus (epi-IIRN) were used. All patients treated with infliximab, adalimumab, vedolizumab, or ustekinumab were included in the analysis. Multivariable cox proportional hazards models with time varying covariates were developed for each biologic therapy to assess the association between antibiotic use and treatment non-persistence, defined as cessation of drug purchases for more than 6 months. The multivariable models included medical treatments including antibiotics, hospitalizations, surgical procedures and laboratory results. Exposure was defined as a drug dispensation or event in the year prior to each time point during the time at risk.

Results: We included 13,513 patients who received at least one biologic. Median ages at treatment initiation ranged between 24 and 28. Most treated patients had Crohn's disease ranging between 59% of patients treated with vedolizumab and 95% of patients treated with ustekinumab. Rates of previous biologic therapy ranged between 19% in infliximab and 96% for ustekinumab. Median times at risk ranged between 1.2 and 2.1 years for ustekinumab, and infliximab respectively. Treatment cessation event were 28, 29, 34, and 39 events per 100 patient years for ustekinumab, adalimumab, vedolizumab, and infliximab respectively. Macrolides and fluoroquinolones were associated with reduced risk of infliximab discontinuation, while metronidazole use increased risk for infliximab cessation (Table 1). Cephalosporins and fluoroquinolones were associated with adalimumab cessation, whereas fluoroquinolones were associated with vedolizumab cessation (Table 1). Antibiotics were not significantly associated with durability of ustekinumab treatment.

Survival Models (aHR, 95% CI)*	Infliximab (n=7,639)	Adalimumab (n=8,686)	Vedolizumab (n=3,232)	Ustekinumab (n=1,246)
Antibiotics	0.98 (0.92, 1.04)	1.03 (0.97, 1.10)	1.07 (0.95, 1.20)	0.90 (0.72, 1.13)
Penicillin	0.98 (0.92, 1.04)	1.03 (0.97, 1.10)	1.03 (0.91, 1.16)	0.85 (0.66, 1.09)
Penicillin-BLI	1.02 (0.95, 1.09)	1.03 (0.96, 1.10)	1.06 (0.95, 1.20)	1.00 (0.80, 1.25)
Cephalosporin	1.00 (0.94, 1.08)	1.10 (1.03, 1.18)	1.04 (0.92, 1.18)	1.09 (0.86, 1.38)
Fluoroquinolones	0.88 (0.82, 0.94)	1.11 (1.03, 1.18)	1.16 (1.03, 1.31)	0.96 (0.76, 1.22)
Macrolides	0.87 (0.80, 0.94)	0.97 (0.90, 1.05)	0.97 (0.85, 1.11)	1.06 (0.82, 1.36)
Metronidazole	1.13 (1.05, 1.20)	1.00 (0.94, 1.08)	1.00 (0.88, 1.14)	0.89 (0.68, 1.15)
Tetracyclin	0.94 (0.80, 1.09)	1.03 (0.89, 1.19)	0.82 (0.63, 1.05)	0.91 (0.59, 1.40)

* Two survival models were developed for each biologic with different primary effects: 1. Any antibiotic exposure; 2. Each antibiotic class as a separate variable.

Table 1. Adjusted hazard ratios for treatment cessation for all antibiotics (model 1) and each antibiotic separately in a combined model (model 2).

The following covariates were included in all models: Crohn's disease; previous biologic therapy; surgery (time varying); hospitalization (time varying); immunomodulators (time varying); steroids (time varying); purchase of a different biologic agent (time varying); albumin (time varying, per 1 g/dL); hemoglobin (time varying, per 1 g/dL).

Conclusion: Specific antibiotic classes are distinctively associated with treatment persistence of biologic agents. These observations may be partially mediated by the effects of antibiotics on immunogenicity, whereas further research is needed to mechanistically understand other associations. Nonetheless, these data suggest a need to customize antibiotic choice in biologics-treated IBD patients.

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P0386

EFFICACY AND SAFETY OF MIRIKIZUMAB AS INDUCTION THERAPY IN PATIENTS WITH MODERATELY TO SEVERELY ACTIVE ULCERATIVE COLITIS: RESULTS FROM THE PHASE 3 LUCENT-1 STUDY

G. D'Haens¹, T. Kobayashi², N. Morris³, T. Lisssoos³, A. Hoover³, X. Li³, V. Arora³, C. Milch³, W.J. Sandborn⁴, B.E. Sands⁵

¹Amsterdam University Medical Centers, Amsterdam, Netherlands, ²Center for Advanced IBD Research and Treatment, Kitasato University Kitasato Institute Hospital, Tokyo, Japan, ³Eli Lilly and Company, Indianapolis, United States, ⁴University of California San Diego, La Jolla, United States, ⁵Division of Gastroenterology, Icahn School of Medicine at Mount Sinai, New York, United States

Contact E-Mail Address: g.dhaens@amsterdamumc.nl

Introduction: Anti-IL23p19 inhibitors are emerging as promising treatment options for ulcerative colitis (UC). Mirikizumab (miri) is a humanized, IgG4 monoclonal antibody directed against the p19 subunit of IL-23, a key mediator in the pathogenesis of inflammatory bowel diseases.

Aims & Methods: We assessed the induction efficacy and safety of miri with a Phase 3, multi-center, randomized, parallel-arm, double-blind, placebo (PBO)-controlled trial (LUCENT 1; NCT03518086) in patients with moderately to severely active UC (Modified Mayo Score 4-9 points and centrally read Mayo endoscopic subscore ≥ 2) who had inadequate response, loss of response, or intolerance to corticosteroids, immunosuppressants, biologic therapies, or tofacitinib.

Adult patients (N=1281) were randomized in a 3:1 ratio to receive blinded intravenous administration of 300 mg miri or PBO every 4 weeks for 12 weeks. Randomization was stratified by biologic failure status, baseline (BL) corticosteroid use, BL disease activity as measured by modified Mayo score, and world region.

The primary objective was to test the hypothesis that miri was superior to PBO in inducing clinical remission at Week 12.

Key secondary objectives were clinical response, endoscopic remission, symptomatic remission, clinical response in biologic-failed patients, histologic-endoscopic mucosal improvement, and improvement in bowel urgency at Week 12. (see table for endpoint definitions).

Results: Overall, 1162 patients (miri: 868, PBO: 294) were included in the analysis. BL characteristics (mean age, years [SD], miri: 42.9 [13.9], PBO: 41.3 [13.8]; disease duration, mean years [SD], miri: 7.2 [6.7], PBO: 6.9 [7.0]; and modified Mayo score, n [%]: moderate (4-6), miri 404 [46.5], PBO: 138 [47.1]; and severe (7-9), miri: 463 [53.3], PBO: 155 [52.9]) were balanced across the two treatment groups.

A significantly greater proportion of patients treated with miri achieved clinical remission at Week 12 (miri: 24.2%; PBO: 13.3%; $\Delta=11.1$ [99.875%CI: 3.2, 19.1]; $p=0.00006$). Miri-treated patients achieved all key secondary endpoints, including a significantly greater average reduction in bowel urgency severity compared to PBO ($p<0.00001$).

The frequencies of treatment-emergent adverse events (TEAEs) in miri-treated patients were similar to PBO (miri: 426 [44.5%], PBO: 148 [46.1]). The most common TEAEs reported (miri, PBO) were nasopharyngitis (39 [4.1%], 10 [3.1%]), anemia (32 [3.3%], 19 [5.9%]), headache (32 [3.3%], 9 [2.8%]), and ulcerative colitis (17 [1.8%], 24 [7.5%]).

There were numerically fewer serious adverse events (miri: 27 [2.8%], PBO: 17 [5.3%]) and discontinuations due to adverse events (miri: 15 [1.6%], PBO: 23 [7.2%]) in miri-treated patients compared to PBO. There were 2 colon malignancies in the miri arm (0.2%) and no deaths during the treatment period.

	Treatment groups	
	Placebo IV N=294	Miri 300 mg IV N=868
Clinical Remission, % patients	13.3	24.2
Common risk difference vs. placebo (99.875% CI)		11.1 (3.2, 19.1)*
Clinical Response, % patients	42.2	63.5
Common risk difference vs. placebo (99.875% CI)		21.4 (10.8, 32.0)**
Clinical Response (Bio-Failed), % patients	29.7	54.6
Common risk difference vs. placebo (99.875% CI)		25.0 (9.0, 41.1)**
Endoscopic Remission, % patients	21.1	36.3
Common risk difference vs. placebo (99.875% CI)		15.4 (6.3, 24.5)**
HEMI, % patients	13.9	27.1
Common risk difference vs. placebo (99.875% CI)		13.4 (5.5, 21.4)**
Symptomatic Remission, W4 % patients	12.9	21.8
Common risk difference vs. placebo (99.875% CI)	27.9	9.2 (1.4, 16.9)***
Symptomatic Remission, W12 % patients		45.5
Common risk difference vs. placebo (99.875% CI)		17.5 (7.5, 27.6)**
Urgency NRSDBL, LSMΔBL	-1.6	-2.6
LSM difference vs. placebo (99.875%CI)		-0.95 (-1.5, -0.4)**

All outcomes are for Week 12 except Symptomatic Remission Week 4. *p=0.00006;

p<0.00001; *p=0.00064

Clinical remission: Stool frequency (SF) subscore = 0 or 1 with a ≥1-point decrease from BL, and Rectal bleeding (RB) subscore = 0, and Endoscopic subscore (ES) = 0 or 1 (excluding friability)

Clinical response: decrease in modified Mayo score of ≥2 points and ≥30% decrease from BL, and decrease of ≥1 point in the RB subscore from BL or an RB score of 0 or 1

Clinical response (bio-failed): clinical response in patients who had previously failed biologic or tofacitinib therapy

Endoscopic remission: ES = 0 or 1 (excluding friability)

HEMI (histologic-endoscopic mucosal improvement): Histologic improvement, defined using Geboes scoring system with neutrophil infiltration in <5% crypts, no crypt destruction, and no erosions, ulcerations, or granulation tissue; and endoscopic remission

Symptomatic remission: SF = 0, or SF = 1 with a ≥1-point decrease from BL and RB = 0

Urgency NRS (numeric rating scale)ΔBL: least square mean change in urgency NRS from BL. Mixed Model for Repeated Measures (MMRM) was used to compare the treatment groups for bowel urgency improvement; for all other endpoints, the Cochran-Mantel Haenszel (CMH) test was used to compare the treatment groups while adjusting for the stratification factors; a p value of 0.00125 was considered significant.

Table: Primary and key secondary outcomes

Conclusion: In this phase 3 UC study, 300mg miri IV demonstrated statistically significant and clinically meaningful improvements vs PBO in all primary and key secondary endpoints across clinical, endoscopic, histologic, and symptomatic measures, with an acceptable safety profile.

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P0387

USTEKINUMAB THERAPY AFTER BIOLOGIC FAILURE IN PATIENTS WITH CROHN'S DISEASE – A REAL-WORLD SINGLE CENTRE EXPERIENCE

S. Majumder^{1,2}, A. Bazarova³, T.L. Parigi^{1,2}, M. Love², J. Davis², S. Ghosh⁴, M. Iacucci^{5,1,2}, U.N. Shivaji^{5,1,2}

¹Institute of Immunology and Immunotherapy, University of Birmingham, Immunology and Immunotherapy, Birmingham, United Kingdom, ²University Hospitals Birmingham NHS Foundation Trust, Gastroenterology, Birmingham, United Kingdom, ³University of Cologne, Institute for Biological Physics, Köln, Germany, ⁴College of Medicine and Health, University College Cork, APC Microbiome, Cork, Ireland, ⁵National Institute for Health Research Birmingham Biomedical Research Centre, Gastroenterology, Birmingham, United Kingdom

Contact E-Mail Address: s.majumder.1@bham.ac.uk

Introduction: Patients with Crohn's disease (CD) often require multiple biological therapies due to loss of response(1). Anti-TNF drugs are generally used as first-line biologic followed by a switch of class. Ustekinumab (UST), an IL-12/23p40 antagonist is used often after anti-TNF failure (2). The aim of the study was to report on outcomes of UST therapy with a median follow-up period of nearly 24 months.

Aims & Methods: All CD patients who commenced UST therapy were identified from EMR at a tertiary referral centre between January 2017 and December 2021. All relevant demographic and clinical data were collected. Data on clinical response (defined as a downgrade in disease activity based on clinician assessment & biochemical parameters), steroid-free duration, and long-term response to UST at 52 and 104 weeks were recorded.

Response was assessed clinically supported by biomarker, cross-sectional imaging, colonoscopic data and sustained maintenance of UST. The data were analysed and statistical analysis carried out using the IBM® SPSS® Statistics software package Version: 28.0.0.0.

Results: Total of 147 CD patients (M=65, 44%; median age 38years) were included in the analysis with a median follow up-period of nearly 24 months (range 5-67 months). 82 (56%) patients had stricturing (B2), penetrating (B3) and perianal phenotype at baseline and 50 (34%) had undergone previous resection/s. 109 (75%) had documented moderate to severe disease activity and 139 (95%) patients were exposed to atleast one biologic prior to treatment with UST. 34 (23%) patients were on concomitant thiopurines at start of treatment.

Of the 147 patients, 143 (97%) in our cohort showed clinical response to UST and all remained on treatment at the end of follow-up period. The distribution of patients as per disease activity at baseline, 52 and 104 weeks is illustrated in table 1. An improvement in haemoglobin levels was observed post-therapy with UST, which was statistically significant at 104 weeks ($p<0.001$), with corresponding significant reduction in faecal calprotectin levels (median reduction from 976 mcg/g to 333 mcg at 104w; $p<0.001$).

Among patients with B2, B3 and perianal disease, nearly 90% responded to UST and remained steroid-free; less than 10% needed surgery for IBD-related indication in this sub-group during follow-up period, with no pause in UST before or after surgery. Almost all patients with history of previous resections responded and remained on UST. Only 13(8.8%) patients had side-effects which were directly attributed to UST therapy.

Assessment Time Point	Mild/Clinical Remission	Moderate Disease Severity	Severe Disease
Baseline	38	52	57
Week 52	53	38	20
Week 104	38	13	06

Table 1:Disease activity of patients during the study period.

Conclusion: UST is an effective therapeutic option in patients with CD who have failed previous biologic therapy. In our cohort with a large proportion of patients with complicated and refractory disease, clinical response was observed regardless of their previous exposure status to biologics, and disease phenotype. UST appears to be well tolerated with a reasonable safety profile. The consistent response rates even after prolonged treatment periods mean that clinicians could safely continue UST for longer durations, to manage CD particularly when options are limited.

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P0388

SWITCHING INTRAVENOUS TO SUBCUTANEOUS INFLIXIMAB WAS SAFE AND SUCCESSFUL SHORT TERM IN ULCERATIVE COLITIS AND CROHN PATIENTS – A BELGIAN SINGLE CENTER EXPERIENCE

L. Cornelis¹, E. De Jonckere¹, E. Lernout¹, J. Bossuyt², H. Vanpoucke³, D. De Wulf¹, L. Desomer¹, F. Baert¹

¹AZ Delta, Gastroenterology, Roeselare, Belgium, ²AZ Delta, Data Management and Analytics, Roeselare, Belgium, ³AZ Delta, Laboratory Medicine, Roeselare, Belgium

Contact E-Mail Address: leander.cornelis@gmail.com

Introduction: Subcutaneous (SC) infliximab CT-P13 (IFX) has recently been registered for the treatment of moderate-to-severe inflammatory bowel disease (IBD). The SC route is an attractive option for patients. However, many open questions remain on how to safely switch patients from maintenance IV to SC administration.

Aims & Methods: To assess switching from IV to SC Infliximab therapy in IBD patients through clinical and biochemical evaluation.

Starting April 2021 for ulcerative colitis (UC) and September 2021 for Crohn patients in durable remission (no symptoms, normal labs and calprotectin) on eight-weekly (or six-weekly) infliximab and therapeutic IFX trough level were offered the option to switch to SC therapy. All patients are monitored prospectively every 3 months with PRO's (with Awell app), labs including IFX concentrations and faecal calprotectin every 6 months. These data were added to our medical file system (HIX) and specific IBD database (URCARE).

Results: April 28 of the year 2022, 57 (40% UC, 60% Crohn) of 127 IBD patients on IFX have chosen to switch to SC IFX therapy with 50 patients (40% UC, 60% Crohn) passing 3 months follow-up, 29 patients (57% UC, 43% Crohn) 6 months and 19 patients (100% UC, 0% Crohn) 9 months respectively (median follow-up 9 months for UC, 5 months for Crohn). Median body weight was 72 kg (range 52-105). Concomitant IBD medication were as follows azathioprine (5), mesalamine (7), beclomethasone (1) or methotrexate (2). The UC cohort median age was 37 years (range 21-74), M:F ratio = 10:13, 50% proctitis, 35% left sided colitis and 15% pancolitis. The Crohn cohort median age was 39 years (range 18-70), M:F ratio = 18:16, 40% small bowel only, 22% colon only and 38% small bowel and colon. Hitherto all patients stayed into deep remission according to clinical Mayo score, CRP and calprotectin. Results are shown in Table 1.

	Last IV dose	3 months follow up	6 months follow up	9 months follow up
	IV	SC		
	N = 57	N = 50	N = 29	N = 18
CRP (mg/L) (±SD)	1.3 (±11.8)	1.2 (±10.8)	1.2 (±1.9)	1.6 (±5.9)
Thrombocytes (x10 ³ /μL) (±SD)	244 (±65)	248 (±57.7)	258 (±71)	247 (±45)
Faecal calprotectin (μg/g) (±SD)	41 (±444)	18 (±77)	21 (±304)	64 (±53)
IFX trough concentration (μg/mL) (±SD)	5.8 (±3)	12 (±2.5)	11 (±2.5)	12 (±0.04)

IFX = Infliximab, IV = intravenous, CRP = C-reactive protein

Table 1.

Median levels of CRP, thrombocytes and calprotectin remained stable from at last IFX infusion to 3,6 and 9 months follow up after switching to SC therapy. IFX serum concentrations doubled after 3 months and remained stable during further follow up. One patient was pre-emptively optimised to weekly injection because of very low serum concentrations (0.7 μg/mL) after 3 months of SC therapy, all other patients are still on standard dose (120 mg SC biweekly) irrespective of body weight. Local pain and injection site reactions were reported in 19% and 10% of patients respectively.

Conclusion: Switching UC and Crohn patients in deep remission and adequate trough levels from maintenance IV to SC infliximab therapy was successful and safe short term. A proportion of patients experienced pain and or injection site reactions. All patients continued SC treatment without request to switch back to IV.

Disclosure: Nothing to disclose.

P0389

PHARMACOKINETICS, SAFETY, AND TOLERABILITY OF ETASIMOD: RESULTS FROM A PHASE 1 DRUG-DRUG INTERACTION STUDY IN HEALTHY VOLUNTEERS

C.A. Lee¹, Y. Tang¹, L. Villa-Caballero¹, K. Shan¹, A. Randle¹, J.S. Grundy¹

¹Arena Pharmaceuticals, a wholly-owned subsidiary of Pfizer Inc, New York, San Diego, United States

Contact E-Mail Address: clee@ARENAPHARM.COM

Introduction: Etrasimod (ETR), a once-daily, oral, selective sphingosine 1-phosphate receptor modulator in clinical development for immune-mediated inflammatory disorders including ulcerative colitis, Crohn's disease, eosinophilic esophagitis, atopic dermatitis, and alopecia areata, is a substrate of cytochrome P450 (CYP)2C8, CYP2C9, and CYP3A4, and to a minor extent, CYP2C19 and CYP2J2. ETR has the potential for drug-drug interaction with CYP2C8, CYP2C9, and CYP3A4 when coadministered with inhibitors or inducers of these enzymes.

This open-label Phase 1 study evaluated the pharmacokinetics (PK) and safety of ETR in the presence of fluconazole (moderate CYP2C9 and CYP3A4 inhibitor; strong CYP2C19 inhibitor), gemfibrozil (strong CYP2C8 inhibitor), or rifampin (moderate CYP2C8 and CYP2C9 inducer; strong CYP3A4 and CYP2J2 inducer).

Aims & Methods: Fifty-six healthy male and female volunteers (18-55 years) were assigned to 1 of 3 treatment groups, each with 2 dosing periods separated by a 7-day washout.

On Day 1 (Period 1), Groups A and B received a single dose of ETR 1mg whereas Group C received a single dose of ETR 2mg. From Days 8–22 (Period 2), Groups A and B received fluconazole once daily (QD) (400mg on Day 8; 200mg on Days 9–22) and gemfibrozil 600mg twice daily, respectively, and a single dose of ETR 1mg on Day 12, whereas Group C received rifampin 600mg QD and a single dose of ETR 2mg on Day 15.

Primary endpoints were plasma C_{max} , AUC_{0-168h} , and $AUC_{0-\infty}$ of ETR in the presence and absence of fluconazole, gemfibrozil, or rifampin. Log-transformed primary PK parameters for ETR were compared using analysis of variance with treatment as fixed effect and participant as random effect.

Results: In the presence of fluconazole or gemfibrozil, there was little impact on ETR C_{max} , but AUC_{0-168h} and $AUC_{0-\infty}$ were mildly-to-moderately increased (Table).

Analyte	C_{max} (ng/mL) GLSMR (90% CI)	AUC_{0-168h} (ng*h/mL) GLSMR (90% CI)	$AUC_{0-\infty}$ (ng*h/mL) GLSMR (90% CI)
Group A (n = 18): [Etrasimod + Fluconazole] / [Etrasimod]			
Etrasimod	1.12 (1.09–1.16)	1.62 (1.52–1.72)	1.84 (1.71–1.99)
Group B (n = 18): [Etrasimod + Gemfibrozil] / [Etrasimod]			
Etrasimod	1.12 (1.06–1.19)	1.27 (1.20–1.35)	1.36 (1.26–1.46)
Group C (n = 18): [Etrasimod + Rifampin] / [Etrasimod]			
Etrasimod	1.24 (0.82–1.88)	0.53 (0.49–0.56)	0.51 (0.47–0.54)

$AUC_{0-\infty}$, area under the plasma concentration-time curve from time 0 to infinity; AUC_{0-168h} , AUC from time 0 to 168 hours; CI, confidence interval; C_{max} , maximum plasma drug concentration; GLSMR, geometric least squares mean ratio.

Table. Statistical Comparison of Etrasimod Plasma Exposure Measures in the Presence and Absence of Fluconazole, Gemfibrozil, or Rifampin.

Geometric mean $t_{1/2}$ of ETR increased from 42 to 87 hours in the presence of fluconazole and from 45 to 70 hours in the presence of gemfibrozil.

When administered in the presence vs absence of rifampin, ETR C_{max} only slightly increased while AUC_{0-168h} and $AUC_{0-\infty}$ moderately decreased. Geometric mean $t_{1/2}$ of ETR decreased by ~50% in the presence of rifampin. All treatments were generally well tolerated. All treatment-emergent adverse events (AEs) were mild or moderate.

One participant discontinued the study due to AEs. No abnormalities were found in laboratory parameters, vital signs, or 12-lead electrocardiograms.

Conclusion: The results of this study are consistent with CYP2C8, CYP2C9, and CYP3A4 being involved in ETR metabolism with no single enzyme appearing to dominate its elimination. The involvement of multiple CYP isoforms reduces the likelihood of ETR having a clinically relevant drug interaction, particularly when only a single CYP isoform is strongly or moderately inhibited/induced by a coadministered drug.

Disclosure: C. A. Lee, Y. Tang, L. Villa-Caballero, K. Shan, A. Randle, and J. S. Grundy are employees of Arena Pharmaceuticals, a wholly-owned subsidiary of Pfizer Inc, New York, NY, USA.

P0390

A PHASE 1 DRUG INTERACTION STUDY EVALUATING THE EFFECTS OF ITRACONAZOLE ON THE PHARMACOKINETICS, SAFETY, AND TOLERABILITY OF ETASIMOD IN HEALTHY VOLUNTEERS

C.A. Lee¹, A. Ramaiya¹, Y. Tang¹, A. Sapone¹, K. Gilder¹, A. Randle¹, J.S. Grundy¹

¹Arena Pharmaceuticals, a wholly-owned subsidiary of Pfizer Inc, New York, San Diego, United States

Contact E-Mail Address: clee@ARENAPHARM.COM

Introduction: Etrasimod (ETR) is a once-daily, oral, selective sphingosine 1-phosphate receptor modulator in clinical development for immune-mediated inflammatory disorders including ulcerative colitis, Crohn's disease, eosinophilic esophagitis, atopic dermatitis, and alopecia areata. ETR is a substrate of cytochrome P450 (CYP)2C8, CYP2C9, and CYP3A4, and to a minor extent, CYP2C19 and CYP2J2.

ETR was previously evaluated in the presence and absence of fluconazole (moderate inhibitor of CYP2C9 and CYP3A4; strong inhibitor of CYP2C19). ETR exposure measures (AUC_{0-168h} and $AUC_{0-\infty}$) increased moderately up to 84% in the presence vs absence of fluconazole, likely due to inhibition of both CYP2C9 and CYP3A4.

To determine the relative contribution of CYP3A4, the pharmacokinetics (PK) and safety of ETR in the presence of itraconazole (strong inhibitor of CYP3A4) were evaluated in this open-label Phase 1 study.

Aims & Methods: Eighteen healthy male and female volunteers (18-55 years) received a single dose of ETR 1mg on Day 1. Starting on Day 10, participants received 200mg itraconazole solution (10mg/mL) once daily for 13 days and a single dose of ETR 1mg on Day 14.

Primary endpoints were plasma C_{max} , AUC_{0-last} , and $AUC_{0-\infty}$ of ETR in the presence and absence of itraconazole. Log-transformed primary PK parameters for ETR were compared using analysis of variance with treatment as fixed effect and participant as random effect.

Results: The presence of itraconazole had little impact on single-dose peak exposure (C_{max}) of ETR, but mildly increased total exposure measures (AUC_{0-last} and $AUC_{0-\infty}$) of ETR by up to 32% (Table). These changes were not considered clinically relevant. Geometric mean $t_{1/2}$ of ETR also mildly increased from 37 to 44 hours in the presence of itraconazole. All treatments were generally well tolerated.

All treatment-emergent adverse events were mild. No abnormalities in laboratory parameters, vital signs, or 12-lead electrocardiogram assessments were noted.

Analyte	C _{max} (ng/mL) GLSMR (90% CI)	AUC _{0-∞} (ng•h/mL) GLSMR (90% CI)	AUC _{0-∞} (ng•h/mL) GLSMR (90% CI)
	[Etrasimod + Itraconazole] / [Etrasimod]		
Etrasimod	1.06 (1.02–1.11)	1.31 (1.26–1.37)	1.32 (1.27–1.38)

AUC_{0-∞}, area under the plasma concentration-time curve from time 0 to infinity; AUC_{0-last}, AUC from time 0 to last quantifiable concentration; CI, confidence interval; C_{max}, maximum plasma drug concentration; GLSMR, geometric least squares mean ratio.

Table. Statistical Comparison of Etrasimod Plasma Exposure Measures in the Presence and Absence of Itraconazole.

Conclusion: The results of this study demonstrate that CYP3A4 is one of several CYP isoforms, along with CYP2C8 and CYP2C9, primarily involved in the disposition of ETR. The involvement of multiple CYP isoforms reduces the likelihood of ETR having a clinically relevant drug interaction, particularly in cases where only a single CYP isoform is strongly or moderately inhibited/induced by a coadministered drug.

Disclosure: C. A. Lee, A. Ramaiya, Y. Tang, A. Sapone, K. Gilder, A. Randle, and J. S. Grundy are employees of Arena Pharmaceuticals, a wholly-owned subsidiary of Pfizer Inc.

P0391

MODEL-PREDICTED LYMPHOCYTE RESPONSE AND RECOVERY PROFILES FOR THE SPHINGOSINE 1-PHOSPHATE RECEPTOR MODULATORS OZANIMOD AND ETASIMOD

C.A. Lee¹, T. Waterhouse², M. Heathman², D.A. Oh¹, H.K. Komori¹, J.S. Grundy¹

¹Arena Pharmaceuticals, a wholly-owned subsidiary of Pfizer Inc, New York, San Diego, United States, ²Metrum Research Group, Tariffville, United States

Contact E-Mail Address: clee@ARENAPHARM.COM

Introduction: Sphingosine 1-phosphate (S1P) receptor modulators inhibit lymphocyte egress from lymph nodes, thereby reducing the number of peripheral circulating lymphocytes and their subsequent recruitment to sites of inflammation. Ozanimod (OZA) is an S1P receptor modulator approved for multiple sclerosis and ulcerative colitis. The lymphocyte response following OZA treatment is mainly driven by the pharmacokinetic (PK) exposure of its active metabolite (CC112273). Etrasimod (ETR) is an S1P receptor modulator in clinical development for ulcerative colitis, Crohn's disease, eosinophilic esophagitis, atopic dermatitis, and alopecia areata. Exposure-response models describing observed/published PK and pharmacodynamic (PD) data can be useful tools for multiple purposes including facilitating comparisons between compounds.

Here we present model-predicted lymphocyte response profiles for once-daily dosing of OZA and ETR as well as lymphocyte recovery profiles following drug discontinuation.

Aims & Methods: A population PK/PD model of lymphocyte response to OZA over time was developed from published summary-level data for CC112273 PK profile and an OZA lymphocyte E_{max} model. Initial model simulation predicted a mean baseline lymphocyte count of 1.97x10⁹/L (slightly higher than the observed mean baseline in the OZA RADIANCE study [1.83x10⁹/L]); thus, a correction factor of 0.93 was applied to subsequent OZA simulations.

A population PK/PD model of lymphocyte response to ETR over time was developed using data from 7 Phase 1 studies in healthy volunteers and 2 Phase 2 studies in participants with either ulcerative colitis or atopic dermatitis. Simulations from both models of 10,000 virtual participants given OZA (initial 7-day dose titration: 0.23mg on Days 1–4, 0.46mg on Days 5–7, 0.92mg on Day 8 and thereafter for 11 weeks) or ETR (2mg for 12 weeks) were produced and compared.

Results: Model-predicted lymphocyte response over time approximately (≥90%) reached median steady-state lymphocyte nadir within 24 days for OZA vs within 5 days for ETR.

After drug discontinuation, the predicted time for lymphocyte counts to return to the lower end of the normal range (of either 0.8x10⁹/L or 1.0x10⁹/L for 90% of virtual participants) was 48 and 81 days, respectively, for OZA and 2 and 4 days, respectively, for ETR. The model predicted results for OZA appear generally consistent with similar observed lymphocyte findings reported in its drug label.

Conclusion: Model predictions of lymphocyte response and recovery profiles indicate that ETR, when compared to OZA, is expected to achieve lymphocyte nadir more quickly as well as require less time to recover to the normal range after drug discontinuation.

Rapid drug washout and reconstitution of the immune system may be desirable when considering resolution of infection, switching therapies, and family planning.

Disclosure: C. A. Lee, D. A. Oh, H. K. Komori and J. S. Grundy are employees of Arena Pharmaceuticals, a wholly-owned subsidiary of Pfizer Inc.

T. Waterhouse and M. Heathman are employees of Metrum Research Group, which received funding from Arena Pharmaceuticals for conduct of the reported analyses.

P0392

HEALTHCARE UTILISATION WITH USTEKINUMAB TREATMENT IN A REAL-WORLD COHORT IN NORTH WEST LONDON: AN ANALYSIS BY AGE AND LINE OF THERAPY

N. Kamperidis¹, M. Shah², S. Young², M. Deshpande³, S. Sweeney³, N. Arebi⁴

¹St Marks Hospital, London, United Kingdom, ²Imperial College Health Partners, London, United Kingdom, ³Janssen-Cilag, Medical Affairs, High Wycombe, United Kingdom, ⁴St Marks Hospital, Dept. of Gastroenterology, London, United Kingdom

Contact E-Mail Address: nkamperidis@yahoo.com

Introduction: Treatment options for moderate to severe Crohn's disease (CD) are evolving. Inherent limitations of clinical trial data related to generalisability of results and restricted outcome measures, are well recognised. Effectiveness studies to include older age groups, the effect of previous exposure to other therapies and other outcomes relevant to patients and healthcare services, offer an understanding of the role of drugs in clinical practice.

Aims & Methods: We aim to describe healthcare utilisation in a real-world cohort of CD patients treated with ustekinumab.

This retrospective cohort study used de-identified data from the prospectively-maintained Whole Systems Integrated Care (Discover) dataset across a population of over 2.5million in Northwest London (NWL)¹. Adult patients with a diagnosis of CD prescribed ustekinumab between 1/1/2016 and 31/3/21 were included. Resource use was captured until 31/12/21.

Outcomes relating to healthcare utilisation, including elective (EL), non-elective hospital admission (NEL) and IBD-related surgery, were analysed according to age at initiation of ustekinumab and previous exposure to other biological drugs during the study period.

Results: 6,251 patients with CD were identified, of which 115 patients prescribed ustekinumab were included.

12% (14/115) were ≥60 years old at ustekinumab prescription. Overall, 25% (29/115) received ustekinumab as a first biologic, 49% (56/115) were as second-biologic and 26% (30/115) were as third-biologic or later. Patient demographics are described in Table 1.

Overall, 177 EL admissions and 122 NEL admissions were recorded in the cohort.

For the 18-59 age group, 67% (91/101) patients prescribed ustekinumab had EL admissions during the study period (median 2 visits), 47% (47/101) NEL admissions (median 2 visits) and 20% (20/101) IBD-related surgery. In the older patient group (≥ 60 years), 50% (7/14) had EL admissions (median 1 visit), 50% (7/14) NEL admissions, (median 2 visits), and 14% (2/14) IBD-related surgery.

When ustekinumab was prescribed as a first, second or third + biologic, the proportion of patients with EL admissions was 52% (15/29), 66% (37/56) and 77% (23/30) respectively with a median of 1, 2 and 2 visits. The proportion recorded for NEL admissions was 45% (13/29), 46% (26/56) and 50% (15/30) respectively each with a median of 2 visits. First-, second- and third + biologic groups experiences IBD-related surgery in 17% (5/29), 21% (12/56) and 17% (5/30) respectively.

	Gender, female N (%)	Age, years median (range)	BMI, kg/m2 median (range)	Ethnicity, white n (%)
Overall cohort (n=115)	57 (50%)	36.0 (18.0-83.0)	23.1 (13.5-39.8)	61 (53%)
≥ 60 years old (n=14)	9 (64%)	-	27.0 (16.9-35.5)	9 (64%)
18- 59 years old (n=101)	48 (48%)	-	22.5 (13.5-39.8)	52 (51%)
1 st biologic (n=29)	16 (55%)	33.0 (18.0-69.0)	23.1 (15.6-35.5)	13 (45%)
2 nd biologic (n=56)	26 (46%)	40.5 (23.0-83.0)	24.5 (13.5-38.2)	32 (57%)
3 rd + biologic (n=30)	15 (50%)	36.5 (24.0-68.0)	23.2 (13.5-39.8)	16 (53%)

Table 1. Patient demographics for whole cohort and subgroups.

Conclusion: In this population cohort, hospital admission and IBD-related surgery rates for older CD patients (≥ 60 years) prescribed ustekinumab were comparable to 18-59 age group. Patients who received ustekinumab as a first biologic during the study showed a numerically lower rates of elective hospital admission compared to those prescribed ustekinumab as a later line of therapy. Further analysis will determine whether this reflects comparable effectiveness for ustekinumab in older people with CD and better outcomes when used as a first line agent.

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P0393

IMPACT OF THE HLA-DQA1*05 ALLELE ON LOSS OF RESPONSE AND PRESENCE OF ANTI-DRUG ANTIBODIES TO USTEKINUMAB IN CROHN'S DISEASE AND ULCERATIVE COLITIS PATIENTS

T. Ahmad¹, M.D. Martín-Arranz², B. Brinkman³, C. Gasink⁴, M. Guan⁵, A. Hart⁶

¹Nuffield Health Exeter Hospital, Exeter, United Kingdom,

²Hospital La Paz, Gastroenterology, Madrid, Spain, ³Janssen

Pharmaceutica, Beerse, Belgium, ⁴Janssen Scientific Affairs, LLC, Horsham, United States, ⁵Janssen Research & Development, LLC, Spring House, United States, ⁶Janssen Research & Development, LLC., Systems Pharmacology & Biomarkers, Spring House, United States

Contact E-Mail Address: tariq.ahmad1@nhs.net

Introduction: Crohn's disease (CD) and ulcerative colitis (UC) patients (pts) with the HLA-DQA1*05 allele and treated with infliximab or adalimumab have a 2-fold risk of anti-drug antibody (ADA) development and subsequent loss of response (LOR). ADA levels to ustekinumab (UST) are comparatively low, at rates <5% in CD and UC through 5 and 3 years in the UNIFI and UNIFI trials.

In UNIFI, the proportion of pts in remission in each dose group decreased by only approximately 5% each year from years 1 through 5. The relationship between the HLA-DQA1*05 allele and UST on ADA development and LOR has not been examined.

Aims & Methods: The UNIFI and UNIFI studies assessed the safety and efficacy of UST induction and maintenance therapy in pts with moderate-to-severe CD and UC, respectively. The cohort comprised pts randomized to UST maintenance as well as delayed responders from the nonrandomized maintenance cohorts from both studies. 343 CD and 332 UC pts had both clinical and genetic data. Pts were genotyped on the Illumina Infinium HumanOmni5.0 (UNIFI) and HumanOmni2.5 (UNIFI) platforms. Utilizing genotype data from chromosome 6, HLA imputation was performed with the Michigan Imputation Server high-resolution HLA reference panel.¹ Antibodies were detected using a drug-specific, drug-tolerant, electrochemiluminescent immunoassay on the Meso Scale Discovery platform.^{2,3} Pts who had ADA detected at 1 or more visits through week (wk) 44 were considered to be positive to ADA.

Two statistical models evaluated association between HLA-DQA1*05 and wk44 LOR or ADA status with PLINK 2.0, $\alpha = 0.05$. The first adjusted for sex, age, and top 5 ancestry principal components (PCs) derived from genetic data, and the second added baseline immunomodulator.

Results: HLA-DQA1*05 allele was detected in 43.15% (148/343) of UNIFI pts and 39.16% (130/332) of UNIFI pts. HLA-DQA1*05 was not significantly associated with UST LOR or ADA positive status in UNIFI or UNIFI regardless of baseline immunomodulator use (Table).

		P-values (based on logistic regression)	
		Response at Week 44	ADA
UNIFI	Model 1 (adjusting for sex, age, and top 5 ancestry principal components)	0.96	0.25
	Model 2 (adjusting for sex, age, top 5 ancestry principal components, and baseline immunomodulator use)	0.95	0.23
UNIFI	Model 1 (adjusting for sex, age, and top 5 ancestry principal components)	0.69	0.85
	Model 2 (adjusting for sex, age, top 5 ancestry principal components, and baseline immunomodulator use)	0.72	0.84

Table. HLA-DQA1*05 allele association results for UNIFI and UNIFI

No meaningful differences were seen in clinical response at wk44 per HLA-DQA1*05 allele carriers vs non-carriers (63.6% [89/140] vs 64.6% [122/189] in UNITI and 73.8% [96/130] vs 74.3% [150/202] in UNIFI, respectively). Similarly, no meaningful differences were seen in ADA positivity through wk44 in pts who had the allele vs those who did not have the allele (2.8% [2/71] vs 3.8% [4/105] in UNITI and 5.5% [6/109] vs 3.9% [7/178] in UNIFI, respectively, 4.4% vs. 3.9% in combined cohorts).

Conclusion: The HLA-DQA1*05 allele was not associated with UST LOR over 44 wks with adequate power in both cohorts. HLA-DQA1*05 was likewise not associated with ADA, although power to detect significance was only ~19% in UNITI and UNIFI for a 2-fold effect given the overall low ADA rate of 4.1%.

Adjusting for immunomodulator use also did not result in any meaningful difference between the HLA-DQA1*05 allele and either LOR or ADA. Thus HLA-DQA1*05 positive pts with IBD, particularly those in whom an immunomodulator is contraindicated, might be attractive candidates for treatment with UST rather than infliximab and adalimumab.

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P0394

REAL-WORLD EVIDENCE OF THE EFFECTIVENESS AND SAFETY OF USTEKINUMAB FOR THE TREATMENT OF CROHN'S DISEASE: SYSTEMATIC REVIEW AND META-ANALYSIS OF OBSERVATIONAL STUDIES

C. Rubín de Célix¹, M. Chaparro Sanchez², J.P. Gisbert^{*1}

¹Hospital Universitario de La Princesa, IIS-Princesa, Universidad Autónoma de Madrid and CIBERehd, Gastroenterology Unit, Madrid, Spain

Contact E-Mail Address: cristina.rubin.92@gmail.com

Introduction: Ustekinumab is a fully human monoclonal IL-12/23 p40 antibody approved for moderate to severe Crohn's disease (CD). Evidence on the outcomes of ustekinumab in real-world CD patients is needed.

Aims & Methods: The aim of this meta-analysis was to evaluate the effectiveness and safety of ustekinumab in CD reported by observational studies. Bibliographical searches were performed in PubMed and EMBASE. Selection: observational studies assessing the effectiveness and safety of ustekinumab in CD.

Exclusion criteria: studies using ustekinumab exclusively as a prophylaxis for the postoperative recurrence or perianal disease. Data synthesis: effectiveness by intention-to-treat (random effects model). Data were stratified by: study design, population included, dose administered and prior treatment with biologics.

We evaluated the dose optimization requirement, the median time to the intensification and the dose optimization response/remission rate. We also evaluated predictors of response. To assess the quality of the observational studies we used the Newcastle-Ottawa Scale.

Results: A total of 63 studies (8,529 patients) were included, almost all focused on biologic experienced patients. Response was achieved in 60% of patients in the short-term (8-12 weeks; 95% confidence interval, 54-67%), 64% in the medium-term (16-24 weeks; 57-71%), and 64% in the long-term (48-52 weeks; 52-74%). Remission was achieved in 37% (28-46%) in the short-term, 42% (36-49%) in the medium-term and 45% (37-53%) in the long-term. Endoscopic remission rate in the medium-term was 24% (13-34%), and 33% (25-40%) in the long-term.

All the performed sub-analyses (study design, the population included, the administered dose of ustekinumab and prior treatment with biologic drugs) did not adequately explain between-study heterogeneity. Nearly one third of the patients needed ustekinumab dose optimization, and in 60% of them it was effective. Eighteen percent of patients lost response during follow-up.

The most frequent predictors of poor clinical response were previous biologic exposure, stricturing or penetrating behaviour, and high Harvey-Bradshaw score at first dose. Twenty-five percent of patients developed adverse events (AEs), the most frequent being infections (4%). Most of the AEs were mild, leading to treatment withdrawal in 7% of the cases.

Conclusion: Ustekinumab is an effective and safe therapy in real-world refractory CD patients. Dose optimization is frequently required, being effective in a high percentage of cases. Our results underline that the clinical benefit of ustekinumab seems to be higher in observational studies compared with clinical trials.

References: Equal contributors as senior authors

Disclosure: Nothing to disclose.

P0395

CORTICOSTEROID-SPARING EFFECTS OF USTEKINUMAB THERAPY FOR ULCERATIVE COLITIS THROUGH 4 YEARS: UNIFI LONG-TERM EXTENSION

R. Arasaradnam¹, E.J. Scherl², D. Rowbotham³, S. Danese⁴, W.J. Sandborn⁵, Y. Miao⁶, H. Zhang⁶, R. Panaccione⁷, W. Afif⁸, T. Hisamatsu⁹, R.W. Leong¹⁰, B.E. Sands¹¹, M.T. Abreu¹², C.W. Marano⁶

¹Warwick Medical School, University of Warwick & University Hospital Coventry, Dept. of Gastroenterology, Coventry Warwickshire, United Kingdom, ²Weill Cornell Medicine, New York Presbyterian Hospital, New York, United States, ³Auckland City Hospital, Gastroenterology & Hepatology, Auckland, New Zealand, ⁴Vita-Salute San Raffaele University - IRCCS San Raffaele Scientific Institute, Gastrointestinal Immunopathology, Milan, Italy, ⁵University of California San Diego, Division of Gastroenterology, San Diego, United States, ⁶Janssen Research & Development, LLC, Spring House, United States, ⁷University of Calgary, Medicine, Calgary, Canada, ⁸McGill University Health Center, Gastroenterology, Montreal, Canada, ⁹Kyorin University, Tokyo, Japan, ¹⁰Concord Hospital Dept. of Gastroenterology, Sydney, Australia, ¹¹Icahn School of Medicine at Mount Sinai, Dr. Henry D. Janowitz Division of Gastroenterology, New York, United States, ¹²University of Miami, Miller School of Medicine, Crohn's and Colitis Center, Miami, United States

Contact E-Mail Address: r.asaradnam@warwick.ac.uk

Introduction: Ustekinumab (UST) is an IL-12/23p40 inhibitor approved for treatment of Crohn's disease and ulcerative colitis (UC). In the UNIFI maintenance study of patients (pts) with moderate to severe UC, >90% of pts who achieved clinical response or remission at week (wk) 44 were not receiving corticosteroids, an important therapeutic goal. In this analysis, we describe the corticosteroid-sparing effects of UST treatment through 4 years (yrs) among pts who were treated in the UNIFI long-term extension (LTE).

Aims & Methods: Overall, 523 intravenous UST induction responders were randomized to subcutaneous (SC) maintenance therapy (placebo [PBO], n=175; UST 90mg every 12 wks [q12w], n=172; or UST 90mg q8w, n=176). A total of 284 UST pts completed wk44 and were treated in the LTE. PBO pts were discontinued after study unblinding.

Based on investigator's clinical judgement of UC disease activity, pts in the LTE were eligible to receive a dose adjustment starting at wk56: PBO to q8w, q12w to q8w, and q8w to q8w (sham adjustment). Pts in PBO or q8w groups were only eligible for dose adjustment or sham dose adjustment before unblinding.

Efficacy was evaluated using symptomatic remission (Mayo stool frequency subscore of 0 or 1 and a rectal bleeding subscore of 0). During the maintenance study, all pts receiving corticosteroids at maintenance baseline were required to initiate tapering.

Through wk200 of the LTE, symptomatic remission endpoints were calculated with treatment failure and missing data nonresponder imputation, and dose adjustment was not considered to be a treatment failure. Missing corticosteroid dose data were managed using last observation carried forward.

Results: Of the 284 pts randomized to UST and treated in the LTE, 139 were receiving corticosteroids at maintenance baseline. Of these, 90.6% (n=126) were no longer receiving corticosteroids at wk200. The average prednisone-equivalent (P.Eq) corticosteroid dose among pts receiving corticosteroids at maintenance baseline in the q8w group was 15.4 mg/day and 1.7, 2.3, and 2.8 mg/day at wks44, 152, 200, respectively. In the q12w group, average P.Eq doses were 15.4, 1.2, 3.6, and 4.0 mg/day, respectively.

Rates of corticosteroid-free symptomatic remission at wk200 were generally similar for the q8w and q12w maintenance doses (Table 1). Of the UST-treated pts who were in symptomatic remission at wk200, 94/96 (97.9%) in the q12w group and 91/96 (94.8%) in the q8w group were corticosteroid free.

Analysis	90 mg UST SC q12w ^a	90 mg UST SC q8w ^a	Combined UST ^a
Randomized patients in maintenance who were treated in the LTE, N	141	143	284
Patients in symptomatic remission, n/N (%)^{d,e,f}			
Week 44	117/141 (83.0%)	119/143 (83.2%)	236/284 (83.1%)
Week 200	96/141 (68.1%)	96/143 (67.1%)	192/284 (67.6%)
Patients in symptomatic remission and not receiving corticosteroids, n/N (%)^{d,e,f}			
Week 44	111/141 (78.7%)	115/143 (80.4%)	226/284 (79.6%)
Week 200	94/141 (66.7%)	91/143 (63.6%)	185/284 (65.1%)
Patients in symptomatic remission and not receiving corticosteroids among patients receiving corticosteroids at maintenance baseline, n/N (%)^{b,c,d,e,f}			
Week 44	49/68 (72.1%)	56/71 (78.9%)	105/139 (75.5%)
Week 200	39/68 (57.4%)	47/71 (66.2%)	86/139 (61.9%)
Patients who were able to eliminate the use of corticosteroids, n/N (%)^{b,c}			
Week 44	61/68 (89.7%)	65/71 (91.5%)	126/139 (90.6%)
Week 200	61/68 (89.7%)	65/71 (91.5%)	126/139 (90.6%)

LTE, long-term extension; q8w, every 8 weeks; q12w, every 12 weeks; SC, subcutaneous; UST, ustekinumab. ^aRandomized group at maintenance Week 0 regardless of whether patients had a dose adjustment during the LTE. ^bPatients who had a missing value in corticosteroid use at the designated visit had their last available value carried forward to the designated visit. ^cDenominator is the number of patients who were receiving concomitant corticosteroids at maintenance baseline. ^dSymptomatic remission is defined as a stool frequency subscore of 0 or 1 and a rectal bleeding subscore of 0. ^ePatients who had both stool frequency and rectal bleeding subscores missing at a visit were considered not to be in symptomatic remission for that visit. ^fPatients who had an ostomy or colectomy, or discontinued study agent due to lack of therapeutic effect or due to an adverse event of worsening of ulcerative colitis prior to the designated visit were considered not to be in symptomatic remission.

Table 1. Symptomatic remission and corticosteroid-sparing effects in patients who were randomized to UST in maintenance and were treated in the long-term extension.

Conclusion: UST maintenance therapy, with both q8w and q12w dosing regimens, was effective in reducing and eliminating the use of corticosteroids in pts with UC through 4 yrs. The majority of pts in symptomatic remission were corticosteroid free through 4 yrs of treatment with UST.

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David S Rowbotham: Reports having received speaker fees from Janssen Research & Development, LLC., and served as an advisory board member for Janssen Research & Development, LLC.

Danese: Reports having received consultancy fees from Janssen and Johnson & Johnson and lecture fees from Janssen.

William J Sandborn: Reports receiving grants and consulting fees from Janssen.

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Maria T Abreu: Reports having received consulting fees from Janssen Research & Development, LLC.

Remo Panaccione: Reports having received consulting fees, speaker fees, and research/educational support from Janssen, and also served on an advisory board for Janssen.

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W Leong: Reports having received grant support from Janssen and consulting fees from Janssen Research & Development, LLC.

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P0396

EFFICACY AND SAFETY OF USTEKINUMAB FOR ULCERATIVE COLITIS THROUGH 4 YEARS: FINAL RESULTS FROM THE UNIFI LONG-TERM EXTENSION

W. Afif¹, M.T. Abreu², S. Danese³, W.J. Sandborn⁴, Y. Miao⁵, H. Zhang⁵, R. Panaccione⁶, T. Hisamatsu⁷, E. Scherl⁸, R.W. Leong⁹, D. Rowbotham¹⁰, R.P. Arasaradnam¹¹, L. Peyrin-Biroulet¹², B.E. Sands¹³, C.W. Marano⁵

¹McGill University Health Center, Gastroenterology, Montreal, Canada, ²University of Miami, Miller School of Medicine, Crohn's and Colitis Center, Miami, United States, ³Vita-Salute San Raffaele University - IRCCS San Raffaele Scientific Institute, Gastrointestinal Immunopathology, Milan, Italy, ⁴University of California San Diego, Division of Gastroenterology, San Diego, United States, ⁵Janssen Research & Development, LLC, Spring House, United States, ⁶University of Calgary, Medicine, Calgary, Canada, ⁷Kyorin University School of Medicine, Department of Gastroenterology and Hepatology, Tokyo, Japan, ⁸Weill Cornell Medicine, New York Presbyterian Hospital, New York, United States, ⁹Concord Hospital, Gastroenterology, Sydney, Australia, ¹⁰Auckland City Hospital, Gastroenterology and Hepatology, Auckland, New Zealand, ¹¹University Hospital Coventry and Warwickshire, Gastroenterology, Coventry Warwickshire, United Kingdom, ¹²Nancy University Hospital, Inserm U 1256 - Team 2 "Inflammation/Cellular Stress and Exposure to Environmental Risks", Vandoeuvre-les-Nancy, France, ¹³Icahn School of Medicine at Mount Sinai, Dr. Henry D. Janowitz Division of Gastroenterology, New York, United States

Contact E-Mail Address: waqqas.afif@mcgill.ca

Introduction: Ustekinumab (UST) is an IL-12/23p40 antagonist approved for treatment of moderate-to-severe ulcerative colitis (UC). Here we report the final results of the UNIFI long-term extension (LTE) study, with efficacy and safety through 4 years (yrs) of subcutaneous (SC) UST treatment.

Aims & Methods: Overall, 523 intravenous UST induction responders were randomized to SC maintenance therapy: 175 SC placebo (PBO); 172 UST 90mg every 12 weeks (q12w); 176 UST 90mg q8w. The nonrandomized population included UST induction nonresponders at week (wk) 8 who received SC UST, responded 8wks later, and continued to receive UST q8w, and responders to PBO induction who received SC PBO. Patients (pts) who completed wk44 were eligible to continue treatment in the LTE. PBO pts were discontinued after study unblinding.

Starting at wk56, randomized pts with UC worsening could adjust to q8w. Efficacy was evaluated in UST-randomized pts (n=284) using symptomatic remission (Mayo stool frequency subscore of 0 or 1 and a rectal bleeding subscore of 0). Safety was evaluated for all 588 pts treated in the LTE, including randomized and nonrandomized populations.

Results: Among all pts randomized to UST at maintenance baseline (intent-to-treat population with nonresponder imputation for missing data and treatment failure criteria), 55.2% were in symptomatic remission at wk200 (biologic naïve 67.2%; biologic failures 41.6%; Table 1); 53.2% of pts achieved corticosteroid-free symptomatic remission at wk200. Overall, 42.7% of biologic failure and 18.8% of biologic naïve pts who were ran-

domized to UST and treated in the LTE discontinued treatment between wks44 and 200. Among randomized pts who continued UST in the LTE, 67.6% were in symptomatic remission at wk200; 72.9% of those in clinical remission at wk44 were in symptomatic remission at wk200; and 85.1% of pts with observed data at wk200 were in symptomatic remission. Safety events were similar among UST-treated pts compared with PBO throughout the study.

From maintenance wk0-220, pts receiving UST and PBO had 1647.4 and 301.7 pt-yrs of follow-up, respectively, and safety events per 100 pt-yrs of follow-up for UST vs PBO were adverse events (AEs): 214.45 vs 288.04, serious AEs: 7.22 vs 10.61, and serious infections: 2.00 vs 3.31.

During the final yr of the LTE, no deaths or major cardiovascular events were reported in UST pts. Among UST pts, 2 cases of colorectal cancer and 1 case of cytomegalovirus were reported.

Analysis	90 mg UST SC q12w ^b	90 mg UST SC q8w ^b	Overall UST
Symptomatic remission in the ITT population^{c,d,e}(treatment failure and missing data nonresponder imputation)			
Week 44, n/N (%)	107/172 (62.2)	119/176 (67.6)	226/348 (64.9)
Week 200, n/N (%)	96/172 (55.8)	96/176 (54.5)	192/348 (55.2)
Symptomatic remission in biologic naïve^f patients			
Week 44, n/N (%)	68/95 (71.6)	57/79 (72.2)	125/174 (71.8)
Week 200, n/N (%)	62/95 (65.3)	55/79 (69.9)	117/174 (67.2)
Symptomatic remission in biologic failure^f patients			
Week 44, n/N (%)	34/70 (48.6)	57/91 (62.6)	91/161 (56.5)
Week 200, n/N (%)	30/70 (42.9)	37/91 (40.7)	67/161 (41.6)
Corticosteroid-free symptomatic remission^{c,d,e,g}			
Week 44, n/N (%)	105/172 (61.0)	116/176 (65.9)	221/348 (63.5)
Week 200, n/N (%)	94/172 (54.7)	91/176 (51.7)	185/348 (53.2)
Symptomatic remission in patients treated in the LTE (treatment failure and missing data nonresponder imputation)^{d,e}			
Week 44, n/N (%)	117/141 (83.0)	119/143 (83.2)	236/284 (83.1)
Week 200, n/N (%)	96/141 (68.1)	96/143 (67.1)	192/284 (67.6)
Symptomatic remission up to the time of dose adjustment with treatment failure rules applied in patients treated in the LTE^d (modified as observed^h)			
Week 44, n/N (%)	117/141 (83.0)	119/143 (83.2)	236/284 (83.1)
Week 200, n/N (%)	58/65 (89.2)	73/89 (82.0)	131/154 (85.1)

AE, adverse event; ITT, intent-to-treat; LTE, long-term extension; q8w, every 8 weeks; q12w, every 12 weeks; SC, subcutaneous; TNF, tumor necrosis factor; UC, ulcerative colitis; UST, ustekinumab

^a Symptomatic remission is defined as a stool frequency subscore of 0 or 1 and a rectal bleeding subscore of 0.

^b Randomized group at maintenance Week 0 regardless of whether or not patients had a dose adjustment during the long-term extension.

^c Patients who had a prohibited change in UC medication, an ostomy or colectomy, or used a rescue medication after clinical flare, or discontinued study agent due to lack of therapeutic effect or due to an AE of worsening of UC prior to the Week 44 visit were considered not to be in symptomatic remission at Week 44.

^d Patients who had an ostomy or colectomy, or discontinued study agent due to lack of therapeutic effect or due to an AE of worsening of UC after Week 44 and prior to Week 200, were considered not to be in symptomatic remission at Week 200.

^e Patients who had both stool frequency and rectal bleeding subscores missing at a visit were considered not to be in symptomatic remission for that visit.

^f Efficacy was evaluated only in patients with a history of biologic failure to ≥1 biologic (anti-TNFα or integrin antagonist) and those who were biologic naïve; 7 UST q12w and 6 UST q8w patients who were biologic-experienced but did not have documentation of biologic failure are excluded.

^g Patients who had a missing value in corticosteroid use had their last value carried forward.

^h The observed data excluded patients with missing data and had not had treatment failure (i.e., an ostomy or colectomy, or discontinued study agent due to lack of therapeutic effect or due to an AE of worsening of UC) prior to the designated visit.

Table 1. Symptomatic remission^a rates during the LTE in randomized patients

Conclusion: Pts receiving SC UST generally maintained clinical benefit through 4yrs. No new safety signals were observed.

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Maria T Abreu: Reports having received consulting fees from Janssen Research & Development, LLC.

Silvio Danese: Reports having received consultancy fees from Janssen and Johnson & Johnson and lecture fees from Janssen.

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Rupert W Leong: Reports having received grant support from Janssen and consulting fees from Janssen Research & Development, LLC.

David S Rowbotham: Reports having received speaker fees from Janssen Research & Development, LLC., and served as an advisory board member for Janssen Research & Development, LLC.

P Arasaradnam: Reports having received grant support and consulting fees from Janssen Research & Development, LLC.

Laurent Peyrin-Biroulet: Reports having received personal fees from Janssen.

Bruce E Sands: Reports having received research grants and consulting fees from Janssen.

Ye Miao, Hongyan Zhang, and Colleen Marano: Employees of Janssen Research & Development, LLC., and own stock/stock options in Johnson & Johnson.

P0397

VIRTUAL BIOLOGICS CLINIC: A STREAMLINED MULTI-DISCIPLINARY TEAM (MDT) APPROACH TO IMPROVE INFLAMMATORY BOWEL DISEASE (IBD) CARE

J. Gertner¹, S. Mann¹, S. Maung¹, Y.M. Thu¹

¹Barnet Hospital, Gastroenterology, London, United Kingdom

Contact E-Mail Address: supyaephyomaung.su@gmail.com

Introduction: The challenges of IBD patients on biologics include complex decision making, securing funding and logistics of administration.

Aims & Methods: Aims: To assess the impact of a Virtual Biologics Clinic (VBC) on clinical decision making and patient outcome.

Methods: Electronic records of IBD patients at Barnet Hospital were retrospectively reviewed. Patients discussed at VBCs conducted by IBD consultant gastroenterologists, nurses and pharmacists from 09/2019 to 01/2022 were included.

Results: 66 patients were reviewed, 2 excluded due to misdiagnosis and death. 24 patients had UC and 40 Crohn's disease; 48% were female and median age was 43.

Of those with UC, 58% had left sided disease only, 42% had pancolitis. Clinically, 55% had mild to moderate disease and 45% moderate to severe. Of those with Crohn's, 80% had terminal ileal disease, 63% colonic disease and 30% perianal disease. 43% had stricturing disease and 38% fistulating disease. Clinically, 30% had mild disease, 50% moderate and 20% severe. 80% of all patients used biologics previously with infliximab (63%), adalimumab (49%), vedolizumab (20%) or ustekinumab (12%). Previous treatments also included azathioprine in 67% of patients, mesalazine 25%, 6-mercaptopurine 16%, methotrexate 8%, sulfasalazine 2%, and tofacitinib 2%.

At VBC, 67% patients were on biologics: infliximab (20%), adalimumab (19%), vedolizumab (14%), or ustekinumab (14%). 92% of patients on infliximab had drug levels and/or antibodies measured.

Of those tested, none had positive antibodies. 81% had faecal calprotectin available and 50% of those had results >1000µg/g; 28% had endoscopies of which there was quiescent disease in 6%, mild 22%, moderate 33%, severe 22%, stricturing 11% and suboptimal views 6%. 44% of endoscopies had histology confirming active disease.

Reasons for VBC discussion were inadequate disease control (64%), funding review (9%), remission (2%), reactions to biologics (3%), or other (22%).

Outcomes from VBC were to switch biologics (23%), continue current treatment (22%), escalate frequency or dose (14%), stop biologics (13%), rediscuss after further investigations (8%), start biologics (6%), re-initiate biologics (5%) or other (9%).

60 VBC outcomes were confirmed as actioned. 1 was not actioned due to patient choice, 2 are pending and 1 patient was uncontactable.

At latest follow up 52% showed clinical response or were in remission and 34% were clinically symptomatic. 14% of patients are awaiting follow up.

Conclusion: VBC is an effective resource for clinical decision making in IBD patients requiring biologics.

Over half the patients reviewed following VBC showed at least clinical improvement.

VBC is a robust approach of ensuring multifaceted management plans are actioned.

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P0398

IMPACT OF BIOLOGIC THERAPIES AND SMALL MOLECULES ON THE RISK OF MAJOR ADVERSE CARDIOVASCULAR EVENTS IN ULCERATIVE COLITIS: A SYSTEMATIC REVIEW AND META-ANALYSIS OF RANDOMIZED CONTROLLED TRIALS

M. Shehab¹, A. Alkazemi², F. Alrashed², P.L. Lakatos³, T. Bessissow³

¹Mubarak Hospital/Kuwait University, Gastroenterology, Aljabreayah, Kuwait, ²Kuwait University, Pharmacy Practice, Aljabreayah, Kuwait, ³McGill University Health Center, Division of Gastroenterology, Montreal, Canada

Contact E-Mail Address: Dr_mshehab@hotmail.com

Introduction: The risk of major adverse cardiovascular events (MACE) in patients with ulcerative colitis (UC) receiving biologic therapies and small molecules is not well documented in the literature.

The aim of this systematic review and meta-analysis is to estimate the risk of MACE in adult patients with UC receiving biologic therapies and small molecule therapy.

Aims & Methods: We systematically searched PubMed/Midline, Cochrane Central Register of Controlled Trials, Scopus, and Embase databases to identify eligible studies that assessed the risk of MACE in patients with UC on biologic therapies or small molecules (age ≥18 years). Eligible studies were phase 3, randomized placebo or active-controlled trials (RCTs).

Our primary outcome was the risk for MACE in patients receiving biologic therapies or small molecules during induction and maintenance phases of RCTs. Random effects model was used to calculate pooled odds ratios (ORs) and 95% CIs. I² statistics was used to assess heterogeneity.

Results: Overall, 45 RCTs involving 22,007 patients with UC were included in our systematic review and meta-analysis. 14,193 (64.5%) patients were receiving biologic therapies and 7,814 (35.5%) patients were receiving small molecules.

There was no statistically significant difference in risk of MACE associated with the use of biologic therapies/small molecules during induction and maintenance therapies; infliximab (OR 0.71, 95% CI 0.23–2.21), adalimumab (OR 0.95, 95% CI 0.05–2.57), etrolizumab (OR 0.93, 95% CI 0.21–4.10), golimumab (OR 0.36, 95% CI 0.21–4.10), ustekinumab (OR 0.31, 95% CI 0.04–2.54), vedolizumab (OR 0.44, 95% CI 0.09–2.15), filgotinib (OR 0.39, 95% CI 0.05–3.08), ozanimod (OR 0.52, 95% CI 0.03–8.30), tofacitinib (OR 1.63, 95% CI 0.28–9.42) and upadactinib (OR 0.31, 95% CI 0.04–2.52).

Conclusion: Biologic therapies and small molecules are not associated with major adverse cardiovascular events (MACE) in ulcerative colitis.

Disclosure: Nothing to disclose

P0399

EARLY INTERVENTION WITH BIOLOGICS IN CROHN’S DISEASE - HOW EARLY IS EARLY?

J. Revés¹, A. Mascarenhas², M.J. Temido³, B. Morão¹, A.C. Bravo¹, B. Abreu¹, C. Nascimento¹, C. Frias Gomes¹, A.R. Franco², R.R. Mendes², C. Palmela¹, M.L. Gloria¹, P. Narra Figueiredo³, F. Silva Portela³, J. Torres¹

¹Hospital Beatriz Ângelo, Gastroenterology Department, Loures, Portugal, ²Centro Hospitalar Lisboa Ocidental, Gastroenterology Department, Lisboa, Portugal, ³Centro Hospitalar e Universitário de Coimbra, Gastroenterology Department, Coimbra, Portugal

Contact E-Mail Address: joanareves94@gmail.com

Introduction: Post-hoc analysis from randomized controlled trials (RCTs) has shown that early intervention (< 24 months) with biologic therapy is associated with better outcomes in Crohn’s disease (CD). We aimed to assess the best time for early biologic therapy initiation.

Aims & Methods: Multicentric retrospective cohort study including newly diagnosed CD patients that started biologic treatment within 24 months from diagnosis. The primary outcome was a composite of switching biologic, hospitalization due to a CD flare and need for intestinal surgery. The secondary outcomes were clinical remission (Harvey-Bradshaw Index - HBI<5), endoscopic healing - EH (SES-CD<3 or absence of ulcers) and transmural healing - TH (absence of active inflammation, extra-enteric signs and CD-related complications), assessed at 12±6 months after therapy initiation. Analysis was performed using cox regression and logistic regression.

Results: 125 patients were included (61% males), with a median age at diagnosis of 26yo (IQR 20-42). Most frequently (46%) patients presented with ileocolonic disease (L3) and 62% had a non-complicated (B1) phenotype. Seventy-two (58%) patients started biologic within 6 months from diagnosis and 102 (82%) within 12 months. The median follow-up time was 33 months (IQR 19-60).

All patients were started on anti-TNF and 52% on combination therapy. Forty-four (35%) patients experienced the primary outcome after a median time of 11 months (IQR 6-22) - 22% switched biologic, 14% were hospitalized and 10% needed surgery.

There was no significant difference in the time to the primary outcome between patients who started biologic ≤6months vs >6 months (HR 1.69, 95%CI 0.90-3.17, p=0.1) and between patients who started biologic ≤12months vs >12 months (HR 0.90, 95%CI 0.41-1.96, p=0.8).

Clinical remission and EH rates were high (86% and 53%, respectively), although there were no significant differences according to the time of initiation of biologic therapy (except for a slight difference between patients

who started biologic ≤6 months and patients who started biologic 13-18 months from diagnosis). The TH rate was 29% and there was no difference between groups (Table 1).

In a multivariate logistic regression analysis adjusted for gender, age at diagnosis, B2/B3 phenotype, perianal disease at diagnosis and use of combination therapy, the time of initiation of biologic treatment (in 6 months categories) remained a non-significant predictor for the achievement of clinical remission (OR 0.76, 95%CI 0.45-1.26, p=0.3), EH (OR 1.03, 95%CI 0.64-1.66, p=0.9) or TH (OR 1.16, 95%CI 0.63-2.14, p=0.6).

Secondary outcomes	≤6 months	7-12 months	13-18 months	19-24 months	p-value*
Clinical remission (Harvey-Bradshaw Index <5)	90% (64/71)	81% (25/31)	67% (8/12)	91% (10/11)	0.1
Endoscopic healing (SES-CD <3 or absence of ulcerations)	53% (27/51)	63% (15/24)	25% (2/8)	57% (4/7)	0.3
Transmural healing (absence of active inflammation, no extra-enteric signs, and no CD-related complications)	25% (14/55)	42% (8/19)	33% (3/9)	0% (0/4)	0.3

*p-value remained non-significant (>0.05) when comparing between groups, except for clinical remission in patients who started biologic ≤6 months and patients who started biologic 13-18 months from diagnosis (90% vs 67%, p=0.03).

Table 1 - Rates of clinical remission, EH and TH according to the time of initiation of biologic therapy

Conclusion: Starting biologic within 24 months of diagnosis is associated with high rates of clinical remission and EH, although TH was obtained in less than 30% of the patients. We found no differences between outcomes and earlier initiation of biologic therapy.

Disclosure: Nothing to disclose

P0400

NON-MEDICAL, MANDATORY SWITCH AMONG ADALIMUMAB BIOSIMILARS AND FROM THE ORIGINATOR ADALIMUMAB TO BIOSIMILARS IN INFLAMMATORY BOWEL DISEASE PATIENTS – A PROSPECTIVE, MULTICENTRE STUDY ON EFFICACY, DRUG SUSTAINABILITY AND SAFETY

L. Lontai¹, L. Gonczi¹, F. Balogh¹, N. Komlodi¹, T. Resál², K. Farkas², T. Molnár², P. Miheller³, P.A. Golovics⁴, E. Schäfer⁴, T. Szamosi⁴, Á. Iliás¹, P.L. Lakatos⁵

¹Semmelweis University, Department of Internal Medicine and Oncology, Budapest, Hungary, ²University of Szeged, I. st Department of Internal Medicine, Szeged, Hungary, ³Semmelweis University, Department of Surgery, Transplantation and Gastroenterology, Budapest, Hungary, ⁴Hungarian Defence Forces Medical Centre, Department of Gastroenterology, Budapest, Hungary, ⁵McGill University Health Center, Division of Gastroenterology, Montreal, Canada

Contact E-Mail Address: lorantgonczi@gmail.com

Introduction: The use of biosimilar adalimumab (ADA) is effective and safe in inflammatory bowel disease (IBD). Switching from the originator to a biosimilar has been successful in multiple IBD cohorts, although clinical data on switching between ADA biosimilars is still rare.

At the end of 2020, a non-medical switch to biosimilar ADA became mandatory in Hungary due to reimbursement policy changes of the National Health Insurance Fund of Hungary (NEAK).

Aims & Methods: The aim of the present study was to evaluate short- and medium term clinical efficacy, drug sustainability and safety comparing non-medical switches from the originator to biosimilar ADA, and between ADA biosimilars. 276 consecutive patients on maintenance ADA therapy (n=205 Crohn's disease[CD], n=71 ulcerative colitis[UC], male/female:n=110/166) were included between September 2019 and December 2020. Data on clinical efficacy, biomarkers and adverse events were collected 8-12 weeks prior switch, at baseline, 8-12 weeks and 20-24 weeks after switch. Drug sustainability following the switch was evaluated at a median 40(IQR:35-42) weeks follow-up.

Results: A total 174 patients underwent a non-medical switch from the originator to a biosimilar, and 102 patients had a biosimilar-to-biosimilar switch. No significant difference was found in clinical remission rates at week 8-12 prior/ baseline /week 8-12 and week 20-24 after switch in patients switching from originator to biosimilar(87.3%/88.5%/86.5%/85.7%) or biosimilar to biosimilar(74.5%/78.4%/85.3%/79.8%).

Among patients in clinical remission at switch/baseline, 93.4% sustained clinical remission at week 8-12 and 89.9% up to week 20-24 in the originator-to-biosimilar group. In the biosimilar-to-biosimilar switch group, 96.3% sustained clinical remission at week 8-12 and 84.9% up to week 20-24. Mean CRP levels were unchanged during follow-up in both cohorts(p=0.856 and p=0.525).

Drug survival was similar between the two cohorts with a probability of 91.6%(SE: 2.2) and 87.0%(SE:3.4) to stay on drug after 40 weeks(log-rank:0.96; p=0.327). Five adverse events were reported, three of them leading to treatment discontinuation.

Conclusion: Clinical benefit was sustained following non-medical switch from originator to biosimilar, or between biosimilars in adalimumab treated IBD patients. Drug sustainability following the switch was high and not different between the two groups.

Disclosure: Nothing to disclose.

P0401

HEALTH-RELATED QUALITY OF LIFE WITH GUSELKUMAB INDUCTION AND MAINTENANCE THERAPY AS MEASURED BY PROMIS-29: RESULTS THROUGH WEEK 48 OF PHASE 2 GALAXI 1 STUDY

G. D'Haens¹, B.E. Sands², R. Panaccione³, C. Han⁴, S. Gonzalez⁵, K. Weisel⁵, M.E. Frustuaci⁵, Z. Yang⁵, A. Sahoo⁵, A. Afzali⁶, J.M. Andrews⁷, S. Danese⁸, T. Hisamatsu⁹, B. Feagan¹⁰, J. Panés¹¹, W. Reinisch¹², W.J. Sandborn¹³, D.T. Rubin¹⁴

¹Amsterdam UMC, Amsterdam, Netherlands, ²Icahn School of Medicine at Mount Sinai, New York, United States, ³University of Calgary, Calgary, Canada, ⁴Janssen Global Services, LLC, Malvern, United States, ⁵Janssen Research & Development, LLC, Spring House, United States, ⁶The Ohio State University Wexner Medical Center, Columbus, United States, ⁷Royal Adelaide Hospital & University of Adelaide, Adelaide, Australia, ⁸IRCCS Ospedale San Raffaele and University Vita-Salute San Raffaele, Gastroenterology and Endoscopy, Milan, Italy, ⁹Kyorin University, Tokyo, Japan, ¹⁰Alimentiv Inc., Gastroenterology, London, Canada, ¹¹Hospital Clínic Barcelona, Gastroenterology, Barcelona, Spain, ¹²Medical University of Vienna, Internal Medicine IV, Division of Gastroenterology and Hepatology, Vienna, Austria, ¹³University of California San Diego, Division of Gastroenterology, San Diego, United States, ¹⁴University of Chicago Medicine, Chicago, United States

Contact E-Mail Address: g.dhaens@amsterdamumc.nl

Introduction: Patients with CD suffer from symptoms that negatively impact their health-related quality of life (HRQOL). In GALAXI 1, a ph2, double-blind, PBO-controlled study of guselkumab (GUS), a selective IL-23 antagonist, for the treatment of pts with moderately to severely active CD who had inadequate response or intolerance to conventional therapies (corticosteroid, immunosuppressant) and/or biologics (tumor necrosis factor antagonist, vedolizumab), HRQoL was evaluated using the Patient-Reported Outcomes Measurement Information System (PROMIS)-29.

Aims & Methods: GALAXI has a treat-through design with pts remaining on randomized treatment (GUS or ustekinumab [UST]) through Wk48. Pts were randomized 1:1:1:1:1 into 5 arms for induction: GUS 200, 600, or 1200mg IV at Weeks (Wks) 0, 4, 8; UST ~6mg/kg IV at Wk0 and 90mg SC at Wk8; or PBO IV. At Wk12, pts transitioned to maintenance as follows: GUS 200mg IV→100mg SC q8w, GUS 600mg IV→ 200mg SC q4w, GUS 1200mg IV→ 200mg SC q4w, PBO non-responders→ UST ~6mg/kg IV→ 90mg SC q8w, and PBO responders→ PBO SC q4w. UST pts continued 90mg SC q8w. Pts randomized to PBO were not included in Wk48 analyses.

PROMIS-29 consists of 7 domains (depression, anxiety, physical function, pain interference, fatigue, sleep disturbance, and social participation) and a pain intensity 0-10 numeric rating scale (NRS). The raw score of each domain is converted into a standardized T-score with a general population mean of 50 and standard deviation (SD) of 10. For physical function and social participation, higher scores indicate better outcomes, while for all other symptom domains like anxiety, higher scores indicate worse outcomes. Clinically meaningful improvement was defined as ≥3-point improvement in pain NRS score and ≥5-point (or 1/2 SD of population) improvement in each domain T-score.

Results: Among pts randomized and evaluated in the primary efficacy analysis, mean PROMIS-29 domain scores were similar between treatment groups at baseline with functional domain score <50 and symptom domain scores >50, indicating impaired HRQOL (Table 1).

Pts treated with GUS had greater improvement in all 7 domain scores at Wk12 compared with PBO. GUS treatment resulted in continued improvement in domain scores from Wk12 to Wk48. For the GUS combined group, mean change from baseline in domain T-scores at Wk12 and Wk48 were

	Placebo (N=61)	GUS 200 mg IV q4w →100 mg SC q8w (N=61)	GUS 600 mg IV q4w →200 mg SC q4w (N=63)	GUS 1200 mg IV q4w →200 mg SC q4w (N=61)	UST ~6 mg/kg IV →90 mg SC q8w (N=63)
Anxiety T-score^{a,b}					
Baseline, mean (SD)	57.68 (10.004), N=57	56.43 (9.344), N=60	56.94 (9.843), N=63	57.29 (9.455), N=61	54.25 (9.068), N=63
Change from baseline, mean (SD), at:					
Wk 12	-0.73 (8.872), N=56	-4.63 (8.869),* N=58	-3.43 (9.178),* N=61	-6.78 (7.805),** N=57	-3.86 (7.908), N=63
Wk 48		-5.66 (10.437), N=56	-4.85 (8.831), N=58	-6.34 (10.188), N=49	-5.09 (6.624), N=59
Depression T-score^{a,b}					
Baseline, mean (SD)		54.33 (9.306), N=60	53.64 (10.567), N=63	54.07 (9.499), N=61	52.20 (8.619), N=63
Change from baseline, mean (SD), at:	54.99 (9.386), N=57	-4.54 (10.567),** N=58	-1.98 (7.123),* N=61	-5.48 (6.999),** N=57	-3.70 (8.217), N=63
Wk 12		-4.91 (11.899), N=56	-3.33 (8.077), N=58	-5.52 (9.559), N=49	-2.86 (7.055), N=59
Wk 48	-0.17 (8.384), N=56				
Fatigue T-score^{a,b}					
Baseline, mean (SD)	57.80 (9.128), N=57	56.36 (9.193), N=60	56.74 (10.097), N=63	58.35 (9.361), N=61	56.03 (8.991), N=63
Change from baseline, mean (SD), at:					
Wk 12	-0.89 (9.640)	-7.33 (9.320),** N=58	-6.30 (9.314),** N=61	-7.27 (8.021),** N=57	-5.91 (10.467), N=63
Wk 48		-7.59 (10.587), N=56	-9.53 (9.903), N=58	-8.03 (9.114), N=49	-7.44 (9.369), N=59
Pain interference T-score^{a,b}					
Baseline, mean (SD)	62.25 (6.625), N=57	60.26 (8.550), N=60	62.26 (6.337), N=63	60.69 (7.418), N=61	60.37 (8.431), N=63
Change from baseline, mean (SD), at:					
Wk 12	-2.43 (7.811), N=56	-8.19 (9.467),** N=58	-9.29 (8.997),** N=61	-6.60 (7.659),** N=57	-7.93 (9.854), N=63
Wk 48		-10.71 (10.989), N=56	-13.44 (9.060), N=58	-10.34 (9.568), N=49	-7.70 (9.334), N=59
Pain intensity NRS score^{a,b}					
Baseline, mean (SD)	5.53 (2.122), N=57	5.13 (2.012), N=60	5.49 (1.925), N=63	5.46 (2.038), N=61	5.37 (2.238), N=63
Change from baseline, mean (SD), at:					
Wk 12	-0.84 (2.380), N=56	-2.41 (2.740),** N=58	-2.82 (2.164),** N=61	-2.30 (2.420),** N=57	-2.21 (2.259), N=63
Wk 48		-3.11 (2.695), N=56	-3.53 (2.494), N=58	-2.88 (2.990), N=49	-2.73 (2.420), N=59
Physical Function T-score^{a,b}					
Baseline, mean (SD)	42.70 (7.491), N=57	44.71 (8.391), N=60	45.24 (7.888), N=63	43.16 (8.275), N=61	45.72 (8.056), N=63
Change from baseline, mean (SD), at:					
Wk 12	1.24 (8.106), N=56	4.64 (8.249),* N=58	3.73 (7.053),* N=61	3.40 (8.037),* N=57	3.30 (7.888), N=63
Wk 48		5.98 (8.851), N=56	5.73 (8.242), N=58	5.18 (8.243), N=49	3.80 (7.307), N=59
Sleep disturbance T-score^{a,b}					
Baseline, mean (SD)	55.06 (8.418), N=57	54.19 (8.062), N=60	54.84 (7.181), N=63	53.23 (7.447), N=61	52.55 (7.408), N=63
Change from baseline, mean (SD), at:					
Wk 12	-0.88 (6.833), N=56	-4.83 (8.489),** N=58	-4.05 (5.805),* N=61	-4.02 (5.727),** N=57	-3.16 (8.143), N=63
Wk 48		-5.36 (8.520), N=56	-6.28 (7.636), N=58	-5.48 (7.018), N=49	-4.61 (7.580), N=59
Ability to participate in social roles and activities T-score^{a,b}					
Baseline, mean (SD)		46.25 (9.278), N=60	46.80 (8.705), N=63	45.40 (9.329), N=61	47.99 (8.827), N=63
Change from baseline, mean (SD), at:					
Wk 12	45.50 (7.990), N=57	6.54 (8.867),** N=58	5.18 (9.922),** N=61	5.49 (7.130),** N=57	4.81 (8.364), N=63
Wk 48	0.58 (7.962), N=56	7.65 (10.842), N=56	8.56 (9.877), N=58	7.10 (8.142), N=49	5.44 (8.757), N=59

*Nominal p-value <0.05 for guselkumab vs placebo at Wk 12. **Nominal p-value <0.001 for guselkumab vs placebo at Wk 12.

^aPatients who had a prohibited change in concomitant Crohn's disease medication, a Crohn's disease-related surgery, or discontinued study agent due to lack of efficacy or an AE of worsening Crohn's disease prior to the designated analysis timepoint had their baseline value carried forward from that timepoint onwards. Patients who had discontinued study agent due to any other reasons prior to the designated analysis timepoint had their observed data used, if available, from that timepoint onwards.

^bPatients who had insufficient data to calculate PROMIS-29 domain score at the designated analysis timepoint did not have their missing data imputed.

NOTE: No comparisons between ustekinumab and placebo were made at Wk 12. No treatment comparisons were made at Wk 48. The p-values for the comparisons of each guselkumab treatment group with the placebo group at Wk 12 were based on MMRM analysis including change from baseline in PROMIS-29 domain score as the response; treatment group, visit, baseline PROMIS-29 domain score, BIO-Failure status (yes, no), baseline CDAI stratification (≤300, >300), an interaction term of visit with treatment group and an interaction term of visit with baseline PROMIS-29 domain score as explanatory variables.

P0401 Table 1. Change from BL at Wk12 and Wk48 for PROMIS-29 Scores

-4.91 and -5.58 for anxiety, -3.96 and -4.53 for depression, -6.95 and -8.41 for fatigue, -8.05 and -11.57 for pain interference, 3.92 and 5.65 for physical function, -4.30 and -5.73 for sleep disturbance, and 5.73 and 7.81 for ability to participate in social roles and activities; mean change from baseline in pain intensity NRS scores at Wk12 and Wk48 were -2.52 and -3.19. GUS-treated pts achieved clinically meaningful improvement in fatigue T-scores (45.9-63.5%), pain interference T-scores (52.5-71.4%) and pain intensity NRS score at Wk48 (56.4-70.2%).

Conclusion: Induction and maintenance treatment with GUS was effective in improving HRQoL as measured by PROMIS-29 domains in pts with moderately to severely active CD at Wk48.

Disclosure: D'Haens: Advisor for Abbvie, Ablynx, Amakem, Amgen, AM Pharma, Avaxia, Biogen, Bristol Meiers Squibb, Boehringer Ingelheim, Celgene/Receptos, Celltrion, Cosmo, Covidien/Medtronic, Ferring, DrFALK Pharma, Eli Lilly, Engene, Galapagos, Genentech/Roche, Gilead, Glaxo Smith Kline, Immunic, Johnson and Johnson, Lycera, Medimetrics, Mil-

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Han, Weisel, Frustaci, Yang, Sahoo: Employees of JNJ and owns company stock/stock options.

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P0402

OZANIMOD EFFICACY BY BASELINE ENDOSCOPIC DISEASE

DISTRIBUTION IN PATIENTS WITH MODERATE TO SEVERE ULCERATIVE COLITIS: A POST HOC ANALYSIS FROM TRUE NORTH

A. Dignass¹, A. Afzali², M. Fischer³, C. Sninsky⁴, A. Armuzzi⁵, C. Wu⁶, H. Ahmad⁶, A. Memaj⁶, S. Harris⁶, J. Canavan⁶, S. Schreiber⁷
¹Agaplesion Markus Hospital, Goethe University, Frankfurt, Germany, ²The Ohio State University Wexner Medical Center, Columbus, United States, ³Indiana University, Indianapolis, United States, ⁴Digestive Disease Associates, Gainesville, United States, ⁵RCCS Humanitas Research Hospital Humanitas University, Milan, Italy, ⁶Bristol Myers Squibb, Princeton, United States, ⁷Department of Internal Medicine I, University Hospital Schleswig-Holstein, Kiel University, Kiel, Germany

Contact E-Mail Address: axel.dignass@agaplesion.de

Introduction: Ozanimod (OZA), an oral small molecule sphingosine 1-phosphate (S1P) receptor modulator with high affinity to S1P₁ and S1P₅, prevents lymphocyte migration to the intestines through S1P receptor internalization. OZA is approved for treating moderately to severely active ulcerative colitis (UC) in Europe and the United States. True North (TN; NCT02435992), a randomized, double-blind, placebo (PBO)-controlled phase 3 trial, showed the efficacy and tolerability of OZA in patients (pts) with UC. Pts with pancolitis may have increased symptomatology and a higher risk of colectomy than pts with left-sided UC.

Aims & Methods: This TN post hoc analysis assessed the effect of baseline endoscopic disease distribution (left-sided vs pancolitis) on clinical outcomes in UC pts treated with OZA. In TN, pts were randomized to OZA

0.92 mg (equivalent to OZA HCl 1 mg) once daily or PBO (Cohort 1) or received open-label OZA (Cohort 2) during the induction period (IP). Pts with clinical response to OZA at Week 10 in either cohort were randomized to double-blind OZA or PBO for the maintenance period (MP). This analysis assessed efficacy outcomes at Weeks 10 (IP) and 52 (MP).

Results: Overall, baseline demographics and disease characteristics were similar between left-sided and extensive UC pts. OZA was more effective than PBO in left-sided and extensive UC pts at Week 10 for all evaluated clinical outcomes (Table).

Treatment effects (OZA vs PBO based on the Cochran-Mantel-Haenszel [CMH] test, stratified by corticosteroid [CS] use at screening and prior anti-tumor necrosis factor use) were generally similar for left-sided and extensive UC pts at Week 10: clinical remission (odds ratio [OR] 4.1 [95% CI 1.9-9.0]; $P=0.0001$ and 2.8 [95% CI 1.0-7.6]; $P=0.0387$), clinical response (3.0 [1.9-4.7]; $P=0.0001$ and 2.3 [1.3-4.2]; $P=0.0066$), endoscopic improvement (2.9 [1.6-5.0]; $P<0.001$ and 2.5 [1.1-5.7]; $P=0.024$), and mucosal healing (5.4 [1.9-15.4]; $P=0.0006$ and 2.1 [0.7-6.5]; $P=0.1675$), respectively. At Week 52, continuous OZA was more effective than OZA-PBO in left-sided and extensive UC pts (Table).

CS remission was achieved in 30.9% and 17.2% OZA-OZA and OZA-PBO left-sided UC pts, and in 33.3% and 15.7% OZA-OZA and OZA-PBO extensive UC pts. Treatment effects (OZA-OZA vs OZA-PBO based on CMH test stratified by remission status at Week 10 and CS use at Week 10) were generally similar for left-sided and extensive UC pts: clinical remission (OR 2.7 [95% CI 1.6-4.5]; $P=0.0003$ and 2.8 [95% CI 1.3-6.2]; $P=0.0084$), clinical response (2.4 [1.5-3.8]; $P=0.0003$ and 2.0 [1.0-3.9]; $P=0.0468$), endoscopic improvement (2.4 [1.5-3.9]; $P<0.001$ and 2.8 [1.3-6.1]; $P=0.007$), CS-free remission (2.3 [1.3-4.0]; $P=0.0040$ and 3.4 [1.5-8.0]; $P=0.0035$), and mucosal healing (2.4 [1.4-4.2]; $P=0.0022$ and 4.0 [1.6-10.6]; $P=0.0033$), respectively.

		IP: Cohort 1		IP: Cohort 2	MP	
Number (%) of pts achieving clinical outcomes		PBO	OZA 0.92 mg	OZA 0.92 mg	OZA-PBO	OZA-OZA
Left-Sided Subgroup (n=639)	Clinical remission	8/134 (6.0%)	55/268 (20.5%)	57/237 (24.1%)	29/157 (18.5%)	57/152 (37.5%)
	Clinical response	36/134 (26.9%)	138/268 (51.5%)	130/237 (54.9%)	65/157 (41.4%)	95/152 (62.5%)
	Endoscopic improvement	18/134 (13.4%)	83/268 (31.0%)	70/237 (29.5%)	45/157 (28.7%)	74/152 (48.7%)
	Mucosal healing	4/134 (3.0%)	38/268 (14.2%)	29/237 (12.2%)	25/157 (15.9%)	47/152 (30.9%)
Extensive Subgroup (n=373)	Clinical remission	5/82 (6.1%)	24/161 (14.9%)	20/130 (15.4%)	13/70 (18.6%)	28/78 (35.9%)
	Clinical response	20/82 (24.4%)	67/161 (41.6%)	63/130 (48.5%)	28/70 (40.0%)	43/78 (55.1%)
	Endoscopic improvement	8/82 (9.8%)	34/161 (21.1%)	30/130 (23.1%)	15/70 (21.4%)	31/78 (39.7%)
	Mucosal healing	4/82 (4.9%)	16/161 (9.9%)	13/130 (10.0%)	7/70 (10.0%)	21/78 (26.9%)

Table.

Conclusion: OZA was more effective than PBO in both left-sided and extensive UC at Weeks 10 and 52. Treatment effects of OZA were similar between left-sided and extensive UC pts across most clinical endpoints.

Disclosure: Axel Dignass: received fees for participation in clinical trials and review activities (eg, data monitoring boards, statistical analysis, and end point committees) from Falk Foundation, AbbVie, Janssen, Gilead, Celgene/Bristol Myers Squibb, and Pfizer; consultancy fees from AbbVie, MSD, Ferring, Roche/Genentech, Takeda, Vifor, Pharmacosmos, Boehringer Ingelheim, Gilead, Galapagos, Biogen, Falk, Janssen, Pfizer, Sandoz/Hexal, Celgene/Bristol Myers Squibb, Tillotts, Eli Lilly, Amgen, and Fresenius Kabi; payment from lectures, including service on speakers bureaus,

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Charles Sninsky: served as a speaker for Janssen, AbbVie, UCB, Pfizer, Bristol Myers Squibb, and Takeda.

Alessandro Armuzzi: received consulting and/or advisory board fees from AbbVie, Allergan, Amgen, Arena, Biogen, Bristol Myers Squibb, Celltrion, Eli Lilly, Ferring, Galapagos, Gilead, Janssen, MSD, Mylan, Pfizer, Protagonist Therapeutics, Roche, Samsung Bioepis, Sandoz, and Takeda; received lecture and/or speaker bureau fees from AbbVie, Amgen, Biogen, Bristol Myers Squibb, Celltrion, Eli Lilly, Ferring, Galapagos, Gilead, Janssen, MSD, Mitsubishi Tanabe, Novartis, Pfizer, Roche, Samsung Bioepis, Sandoz, Takeda, and TiGenix; and received research grants from MSD, Pfizer, and Takeda.

Chun Wu, Harris Ahmad, Arteid Memaj, Sarah Harris, and James Canavan: employees and may be shareholders of Bristol Myers Squibb.

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P0403

EVALUATION OF OZANIMOD EFFICACY AND SAFETY IN OLDER PATIENTS WITH ULCERATIVE COLITIS: POST HOC ANALYSIS FROM THE PHASE 3 TRUE NORTH STUDY

P. Irving¹, A. Ananthakrishnan², I. Blumenstein³, S. Horst⁴, H. Ahmad⁵, G. Lawlor⁵, V. Hobbs⁵, A. Jain⁵, A. Memaj⁵, N. Khan⁶
¹Guy's and St Thomas' NHS Foundation Trust, London, United Kingdom, ²Massachusetts General Hospital & Harvard Medical School, Boston, United States, ³Goethe University Hospital, Frankfurt, Germany, ⁴Vanderbilt University Medical Center, Nashville, United States, ⁵Bristol Myers Squibb, Princeton, United States, ⁶Corporal Michael J Crescenz VA Medical Center, Philadelphia, United States

Contact E-Mail Address: peter.irving@gstt.nhs.uk

Introduction: Ozanimod (OZA), an oral sphingosine 1-phosphate (S1P) receptor modulator, is approved for the treatment of moderately to severely active ulcerative colitis (UC) in Europe and the United States. OZA induces S1P receptor internalization in lymphoid tissue, reducing lymphocyte egress to inflamed tissue.

The prevalence of inflammatory bowel disease (IBD) is increasing in the older population; currently, 25%–30% of patients (pts) with IBD are aged ≥60 years.^{1,2} Older pts, who generally have more comorbidities than younger pts, represent an understudied population in IBD.

Aims & Methods: This post hoc analysis from the phase 3 True North (TN) trial (NCT02435992)³ examined the efficacy and safety of OZA in pts aged <60 y and ≥60 y. Pts were randomized to double-blind OZA 0.92 mg (equivalent to OZA HCl 1 mg) or placebo (PBO; Cohort 1) or received open-label OZA (Cohort 2) during the 10-week (wk) induction period (IP). Pts with clinical response to OZA at Wk 10 were re-randomized to double-blind OZA or PBO for maintenance through Wk 52.

Efficacy endpoints (clinical remission, clinical response, endoscopic improvement, and mucosal healing) were assessed at Wks 10 and 52; adjusted treatment differences for OZA vs PBO were calculated using the Cochran-Mantel-Haenszel test. Treatment-emergent adverse events (TEAEs) and adverse events of special interest (AESIs) were assessed throughout the study.

Results: A total of 562 pts aged <60 y (OZA, n=376; PBO, n=186) and 83 pts aged ≥60 y (OZA, n=53; PBO, n=30) from Cohort 1 and 315 pts (<60 y) and 52 pts (≥60 y) from Cohort 2 were included in this analysis. During maintenance, 196 pts (<60 y) and 34 pts (≥60 y) continued on OZA treatment; 196 pts (<60 y) and 31 pts (≥60 y) were re-randomized to PBO.

Demographics and baseline disease characteristics were generally well balanced across treatment and age groups, but older pts had less-extensive disease, lower baseline fecal calprotectin levels, and more polypharmacy.

Adjusted treatment differences favored OZA vs PBO and were generally similar between the age groups across all efficacy endpoints at Wks 10 and 52. PBO response rates were higher in older vs younger pts. During IP, incidence of TEAEs with OZA in Cohorts 1 and 2 was lower in older (36% and 31%) vs younger pts (41% and 41%). Rates of serious TEAEs were similar in older (6% and 4%) vs younger (4% and 7%) pts, and TEAEs leading to treatment discontinuation were comparable in older (2% and 6%) and younger pts (3.5% and 3.5%).

With continued OZA treatment during maintenance, TEAEs occurred more frequently in older (56%) vs younger (48%) pts; however, serious TEAEs were less frequent in older pts (3% vs 6%). TEAEs leading to treatment discontinuation were similar in older (3%) vs younger (1%) pts.

AESIs were generally low overall, with the most common being infection (≥60 y: 2 pts vs <60 y: 3 pts), hepatic effects (≥60 y: 0 pts vs <60 y: 2 pts), macular edema (≥60 y: 1 pt vs <60 y: 0 pts), malignancy (≥60 y: 0 pts vs <60 y: 2 pts), and pulmonary effects (≥60 y: 0 pts vs <60 y: 1 pt). One death from acute respiratory distress syndrome due to viral pneumonia occurred during IP in an older pt (64y) on OZA but was deemed unrelated to treatment.

Conclusion: OZA is a safe, tolerable oral treatment option for older UC patients with an absence of concerning serious adverse events. Further, efficacy in older patients was comparable to younger patients. A key limitation of this study is the small sample size warranting future studies with larger, real-world cohorts.

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Disclosure: Peter Irving:received lecture fees from AbbVie, Bristol Myers Squibb, Celgene, Celltrion, Dr. Falk Pharma, Ferring, Galapagos, Gilead, MSD, Janssen, Pfizer, Takeda, Tillotts, Sapphire Medical, Sandoz, Shire, and Warner Chilcott; received financial support for research from Celltrion, MSD, Pfizer, and Takeda; received advisory fees from AbbVie, Arena, Boehringer Ingelheim, Bristol Myers Squibb, Celgene, Celltrion, Genentech, Gilead, Hospira, Janssen, Eli Lilly, MSD, Pfizer, Pharmacosmos, Prometheus Biosciences, Roche, Sandoz, Samsung Bioepis, Takeda, Topivert, VH2, Vifor, and Warner Chilcott.

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Sara Horst: consultant for AbbVie, Janssen, and Takeda.

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P0404

ASSOCIATION BETWEEN ABSOLUTE LYMPHOCYTE COUNT AND OZANIMOD EFFICACY AND SAFETY IN PATIENTS WITH MODERATELY TO SEVERELY ACTIVE ULCERATIVE COLITIS: RESULTS FROM THE PHASE 3 TRUE NORTH STUDY

S. Harris¹, R. Maddux¹, C. Wu¹, S. Hu¹, A. Petersen¹

¹Bristol Myers Squibb, Princeton, United States

Contact E-Mail Address: sarah.harris@bms.com

Introduction: Ozanimod, a sphingosine 1-phosphate (S1P) receptor modulator selectively targeting S1P₁ and S1P₅, is approved in Europe and the United States for the treatment of moderately to severely active ulcerative colitis (UC). Binding with ozanimod results in internalization of S1P₁ receptors, reducing egress of lymphocyte subsets into circulation with preservation of immunosurveillance. Ozanimod demonstrated efficacy and safety in the phase 3 True North trial in patients with moderately to severely active UC (NCT02435992).

Aims & Methods: This analysis assessed the association between absolute lymphocyte count (ALC) and ozanimod efficacy and safety during the induction and maintenance periods of True North. Patients were randomized to double-blind ozanimod 0.92 mg (equivalent to ozanimod HCl 1 mg) or placebo once daily (Cohort 1) or received open-label ozanimod 0.92 mg once daily (Cohort 2) during the 10-week induction period; patients with a clinical response to ozanimod at Week 10 were re-randomized to double-blind ozanimod or placebo for maintenance through Week 52. Clinical outcomes (rectal bleeding score [RBS], stool frequency score [SFS], composite Mayo score, Physician's Global Assessment [PGA] score, and endoscopy score) were assessed at baseline and Weeks 10 and 52. Efficacy endpoints (clinical remission, clinical response, endoscopic improvement, mucosal healing, and histologic remission) were also assessed at Weeks 10 and 52. Occurrence of treatment-emergent adverse events (TEAEs) and ALCs were evaluated at baseline and Weeks 5, 10, 18, 28, 40, and 52.

Results: A total of 645 patients received double-blind ozanimod (n=429) or placebo (n=216), and 367 received open-label ozanimod during induction; 230 and 227 ozanimod-treated patients were re-randomized to ozanimod and placebo, respectively, for maintenance. Baseline ALC was not significantly correlated with clinical outcome at Weeks 10 or 52 as measured by changes from baseline RBS, SFS, Mayo score, PGA score, and endoscopy score in patients who received ozanimod or placebo.

Additionally, baseline ALC was neither predictive nor prognostic for Weeks 10 and 52 responses based on all efficacy endpoints assessed. Reductions from baseline in mean ALC occurred by Week 5 with ozanimod and were significantly greater in patients who received ozanimod (53-54%) vs placebo (2.3%; $P<0.001$). ALC plateaued by Week 10 and was maintained through Week 52 in patients on continuous ozanimod. ALC returned to placebo levels by Week 52 in patients who switched to placebo during maintenance. Change in ALC at Week 10 was generally not significantly correlated with changes in clinical outcomes at Weeks 10 or 52.

Additionally, change in ALC at Week 5 was not predictive of Week 10 response, and change in ALC at Week 10 was not predictive of Week 52 response based on all efficacy endpoints assessed. Reductions from baseline in ALC at all weeks were similar in ozanimod-treated patients with or without ≥ 1 TEAE and with or without infection-related TEAEs.

Conclusion: ALC reductions, which were reversed upon treatment discontinuation, occurred with ozanimod and were not associated with occurrence of TEAEs, including infections. Baseline ALC was not predictive or

prognostic for response, nor were reductions in ALC. These findings support the use of ALC as a pharmacodynamic biomarker but not as a prognostic biomarker in UC or as a predictive biomarker for ozanimod.

Disclosure: Sarah Harris, Chun Wu, Sarah Hu, and AnnKatrin Petersen: employees and stakeholders of Bristol Myers Squibb.

Rachel Maddux: employee of Bristol Myers Squibb.

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P0405

IMPACT OF OZANIMOD ON FECAL CALPROTECTIN LEVELS AND THE ASSOCIATION WITH OZANIMOD EFFICACY IN PATIENTS WITH MODERATELY TO SEVERELY ACTIVE ULCERATIVE COLITIS: RESULTS FROM THE PHASE 3 TRUE NORTH STUDY

S. Harris¹, R. Maddux¹, Y. Li², S. Hu¹, C. Wu¹, A. Petersen¹

¹Bristol Myers Squibb, Princeton, United States, ²Parexel International, Durham, United States

Contact E-Mail Address: sarah.harris@bms.com

Introduction: Ozanimod, a sphingosine 1-phosphate (S1P) receptor modulator, is approved in Europe and the United States for the treatment of moderately to severely active ulcerative colitis (UC). Ozanimod demonstrated efficacy in the phase 3 True North trial in patients with moderately to severely active UC (NCT02435992).

Infiltration of neutrophils in intestinal mucosa contributes to inflammation in inflammatory bowel diseases. Calprotectin, which is released by neutrophils, reflects neutrophilic activity and is useful in monitoring disease activity in UC.

Aims & Methods: This analysis assessed the effect of ozanimod on fecal calprotectin (FCP) levels and the association with ozanimod efficacy in True North. During the 10-week induction period, patients were randomized to double-blind ozanimod 0.92 mg (equivalent to ozanimod HCl 1 mg) or placebo once daily (Cohort 1) or received open-label ozanimod 0.92 mg once daily (Cohort 2).

Patients with clinical response to ozanimod at Week 10 were re-randomized to double-blind ozanimod or placebo for maintenance through Week 52. Efficacy endpoints (clinical remission, clinical response, endoscopic improvement, mucosal healing, and histologic remission) and FCP levels were assessed at Weeks 10 and 52.

Results: Change in FCP from baseline to Week 10 was assessed in 517 patients who received double-blind ozanimod (n=347) or placebo (n=170), and 293 who received open-label ozanimod. Patients on ozanimod demonstrated reductions from baseline in FCP at Week 10, which was significant vs placebo ($P<0.001$, both cohorts) (Table). FCP reductions were significantly greater in patients with vs without clinical response at Week 10 in all treatment groups ($P<0.001$, all groups) (Table).

Change in FCP from baseline to Week 52 was assessed in 149 patients remaining on ozanimod and 109 who switched to placebo. FCP levels remained low through Week 52; patients on continuous ozanimod had significantly greater FCP reductions at Week 52 vs patients who switched to placebo ($P=0.0002$) (Table).

FCP reductions were significantly greater in patients with vs without clinical response at Week 52 in the ozanimod and ozanimod-placebo groups ($P<0.01$, both groups) (Table).

Significantly greater reductions from baseline in FCP occurred with ozanimod vs placebo at Weeks 10 and 52 regardless of prior biologic or tumor necrosis factor inhibitor exposure ($P<0.05$, all groups). Baseline FCP level was predictive of clinical response and histologic remission at Week 10 ($P<0.05$, both endpoints). Reduction from baseline in FCP at Week 10 was predictive and prognostic for all endpoints except clinical response at Week 52 ($P<0.05$, all endpoints).

FCP adjusted mean percent change (95% CI)	Induction (Week 10)		Maintenance (Week 52)		
	Cohort 1		Cohort 2		
	Placebo (n=170)	Ozanimod (n=347)	Ozanimod (n=293)	Ozanimod-placebo (n=109)	Ozanimod-ozanimod (n=149)
All patients	18.8 (-11.6, 59.6)	-59.3 (-67.1, -49.7)	-71.6 (-77.2, -64.5)	-70.7 (-79.6, -57.7)	-87.7 (-91.0, -83.3)
Responders ^a	-48.7 (-68.7, -16.0)	-83.9 (-87.8, -78.8)	-86.2 (-89.5, -81.8)	-81.5 (-87.8, -71.7)	-91.0 (-93.7, -87.1)
Nonresponders ^b	54.9 (12.4, 113.5)	-12.1 (-32.4, 14.4)	-33.3 (-50.9, -9.5)	-10.5 (-53.6, 72.9)	-75.4 (-85.9, -57.2)

^aResponders are patients who achieved clinical response at Week 10 for the induction period and at Week 52 for the maintenance period. ^bNonresponders are patients who did not achieve clinical response at Week 10 for the induction period and at Week 52 for the maintenance period.

Table. Change from baseline in FCP at Weeks 10 and 52

Conclusion: Ozanimod led to FCP reductions, indicative of decreases in intestinal neutrophil levels. Baseline FCP was predictive of ozanimod response. FCP reductions were predictive for ozanimod response and prognostic for UC. These findings may help support the use of FCP as a predictive biomarker for ozanimod response and prognostic biomarker in UC.

Disclosure: Sarah Harris, Sarah Hu, Chun Wu, and AnnKatrin Petersen: employees and shareholders of Bristol Myers Squibb.

Rachel Maddux: employee of Bristol Myers Squibb.

Yicong Li: employee of Parexel International and a consultant for Bristol Myers Squibb.

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P0406

COMBINATION THERAPY IS NOT ASSOCIATED WITH IMPROVED RATES OF CLINICAL OR ENDOSCOPIC REMISSION IN PATIENTS WITH INFLAMMATORY BOWEL DISEASE TREATED WITH USTEKINUMAB OR VEDOLIZUMAB

A.W. Jeffrey¹, S. Picardo¹, S. Menon¹, K. So¹, K. Venugopal¹

¹Royal Perth Hospital, Department of Gastroenterology, Perth, Australia

Contact E-Mail Address: angus.jeffrey@health.wa.gov.au

Introduction: Combination therapy with Anti-TNF and immunomodulators has been demonstrated to be superior than monotherapy in Crohn's Disease (CD) and Ulcerative Colitis (UC). This is due to mechanistic effects of immunomodulators as well as reducing immunogenicity. Lower rates of immunogenicity have been found with Ustekinumab (UST) and Vedolizumab (VDZ). Emerging data suggests combination therapy is not required for these agents, however there is no data from the Australian cohort.

Aims & Methods: The aim of this retrospective cohort study was to determine if there was a difference in clinical and endoscopic outcomes for UST or VDZ as a monotherapy compared to a combination with thiopurines or methotrexate. Primary outcome was clinical remission or response as calculated by partial MAYO score (remission <3, response is a decrease >1) for UC or Harvey Bradshaw Index for CD (remission <5, response is a decrease >2) at week 14, 26 and 52. Secondary endpoints were treatment failure or relapse, and endoscopic remission at one year, where treatment failure or relapse is a combination endpoint of need for dose escalation, reinduction, ceasing biologic, and IBD related hospital admission or surgery.

Results: 85 patients on VDZ (61 with UC, 24 with CD) and 74 on UST (all with CD) were identified at a single centre in Australia between October 2015 and March 2022. Of these patients, 53 (72%) on UST and 56 (66%) on VDZ were treated with monotherapy. With the combination therapy, 16 (76%) on UST received thiopurines and 5 (24%) methotrexate compared

to 26 (90%) and 3 (10%) on VDZ respectively. There was no difference in clinical response or remission for VDZ monotherapy compared to combination therapy (Table 1) at Week 12 or 26 (p=0.38, p=0.83). Similarly, there was no difference in outcome for UST at the same intervals (p=0.21, p=0.74). At Week 52, 42 (82%) of patients on VDZ monotherapy had clinical response or remission compared to 21 (91%) on combination therapy (p=0.32). For UST this was 29 (97%) and 14 (88%) respectively (p=0.23). Remission and response rates were calculated from those patients who were still on treatment and had data available at each time interval. Treatment failure or relapse at one year occurred in 13 (23%) of patients on VDZ monotherapy compared to 5 (19%) on combination therapy (p=0.80). For UST this was 11 (21%) and 5 (24%) respectively (p=0.17). 52 patients on VDZ and 28 patients on UST had an interval colonoscopy at approximately one year. 23 (66%) patients on VDZ monotherapy and 14 (78%) on combination therapy achieved endoscopic remission (p=0.36). For UST this was 14 (70%) and 5 (63%) respectively (p=0.70).

Outcome	Number of Patients	Combination (%)	Number of Patients	Monotherapy (%)	p-value	Number of Patients	Combination (%)	Number of Patients	Monotherapy (%)	p-value
Vedolizumab						Ustekinumab				
Clinical Response or remission	29		56			21		53		
Week 12	27	19 (70%)	44	35 (80%)	0.38	14	13 (93%)	45	35 (78%)	0.21
Week 26	25	20 (80%)	50	41 (82%)	0.83	18	16 (89%)	42	36 (86%)	0.74
Week 52	23	21 (91%)	51	42 (82%)	0.32	16	14 (88%)	30	29 (97%)	0.23
Endoscopic Remission	18	14 (78%)	35	23 (66%)	0.36	8	5 (63%)	20	14 (70%)	0.70
Treatment Failure or Relapse	29	5 (19%)	56	13 (23%)	0.80	21	5 (24%)	53	11 (21%)	0.17

Table 1. Outcomes for Patients with Inflammatory Bowel Disease on Vedolizumab or Ustekinumab Monotherapy or in combination with another Immunomodulator.

Conclusion: For patients with IBD who are commencing either VDZ or UST, monotherapy is effective at achieving both clinical response or remission and endoscopic remission up to one year from starting treatment.

Disclosure: Nothing to disclose.

P0407

HIGH C-REACTIVE PROTEIN LEVEL OF ACUTE SEVERE ULCERATIVE COLITIS IS ASSOCIATED WITH RE-ADMISSION DUE TO AGGRAVATION OF ULCERATIVE COLITIS: A KASID MULTICENTER STUDY

D.H. Kim¹, H.-S. Kim¹, S.-J. Kim², J. Lee², E.S. Kim³, K.O. Kim⁴, Y.J. Lee⁵, S.H. Park⁶, E.M. Song⁷, D.S. Kim⁸, K. Oh⁹, H.S. You¹⁰, IBD Research Group in Korean Association for the Study of the Intestinal Diseases (KASID)

¹Chonnam National University Hospital and Medical School, Division of Gastroenterology, Department of Internal Medicine, Gwangju, Korea (Republic of), ²Chosun University Hospital, Department of Internal Medicine, School of Medicine, Gwangju, Korea (Republic of), ³Kyungpook University Hospital, Daegu, Korea (Republic of), ⁴Yeungnam University Hospital, Daegu, Korea (Republic of), ⁵Keimyung University Hospital, Daegu, Korea (Republic of), ⁶Asan Medical Center, Seoul, Korea (Republic of), ⁷Ewha Womans University Seoul Hospital, Seoul, Korea (Republic of), ⁸kumari2@hanmail.net, Daejeon, Korea (Republic of), ⁹Sejong General Hospital, Bucheon, Korea (Republic of), ¹⁰Chonnam National University Hospital, Gastroenterology, Gwangju, Korea (Republic of)

Contact E-Mail Address: go6003@naver.com

Introduction: Acute severe ulcerative colitis (ASUC) is a life-threatening disease.¹ Even after recovery, maintenance treatment is required for a long time, and re-exacerbation of ulcerative colitis can occur frequently.² A high CRP level is a poor prognostic factor in ASUC and increases the likelihood of colectomy.³⁻⁵

However, there are insufficient studies on the prediction of readmission due to exacerbation of ulcerative colitis.

Aims & Methods: We retrospectively included patients who were hospitalized at four tertiary medical centers for ASUC management between January 2015 to December 2020, and data on the underlying disease, disease activity, treatment method and readmission due to ulcerative colitis aggravation were checked.

Results: A total of 145 patients (mean age 44.4 years, 68 female) were investigated. Initial partial mayo score, mayo endoscopic sub-score, ulcerative colitis endoscopic index of severity scores were 7.6±0.8, 2.7±0.5, and 6.0±1.4, respectively. When divided into two groups with an initial CRP level above 5 and below, there was no significant difference in baseline characteristics.

Variables	cHR	95% CI	p-value	aHR	95% CI	p-value
Age	0.97	0.94-0.997	0.03			
Sex, male	0.67	0.33-1.36	0.26			
CRP ≥ 5	2.83	1.42-5.65	<0.01	2.38	1.26-4.49	<0.01
Albumin	0.89	0.47-1.70	0.73			
WBC	1.00	1.00-1.00	0.29			
Platelet	1.00	0.997-1.001	0.25			
UCEIS	0.95	0.76-1.20	0.68			
Partial Mayo score	0.94	0.63-1.40	0.75			
CCI	1.81	0.97-3.38	0.06			

aHR, adjusted hazard ratio; cHR, crude hazard ratio; CCI, Charlson comorbidity index; CI, confidential interval; CRP, C-reactive protein; UCEIS, ulcerative colitis endoscopic index of severity; WBC, white blood cell

Table 1. Univariate and multivariate analysis of risk factors for increased readmission due to exacerbation of ulcerative colitis using cox-regression.

However, in the group with CRP≥5, longer hospital stay (18 versus 12 days, p<0.01), lower albumin levels (3.1 versus 3.5 mg/dL, p<0.01), higher leukocyte counts (10652 versus 9148 /mm³, p=0.02), and higher platelet counts (417 versus 364 x10³/mm³, p=0.03) were observed compared with CRP<5. Readmission occurred in 69 (47.6%) patients on the median of 531 days (range, 7-4019).

The cumulative incidence rate of readmission at 1, 6, 12, 24 months were 2.8%, 12.4%, 19.3%, and 27.6%, respectively. Significantly more readmissions occurred in Kaplan Meier analysis in patients with CRP≥5 (p<0.01). In Cox regression analysis, readmission more frequently occurred in patients with CRP≥5 compared to patients with CRP<5 (aHR 2.38, CI: 1.26-4.49, p<0.01).

Conclusion: A total of 47.5% of readmission due to exacerbation of ulcerative colitis occurred during follow-up after ASUC recovery. High initial CRP levels were associated with readmissions for exacerbation of ulcerative colitis.

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P0408

TOFACITINIB FOR THE TREATMENT OF MODERATE-SEVERE ULCERATIVE COLITIS. THE GREEK EXPERIENCE

N. Viazis¹, D.K. Christodoulou², O. Gioulema³, A. Theodoropoulou⁴, G. Bamias⁵, E. Zampeli⁶, I. Koutroubakis⁷, M. Tzouvala⁸, K. Karmiris⁴, I. Mousavere², K.H. Katsanos², M. Katsaros³, V. Kitsou⁵, G. Axiaris⁶, S. Michopoulos⁶, K. Foteinogiannopoulou⁷, E. Zacharopoulou⁸, G. Tribonias⁸, K. Mountaki¹, G.J. Mantzaris¹
¹*Evangelismos General Hospital, Gastroenterology, Athens, Greece,* ²*University Hospital of Ioannina, Gastroenterology, Ioannina, Greece,* ³*2nd Propeadeutic Department of Internal Medicine, General Hospital "Hippokratio", Gastroenterology, Thessaloniki, Greece,* ⁴*Venizeleio General Hospital, Gastroenterology, Heraklion, Crete, Greece,* ⁵*3rd Academic Department of Internal Medicine, National and Kapodistrian University of Athens, Sotiria Hospital, Gastroenterology, Athens, Greece,* ⁶*Alexandra Hospital, Gastroenterology, Athens, Greece,* ⁷*University Hospital of Heraklion Crete, Gastroenterology, Heraklion, Greece,* ⁸*General Hospital Nikaia Piraeus Agios Panteleimon - General Hospital Dytikis Attikis Agia Varvara, Gastroenterology, Athens, Greece*

Contact E-Mail Address: gjmantzaris@gmail.com

Introduction: Tofacitinib is a pan-JAK inhibitor approved for the treatment of moderate-severe ulcerative colitis (UC). We aimed to assess the rates of clinical response at week 8, and biochemical response, steroid-free clinical remission, and endoscopic healing at week 26 to tofacitinib in patients with mostly treatment-refractory moderate-severe UC.

Aims & Methods: This was a retrospective analysis of prospectively collected data extracted from the notes of patients with moderate-severe UC who were treated with tofacitinib in the last 2 years in 8 Greek IBD centers and who had a follow up of at least 26 weeks after initiation of treatment. Tofacitinib was administered at a dose of 10 mg *bid* for 8 weeks followed by a maintenance dose of 5mg *bid* thereafter. Week-8 clinical response was defined as the reduction in the partial Mayo score of at least 2 points, without concomitant use of any steroid preparation [budesonide, prednis(ol)one, or methylprednisolone]. Steroid free clinical remission at week 26 was defined as a partial Mayo score of ≤1 points without concomitant use of any steroid preparation. Biochemical response at week 26 was defined as any reduction in fecal calprotectin or plasma C-reactive protein concentrations over their baseline levels. Mucosal healing at week 26 was defined as Mayo endoscopic sub-score of ≤1. A safety list of all reported adverse events was completed. Treatment discontinuation due to adverse events was considered as treatment failure, whereas patients needing escalation of the maintenance dose were also considered as non-responders.

Results: Overall, 74 patients (41 males), aged (mean, SD) 39.2 (15.4) years and disease duration of (mean, SD) 10.6 (9.7) years were included. UC was extensive in 47, left-sided in 24, and proctitis in 3 patients. Four patients were naïve to biologics, whereas 12, 28 and 30 patients had failed treatment with 1, 2 and 3 biologics, respectively. Clinical response at week 8 was seen in 58 patients (78.4%). Biochemical response and steroid free clinical remission at week 26 were seen in 32 (43.2%) and 31 (41.9%) patients, respectively. Endoscopy at week 26 was performed in 28 patients and endoscopic healing was seen in 13 (46.4%) patients. Adverse events which did not lead onto treatment discontinuation occurred in 7 patients (hyperlipidemia n=5, elevated liver enzymes n=2). One patient experienced pulmonary embolism and treatment was discontinued.

Conclusion: In this retrospective real-world cohort tofacitinib demonstrated clinical response at week 8 in more than three quarters and steroid free clinical remission at week 26 in almost half of the patients with treatment refractory moderate-severe UC.

Disclosure: Nothing to disclose.

P0409

EFFECTIVENESS AND SAFETY OF VEDOLIZUMAB AND USTEKINUMAB THERAPY FOR COMPLEX PERIANAL FISTULA IN CROHN'S DISEASE: THE HEAL STUDY

M.J. Casanova¹, M. Chaparro Sanchez¹, B. Caballol², M.J. García³, F. Mesonero⁴, C. Rubín de Célix¹, P. Suárez-Álvarez⁵, R. Ferreira-Iglesias⁶, M.d.M. Martín-Rodríguez⁷, R. de Francisco⁸, P. Varela-Trastoy⁹, G. Bastida¹⁰, M. Carrillo-Palau¹¹, A. Núñez-Ortiz¹², P. Ramírez-de la Piscina¹³, D. Ceballos¹⁴, D. Hervías-Cruz¹⁵, R. Muñoz-Pérez¹⁶, B. Velayos¹⁷, F. Bermejo¹⁸, D. Busquets¹⁹, M. Cabacino²⁰, P. Camo-Monterde²¹, I. Marín-Jiménez²², C. Muñoz²³, L.C. de la Peña-Negro²⁴, E. Sierra-Moros²⁵, J. Barrio²⁶, E. Brunet-Mas²⁷, L. Bujanda²⁸, F. Cañete²⁹, F. Gomollon³⁰, N. Manceñido-Marcos³¹, I. Rodríguez-Lago³², M.C. Rodríguez-Grau³³, B.S. Sicilia³⁴, S. Torra-Alsina³⁵, L. Arranz-Hernández³⁶, D. Carpio³⁷, M.F. García-Sepulcre³⁸, C. González-Muñoz³⁹, J.M. Huguet⁴⁰, L. Márquez-Mosquera⁴¹, M.P. López-Serrano⁴², Á. Ponferrada-Díaz⁴³, J.P. Gisbert¹,
 on behalf of the HEAL Study Group of GETECCU

¹*Hospital Universitario de La Princesa, IIS-Princesa, UAM and CIBERehd, Gastroenterology Unit, Madrid, Spain,* ²*Hospital Clínic i Provincial, Institut d'Investigacions Biomèdiques August Pi i Sunyer (IDIBAPS), and CIBEREHD, Gastroenterology Unit, Barcelona, Spain,* ³*Hospital Universitario Marqués de Valdecilla and Instituto de Investigación Sanitaria Valdecilla (IDIVAL), Gastroenterology Unit, Santander, Spain,* ⁴*Hospital Universitario Ramón y Cajal, Gastroenterology Unit, Madrid, Spain,* ⁵*Complejo Asistencial Universitario de León, Gastroenterology Unit, León, Spain,* ⁶*Hospital Clínico Universitario de Santiago de Compostela, Gastroenterology Unit, Santiago de Compostela, Spain,* ⁷*Hospital Universitario Virgen de las Nieves, Gastroenterology Unit, Granada, Spain,* ⁸*Hospital Universitario Central de Asturias and Instituto de Investigación Sanitaria del Principado de Asturias (ISPA), Gastroenterology Unit, Oviedo, Spain,* ⁹*Hospital Universitario de Cabueñes, Gastroenterology Unit, Gijón, Spain,* ¹⁰*Hospital Universitario La Fe, and CIBEREHD, Gastroenterology Unit, Valencia, Spain,* ¹¹*Hospital Universitario de Canarias, Gastroenterology Unit, La Laguna, Spain,* ¹²*Hospital Universitario Virgen del Rocío, Gastroenterology Unit, Sevilla, Spain,* ¹³*Hospital HUA Álava, Gastroenterology Unit, Vitoria, Spain,* ¹⁴*Hospital Universitario de Gran Canaria Dr. Negrín, Gastroenterology Unit, Las Palmas de Gran Canaria, Spain,* ¹⁵*Hospital General Universitario de Ciudad Real, Gastroenterology Unit, Ciudad Real, Spain,* ¹⁶*Hospital General Universitario Dr. Balmis, and CIBEREHD, Gastroenterology Unit, Alicante, Spain,* ¹⁷*Hospital Clínico de Valladolid, Gastroenterology Unit, Valladolid, Spain,* ¹⁸*Hospital Universitario de Fuenlabrada and Instituto de Investigación Hospital Universitario La Paz (IdiPAZ), Gastroenterology Unit, Madrid, Spain,* ¹⁹*Hospital Universitari de Girona Doctor Josep Trueta, Gastroenterology Unit, Girona, Spain,* ²⁰*Hospital General Universitario de Castellón, Gastroenterology Unit, Castellón, Spain,* ²¹*Hospital General San Jorge, Gastroenterology Unit, Huesca, Spain,* ²²*Hospital Universitario Gregorio Marañón, Instituto de Investigación Sanitaria Gregorio Marañón (IISGM), and Universidad Complutense de Madrid, Gastroenterology Unit, Madrid, Spain,* ²³*Hospital Universitario Basurto, Gastroenterology Unit, Bilbao, Spain,* ²⁴*Hospital Universitario de Bellvitge, Gastroenterology Unit, Barcelona, Spain,* ²⁵*Hospital Universitario Miguel Servet, Gastroenterology Unit, Zaragoza, Spain,* ²⁶*Hospital Universitario Río Hortega, Gastroenterology Unit, Valladolid, Spain,* ²⁷*Hospital*

Universitari Parc Taulí, Gastroenterology Unit, Sabadell, Spain, ²⁸Hospital Universitario de Donostia, Biodonostia Health Research Institute, Universidad del País Vasco (UPV/EHU), and CIBEREHD, Gastroenterology Unit, Donostia, Spain, ²⁹Hospital Universitario Germans Trias i Pujol, and CIBEREHD, Gastroenterology Unit, Badalona, Spain, ³⁰Hospital Clínico Universitario Lozano Blesa, Instituto de Investigación Sanitaria Aragón (IIS Aragón), and CIBEREHD, Servicio de Aparato Digestivo, Zaragoza, Spain, ³¹Hospital Universitario Infanta Sofía, Gastroenterology Unit, Madrid, Spain, ³²Hospital Universitario de Galdakao, Biocruces Bizkaia Health Research Institute, Gastroenterology Unit, Galdakao, Spain, ³³Hospital Universitario del Henares, Gastroenterology Unit, Madrid, Spain, ³⁴Hospital Universitario de Burgos, Gastroenterology Unit, Burgos, Spain, ³⁵Parc Sanitari Sant Joan de Déu, Gastroenterology Unit, Sant Boi de Llobregat, Spain, ³⁶Hospital Universitario Nuestra Señora de Candelaria, Gastroenterology Unit, Santa Cruz de Tenerife, Spain, ³⁷Complejo Hospitalario Universitario de Pontevedra, Gastroenterology Unit, Pontevedra, Spain, ³⁸Hospital General Universitario de Elche, Gastroenterology Unit, Elche, Spain, ³⁹Hospital Santa Creu i Sant Pau, Gastroenterology Unit, Barcelona, Spain, ⁴⁰Consorcio Hospital General Universitario de Valencia, Gastroenterology Unit, Valencia, Spain, ⁴¹Hospital del Mar and Hospital del Mar Medical Research Institute (IMIM), Gastroenterology Unit, Barcelona, Spain, ⁴²Hospital Universitario Fundación de Alcorcón, Gastroenterology Unit, Madrid, Spain, ⁴³Hospital Universitario Infanta Leonor, Gastroenterology Unit, Madrid, Spain

Contact E-Mail Address: mjcasanova.g@gmail.com

Introduction: The effectiveness of vedolizumab and ustekinumab for the treatment of complex perianal fistula (CPF) in Crohn's disease (CD) patients has been barely studied.

Aims & Methods: To evaluate drug persistence, the effectiveness, and safety of vedolizumab and ustekinumab in CPF.

Retrospective, multicenter study conducted in 43 Spanish sites. Patients who had received vedolizumab or ustekinumab for the indication of active CPF and had started the study drugs at least 6 months before study entry, were included. Patients who received both drugs were included in both groups for the data analysis. Clinical remission was defined according to Fistula Drainage Assessment Index (no drainage through the fistula upon gentle pressure) according to physicians' assessment.

Results: 155 patients were included (39% women, mean age at CD diagnosis 28 years, 96% previously exposed to anti-TNFs): 136 patients received ustekinumab, and 35 vedolizumab (16 patients had been treated with both drugs). Of the 136 patients who received ustekinumab, 95% had been previously treated with anti-TNFs. The indications for ustekinumab were: anti-TNF failure in 68% of the patients, anti-TNFs intolerance in 15%, vedolizumab failure in 10%, and other reasons in 6%. At ustekinumab start, 82% of the patients had also active luminal disease and 30% had undergone a surgical procedure on the CPF just before starting the treatment. The median follow-up time was 27 months (IQR=15-38). A total of 19% (24/136) of the patients discontinued ustekinumab during follow-up. The incidence rate of ustekinumab discontinuation was 8% per patient-year (95%CI=5-11%). Ustekinumab persistence was: 89% at 1 year, and 82% at 2 years. In the short-term, remission was achieved in 54% of the patients –median time to achieve clinical remission was 6 months (IQR=4-9)– of them, 27% (20/74) relapsed during follow-up. The incidence rate of relapse was 11% (95%CI=7-17%) per patient-year. The probability of relapse was: 10% at 1 year, and 25% at 2 years. In the multivariable analysis, no variable was associated either with the likelihood of discontinuation or with the risk of relapse. 6% of the patients on ustekinumab had adverse events, most of them mild. Of the 35 patients who received vedolizumab,

100% had been previously treated with anti-TNFs. The indications for vedolizumab were: anti-TNF failure in 74% of the patients, anti-TNF intolerance in 14%, ustekinumab failure in 7%, and other reasons in 3%. At vedolizumab start, 8% of the patients had also active luminal disease and 37% had undergone a surgical procedure on the CPF just before starting the treatment. The median follow-up time was 19 months (IQR=9-31). A total of 63% (22/35) patients discontinued vedolizumab. The incidence rate of vedolizumab discontinuation was 33% per patient-year (95%CI=22-45%). Vedolizumab persistence was: 65% at 1 year, and 42% at 2 years. In the short-term, remission was achieved in 46% of the patients –median time to achieve clinical remission was 8 months (IQR=3-8)– of them, 20% (3/19) relapsed during follow-up. The incidence rate of relapse was 7% (95%CI=2-19%) per patient-year. In the multivariable analysis, no variable was associated either with the likelihood of discontinuation or with the risk of relapse. 8% of the patients had adverse events, all mild.

Conclusion: Ustekinumab and vedolizumab seem to be effective for CPF, inducing clinical remission in about half of the patients, although a relevant proportion of patients withdraw the treatment over time. The safety profile of both drugs is good.

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María Chaparro¹, has served as a speaker, or has received research or education funding from MSD, Abbvie, Hospira, Pfizer, Takeda, Janssen.

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María Pilar López-Serrano⁴² has served as speaker or has received research and education funding from MSD, Ferring, AbbVie, Janssen, Biogen, and Takeda.

Ángel Ponferrada-Díaz⁴³ has served as speaker or a consultant and advisory member for Ferring, Shire, Janssen, Abbvie, and MSD.

Rest of the authors: none.

P0410

EFFECT OF A GLUTEN-FREE DIET ON THE DISEASES SEVERITY, QUALITY OF LIFE, AND INFLAMMATORY MARKERS AMONG PATIENTS WITH MILD TO MODERATE ULCERATIVE COLITIS: A TRIPLE-BLIND RANDOMIZED PLACEBO-CONTROLLED TRIAL

F. Alborziavanaki¹, R. Hadi², N. Aletaha², N. Ebrahimi², A. Mirolyaii¹

¹Tehran University of Medical Sciences, Gastroenterology, Tehran, Iran (Islamic Republic of), ²Tehran University of Medical Sciences, Tehran, Iran (Islamic Republic of)

Contact E-Mail Address: mynameisrezahadi@gmail.com

Introduction: Dietary regimen has been introduced as an important underlying factor in ulcerative colitis disease. Some patients have also reported symptoms associated with using a specific diet. The aim of the present study was to investigate the effect of a gluten-free diet on disease severity, quality of life, and inflammatory markers in patients with ulcerative colitis.

Aims & Methods: In this triple-blind randomized placebo-controlled clinical trial, we evaluated the effect of a gluten-free regimen on the ESR, CRP, fecal calprotectin, disease severity, and quality of life in patients with mild to moderate ulcerative colitis. Patients' quality of life and severity of symptoms were evaluated using Inflammatory Bowel Disease Questionnaire (IBDQ) and Simple Clinical Colitis Activity Index (SCCAI) respectively. Patients received this regimen for six weeks and were evaluated before and after receiving it. Data were analyzed using SPSS version 22.

Results: Mean (standard deviation) age of patients (n=26) was 39.31 (9.34) years. Among our patients there were 19 (73.1%) females. In both study groups, mean ESR, CRP, quality-of-life (IBDQ) and SCCAI severity score decreased, after receiving diet. These decreases were stronger in intervention group, but none of them were statistically significant. Additionally, both in the control and intervention groups, mean fecal calprotectin increased. However, none of the changes were statistically significant (P-Value> 0.05).

Conclusion: Although in our study, inflammatory markers, quality of life, and disease severity improved in the gluten-free group compared to the control group, but none of the changes were statistically significant. It is too early to suggest the gluten-free diet as a safe and beneficial regimen for UC patients and still, there is a need for further investigations with larger sample sizes in the context of clinical trial and cohort studies, to obtain more reliable results.

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P0411 WITHDRAWN

P0412

ONE YEAR OF USTEKINUMAB THERAPY IMPROVES NUTRITIONAL STATUS IN PATIENTS WITH CROHN'S DISEASE

L. Bertani¹, C. D'Alessandro¹, M. Fornili², F. Coppini¹, F. Zanzi¹, F. Geri¹, M.G. Mumolo³, L. Ceccarelli³, L. Baglietto², M. Bellini¹, F. Costa³, N. de Bortoli¹

¹University of Pisa, Translational Research and New Technologies in Medicine and Surgery, Pisa, Italy, ²University of Pisa, Clinical and Experimental Medicine, Pisa, Italy, ³Pisa University Hospital, General Surgery and Gastroenterology, Pisa, Italy

Contact E-Mail Address: lorenzobertani@gmail.com

Introduction: Patients with Crohn's disease (CD) display high rates of nutritional deficiencies and metabolic imbalances, primarily due to mucosal damage induced by inflammation. In particular, the loss of lean muscle mass configures a condition known as sarcopenia, which is not necessary associated with a low Body Mass Index (BMI). The presence of sarcopenia has been associated with a worst outcome of IBD. At present, no studies evaluated the impact of Ustekinumab (UST) in terms of its effects on body composition.

The aim of this study was to evaluate whether UST treatment could modify the parameters of body composition assessed by Bioelectrical Impedance Assay (BIA) in patients with CD. In particular, we evaluated phase angle, which represents the most clinically established impedance parameter and it might be considered as a reliable and optimal marker of nutritional status.

Aims & Methods: We enrolled all consecutive CD patients treated with UST prospectively, following the current guidelines. BIA was performed at baseline and at week 48, assessing Body Cellular Mass (BCM), total body water, phase angle and BMI. At the same time-points, a colonoscopy was performed in order to evaluate the therapeutic outcome in terms of mucosal healing, defined as a Simple Endoscopic Score for CD <2. We evaluated also clinical remission, defined as a Harvey-Bradshaw Index <5 at week 48.

Results: Out of 44 patients enrolled, 26 (59%) presented clinical remission and 22 (50%) achieve mucosal healing at the end of follow up. No significant differences were observed at baseline in all the BIA parameters between responders and non-responders. Phase angle increased over time in responders, while this was not observed in non-responders (test for the interaction between time and outcome, p-value=0.010 and 0.008 for clinical remission and mucosal healing, respectively). The same differential increase was observed for BCM (test for the interaction between time and outcome, p-value=0.037 and 0.076 for clinical remission and mucosal healing, respectively). No other significant differences were observed regarding the other BIA parameters.

Conclusion: UST therapy seems to be able to modify body composition of patients with CD. In particular, the increase in phase angle in responders suggests that a significant improvement of nutritional status occurred in these patients. Our results are in line to what was shown by a previous study performed in patients with psoriasis treated with UST.

Disclosure: None of the authors have conflicts of interest regarding this study

P0413

EFFECTIVENESS AND SAFETY OF RISANKIZUMAB INDUCTION THERAPY IN PATIENTS WITH CROHN'S DISEASE: A GETAID COHORT STUDY

M. Fumery¹, A. Defrance², X. Roblin³, C. Stefanescu⁴, B. Caron⁵, X. Hebuterne⁶, R. Altwegg⁷, C. Leberre⁸, M. Nachury⁹, A. Meyer¹⁰, P. Ah-Soune¹¹, C. Gilletta De Saint Joseph¹², N. Duveau¹³, M. Uzzan¹⁴, A. Biron¹⁵, D. Laharie¹⁶, S. Nancey¹⁷, M.-L. Tran-minh¹⁸, L. Caillou¹⁹, T. Paupard²⁰, Y. Elgharabawy², L. Peyrin-Biroulet²¹
¹Amiens University Hospital, Gastroenterology Department, Amiens, France, ²GETAID, Paris, France, ³University of St. Etienne Dept. de Gastroenterologie, Saint Etienne, France, ⁴Hopital Beaujon, Service de Gastroenterologie et assistance nutritive, Clichy, France, ⁵CHU Nancy, Gastroenterologie, Nancy, France, ⁶Hospital Archet 2, Nice, Department of Gastroenterology and Clinical Nutrition, Nice, France, ⁷Hopital Saint Eloi Hepatologie Gastro Enterologie, Montpellier, France, ⁸CHU Nantes, Gastroenterologie, Nantes, France, ⁹CHRU Lille, Gastroenterology, Courbevoie Cedex, France, ¹⁰Hôpital Bicêtre, Gastroenterology, Bicetre, France, ¹¹CH Toulon, Gastroenterology, Toulon, France, ¹²Hopital Rangueil, Toulouse, France, ¹³CH Roubaix, Roubaix Cedex 1, France, ¹⁴Hôpital Mondor, Gastroenterology, Paris, France, ¹⁵CHU Reims, Gastroenterology, Reims, France, ¹⁶CHU de Bordeaux, Gastroenterology, Pessac cedex, France, ¹⁷CHU Lyon, Dept. de Gastroenterologie, Pierre Benite, France, ¹⁸Hopital Saint-Louis, Gastroenterology, Paris, France, ¹⁹CHU de Nîmes, Gastroenterology, Nîmes, France, ²⁰CH Dunkerque, Gastroenterology, Dunkerque, France, ²¹Nancy University Hospital, Gastroenterology, Vandoeuvre-les-Nancy, France

Contact E-Mail Address: mathurinf@hotmail.fr

Introduction: Phase III trials have demonstrated the efficacy of risankizumab in moderate-to-severe Crohn's disease (CD), but no real-world data are currently available. We aimed to assess the short-term effectiveness and safety of risankizumab in patients with CD.

Aims & Methods: From April 2021 to March 2022, all patients with refractory luminal CD treated with risankizumab in 18 French GETAID centres were retrospectively included. The primary endpoint was steroid-free clinical remission at week 12 (Harvey-Bradshaw (HB) score <5).

Secondary endpoints included clinical response (≥ 3 -point decrease of HB score and/or (HB) score <5), biological remission (CRP ≤ 5 mg/L), morphological response (endoscopy, MRI or intestinal ultrasound), need for CD-related surgery, and adverse events.

Results: Data at week 12 were available for 70 patients. All (100%) had been previously exposed to anti-TNF agents, 64/70 (92%) to vedolizumab and 68/70 (97%) to ustekinumab. All patients were exposed to at least three biologics and 45/70 (65%) had previous intestinal resection. All but two (68/70, 97%) received 600 mg intravenous induction at weeks 0-4-8. At weeks 12, clinical response was observed in 55/70 (78%), clinical remission and steroid-free clinical remission in 40/70 (57%) and 31/70 (44%), respectively. Absence/mild abdominal pain with normal stool frequency was noted in 20/70 (29%) patients. Twenty-five patients had extra-intestinal manifestations at baseline versus 13 at week 12. Biological remission was observed in 38/70 (54%) patients. Among the 17 patients with colonoscopy, MRI or IUS at both baseline and week 12, response was observed in nine. Seven (10%) patients discontinued risankizumab and 5 (7.4%) underwent surgery during follow-up. In multivariable analysis, steroids at risankizumab initiation (Odds Ratio (OR), 0.24; 95%CI, 0.06 - 0.89; p=0.037) and non-smoker status (OR, 7.01; 95%CI, 1.26 - 59.0; p=0.04) were significantly associated with steroid-free clinical remission at weeks 12. Adverse events occurred in 10/70 (14%) of patients and serious adverse events in 3/70 (4.3%) of patients.

Conclusion: In a cohort of highly refractory patients with CD with multiple prior drug failures including ustekinumab, risankizumab induction provided clinical response in about 3 out of 4 patients and steroid-free clinical remission in about 40%.

Disclosure: Nothing to disclose.

P0414

BIOLOGICALS AND SMALL MOLECULE COMBOTHERAPIES: PROMISING EXPERIENCE IN REFRACTORY IBD PATIENTS

P. Juillerat^{1,2}, M. Martinho Grueber¹, P. Michetti^{1,3}

¹La Source-Beaulieu Crohn's and Colitis Center, Gastroenterology, Lausanne, Switzerland, ²Bern University Hospital, Gastroenterology, Bern, Switzerland, ³Lausanne University Hospital, Gastroenterology, Lausanne, Switzerland

Contact E-Mail Address: pjuillerat@gesb.ch

Introduction: It has been hypothesized that combination of two biologics or with a small molecule could "break the ceiling" of the efficacy (~60%) of currently available biological therapies for IBD patients. The best combinations and their safety are, however, unknown.

Aims & Methods: A chart review of Inselspital, Bern University hospital, of IBD patients on combination therapy have been performed. Data on disease phenotype, previous treatment and efficacy and safety of the new combinations have been collected and studied to help moving forward the use of this armamentarium.

Results: Among 18 identified IBD patients (39% women, 10 ulcerative colitis, 8 Crohn's disease) with extended and refractory luminal disease (indication) who received 21 combination therapies between June 2017 and November 2021. They suffered from steroid-dependency and half of them were refractory to at least two anti-TNF alpha agents. These treatments have been started after a median duration of disease of 6 years (range 1-25) for a mean period of combo treatment of 11 months (range 1-52), 8 were still ongoing. Various combotherapies and clinical response (arrows; red=bad, green=good response) are presented in Table 1.

Disease	Type of combo	Success	Duration (range)	Adverse events (AE)
ulcerative colitis	5x Vedo/ Tofa	2/5 (40%)	5 mois (1-11)	None
	3x Vedo/ Anti-TNFs	1/3 (33%)	8 mois (1-12)	None
	3x Vedo / CysA.	2/3 (66%)	8 mois (6-11)	None
	1x Ustek/ CysA	1/ 1 (100%)	16 mois	None
Crohn's disease	4x Ustek/ Anti-TNFs	4/ 4 (100%)	3 mois (1-9)	Left parotide tumefaction, eczema
	2x Ustek/ JAK	2/2 (100%)	14 mois (2-25)	Lymphopenia (2x), skin mycosis, otitis media Non Hodgkin lymphoma
	3x Vedo/ Anti-TNFs	2/3 (66%)	37 mois (6-52)	None
IBD	14x Vedo, 10x Anti-TNFs, 7x Ustek, 7x JAKs, 4x CysA	13/ 19 (68%) partial or complete response CRP -11, Calpro - 1234	~ 12 months (1-52)	2 Infections, 4 Minor AE, 1 SAE (Lymphoma)

Table 1.

A partial or complete response was observed in 15/21 therapies (71%) with a mean decrease of CRP of 11 mg/l (range+23 to -59) and calprotectin of 399 mcg/g (range 0 – 1745) among the responders. Concerning safety, 2 infections (otitis media, skin mycosis), 1 non hodgkin Lymphoma and 4 minor adverse events (tumefaction left parotide, eczema, 2x lymphopenia) have been reported, mostly when small molecules have been involved.

Conclusion: Ustekinumab combined with anti-TNF agents in Crohn's disease is more effective than vedolizumab and tofacitinib in ulcerative colitis. Combining with small molecules increases the risk of lymphopenia, of cancer (1 case of non hodgkin lymphoma) and minor infections in severe refractory and steroid-dependent inflammatory bowel disease patients.

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P0415

DELAYED IBD DIAGNOSIS INCREASES RISK OF REQUIRING BIOLOGICS IN FIRST 4-YEARS - AN INCEPTION COHORT STUDY

A. Rao¹, A. Bazarova², P. Mitra³, T.L. Parigi^{4,1}, S. Majumder^{4,1,5}, S. Ghosh⁶, M. Iacucci^{7,4,1}, U.N. Shivaji^{7,4,1}

¹University Hospitals Birmingham NHS Foundation Trust, Gastroenterology, Birmingham, United Kingdom, ²University of Cologne, Institute for Biological Physics, Köln, Germany, ³University of Birmingham, Biomedical Sciences, Birmingham, United Kingdom, ⁴Institute of Immunology and Immunotherapy, University of Birmingham, Immunology and Immunotherapy, Birmingham, United Kingdom, ⁵University of Birmingham, India Institute, Birmingham, United Kingdom, ⁶College of Medicine and Health, University College Cork, APC Microbiome, Ireland, Cork, Ireland, ⁷National Institute for Health Research NIHR Birmingham Biomedical Research Centre, University Hospitals Birmingham, Gastroenterology, Birmingham, United Kingdom

Contact E-Mail Address: abs.rao@doctors.org.uk

Introduction: Delays in diagnosis could be due to patient-related and health-system related factors. The impact of such delays in Inflammatory Bowel Diseases (IBD), particularly on biological therapies, continues to be a subject of interest.

The aim of the study was to investigate if delays could predict need for biologics and report on related adverse outcomes (AOs).

Aims & Methods: New patients referred for suspected IBD to a single tertiary care centre between Jan 2013 to Dec 2017 were identified using EMR. For purposes of the study, delay-types and cut-off times for each type was set by investigators based on best average hospital waiting times. The reasons for delays until start of treatment were recorded; data on the start of biologics, duration, and reasons for switch (if required) were recorded. The data were analysed using multiple Pearson correlations and Cox proportional Hazard model to determine whether any delay-type/s could predict need for biologics and compare the risk between patients with or without a delay.

Results: Total of 105 patients were identified using stringent criteria (M=58; median age=32y) with a long median follow-up of 55 months. 65, 27 and 13 patients had final diagnosis of Ulcerative colitis, Crohn's disease, and Unclassified colitis respectively, and were analysed collectively.

In our cohort, a model that combined delay in seeking medical attention, and time taken from specialty review to index endoscopy exhibited the best predictive power with average AUROC of 0.67.

When individual delay-types were analysed, it was noted that most delay-types increased the risk of biologic use-

a. Delay in seeking medical attention [OR-1.08 (1.03 1.17)]

b. Delay from GP referral to specialty review [OR-1.10 (1.0 1.23)]
 c. Delay from specialty review to index endoscopy [OR-1.09 (1.01 1.21)]
 On further analysis of patient-related delay and health-system related delays, there was a statistically significant increase noted in the risk of requiring biologics at any time during the follow-up period.
 Survival without biologics when there is a delay of >2 weeks in seeking medical attention was statistically significant ($p=0.042$) and so was survival without biologics when there is delay of >6 weeks from GP referral to index endoscopy procedure ($p=0.021$).

Conclusion: The risk of requiring biologic therapy is higher in those patients who have faced any type of delay in their diagnosis of IBD. A patient-related delay of >2weeks and cumulative health-system related delay of >6weeks increase the risk of requiring biologic therapy at any time during their follow-up.
 Both primary and secondary care must work to reduce any delays as this has long-term implications for patients and economic implications for the health care providers.

Disclosure: Nothing to disclose.

P0416

6-THIOGUANINE NUCLEOTIDE LEVELS AND ANTI-TUMOUR NECROSIS FACTOR ALPHA TROUGH LEVELS IN INFLAMMATORY BOWEL DISEASE PATIENTS ON COMBINATION THERAPY: A RETROSPECTIVE MULTICENTRE STUDY

N. Yu¹, D. Tassone¹, T. Lee¹, S. Phan², D.M. Wu², J. Zhang³, L. Wang⁴, J. Tjahyad⁵, K. Dutt⁵, H. Liou⁶, C. Basnayake^{1,7}, E. Wright^{1,7}, M. Lust¹, O. Niewiadomski¹, M.A. Kamm^{1,7}, W. Connell^{1,7}, A. Thompson^{1,7}, I. Hilmi⁸, R.A. Raja Ali⁹, S.C. Wei⁶, P. De Cruz^{2,7}, A.B. Friedman³, G.T. Moore^{4,10}, D. van Langenberg^{5,10}, N.S. Ding^{1,7}

¹St Vincent's Hospital Melbourne, Gastroenterology, Melbourne, Australia, ²Austin Health, Gastroenterology, Melbourne, Australia, ³Alfred Health and Monash University, Gastroenterology, Melbourne, Australia, ⁴Monash Health, Gastroenterology, Melbourne, Australia, ⁵Eastern Health, Gastroenterology, Melbourne, Australia, ⁶National Taiwan University Hospital, Internal Medicine, Taipei, Taiwan, ⁷The University of Melbourne, Medicine, Melbourne, Australia, ⁸University of Malaya Medical Centre, Medicine, Kuala Lumpur, Malaysia, ⁹Hospital Universiti Kebangsaan Malaysia, Medicine, Kuala Lumpur, Malaysia, ¹⁰Monash University, Medicine, Melbourne, Australia

Contact E-Mail Address: natalieyu24@gmail.com

Introduction: Thiopurine co-therapy with anti-tumour necrosis factor alpha (anti-TNF α) agents is associated with higher anti-TNF α drug levels and reduced immunogenicity in patients with Inflammatory Bowel Disease (IBD). However, the 6-thioguanine nucleotide (6-TGN) threshold level required to confer this benefit remains unclear.

Aims & Methods: This study aimed to evaluate the relationship between serum 6-TGN levels and trough levels of infliximab (IFX) and adalimumab (ADA) in IBD patients on combination therapy. We performed a retrospective multicentre study of IBD patients receiving combination anti-TNF α and thiopurine maintenance therapy for at least 3 months duration with stable doses for at least 2 months. All 6-TGN levels measured within 3 months prior to or on the same date as IFX or ADA trough levels, between January 2015 and August 2021, were included. Undetectable 6-TGN levels (<5pmol/8x10⁸ RBC) were excluded.

Primary outcomes were IFX and ADA levels. Secondary outcomes were antibodies to IFX (ATI) or ADA (ATA). Spearman's rho was used to correlate 6-TGN and anti-TNF α levels. Receiver operator characteristic curves were

used to define the optimal 6-TGN cut-off levels associated with therapeutic anti-TNF α levels ($\geq 5\text{mcg/ml}$ for IFX, $\geq 7.5\text{mcg/ml}$ for ADA), using the Liu index. The Mann-Whitney U test was used to compare 6-TGN levels between patients with and without detectable ATI.

Results: A total of 743 paired 6-TGN and anti-TNF α levels (640 IFX, 103 ADA) from 354 patients (263 IFX, 91 ADA) were included. 363/640 (57%) IFX levels and 65/103 (63%) ADA levels were measured in patients on standard anti-TNF α dosing (5mg/kg every 8 weeks for IFX, 40mg every 2 weeks for ADA). The median 6-TGN level was 252pmol/8x10⁸ RBC, median IFX level was 6.45mcg/ml and median ADA level was 7.70mcg/ml. 6-TGN and IFX levels were significantly positively correlated ($\rho=0.132$, $p=0.0008$), however the correlation between 6-TGN and ADA levels was not significant ($\rho=0.145$, $p=0.143$).

The optimal 6-TGN cut-off that predicted therapeutic IFX levels was 261pmol/8x10⁸ RBC (area under the curve (AUC) 0.57, sensitivity 0.58, specificity 0.56) for patients on standard IFX dosing and 227.5pmol/8x10⁸ RBC (AUC 0.58, sensitivity 0.57, specificity 0.58) for patients on escalated IFX dosing.

The optimal 6-TGN cut-off that predicted therapeutic ADA levels was 245pmol/8x10⁸ RBC (AUC 0.57, sensitivity 0.62, specificity 0.53) for patients on standard ADA dosing and 201pmol/8x10⁸ RBC (AUC 0.63, sensitivity 0.80, specificity 0.46) for patients on escalated ADA dosing. Seven patients had detectable ATI. Patients with ATI had significantly lower 6-TGN levels compared to those without ATI (median 6-TGN 133 vs 253pmol/8x10⁸ RBC, $p=0.010$). No patients had detectable ATA.

Conclusion: 6-TGN levels are associated with IFX trough levels, however the association between 6-TGN and ADA levels remains unclear. Target 6-TGN levels in the lower end of the therapeutic 6-TGN range may be adequate to maintain therapeutic anti-TNF α levels, particularly in patients on escalated anti-TNF α dosing.

However, the optimal 6-TGN cut-offs associated with therapeutic IFX and ADA levels that were calculated from our multicentre data showed poor predictive ability, and may differ depending on individual laboratory assays.

Disclosure: Nothing to disclose.

P0417

INCREASE IN CIRCULATING T AND B LYMPHOCYTE SUBSETS AFTER TREATMENT WITH THE POTENT, SELECTIVE, ORAL, SMALL MOLECULE $\alpha_4\beta_7$ INHIBITOR MORF-057 IN HEALTHY SUBJECTS

A. Hussain¹, M. Mangada¹, J. Wong¹, A.S. Ray¹, G. Bain¹

¹Morphic Therapeutic, Waltham, United States

Contact E-Mail Address: ali.hussain@morphictx.com

Introduction: The expanding role of small molecule drugs in modulating the immune system provides innovative opportunities in targeting autoimmune diseases. Unraveling the complex molecular mechanisms behind immune trafficking have aided in the development of tissue-specific therapeutic agents. Patients experiencing chronic inflammation in their gut have benefited from biologics targeting the $\alpha_4\beta_7$ /MAdCAM-1 axis. Integrin heterodimer $\alpha_4\beta_7$ is expressed on a subset of lymphocytes, mediating their extravasation upon binding to the corresponding gut-specific ligand MAdCAM-1. Inhibiting this interaction blocks lymphocytes from infiltrating into the intestinal lamina propria, leading to measurable increases in their circulating levels.^{1,2,3}

In this study, we explored target engagement and lymphocyte trafficking as pharmacodynamic (PD) readouts in healthy subjects treated with an orally administered, small molecule inhibitor of $\alpha_4\beta_7$ MORF-057.

Aims & Methods: A randomized, double-blinded, placebo-controlled multiple ascending dose (MAD) study (NCT04580745) was conducted on 21 healthy subjects (16 active + 5 placebo) to evaluate the safety, tolerability, and pharmacokinetics (PK) of MORF-057. Subjects recruited in the MAD study were grouped into 3 cohorts based on MORF-057 treatment dosages (25 mg BID, 50 mg BID, 100 mg BID). Blood was serially collected to assess PK/PD readouts over a period of 14 days.

Changes in $\alpha_4\beta_7$ receptor occupancy (RO) and lymphocyte trafficking were explored using flow cytometry-based assays on days 0 (pre-treatment), 1, 7, and 14. Whole blood samples were assayed under physiological conditions to quantify $\alpha_4\beta_7$ occupancy. PBMC samples were isolated to quantify CD4+ naïve, CD4+ central memory (T_{CM}), CD4+ effector memory (T_{EM}) T cells, and switched memory B cells (B_{SM}). Post-treatment PBMC data were normalized to baseline pre-treatment levels for comparison with placebo using the Mann-Whitney U test.

Results: On Day 14, trough $\alpha_4\beta_7$ RO was high in all groups and saturating (RO > 99%) in the 100 mg BID cohort (Table). Subjects receiving MORF-057 100 mg BID had a significant increase in their circulating levels of β_7 + CD4+ T_{CM} cells. Similarly, β_7 high CD4+ T_{EM} subset showed an increasing trend in circulation for the 100 mg BID dose group. As for the β_7 + B_{SM} cell subset, the percent change from baseline was significantly greater for the top two dose groups. No significant changes in naïve B and naïve CD4+ T cells were observed in all dose groups.

	POOLED PLACEBO (n=5)	25 mg BID (n=5)	50 mg BID (n=6)	100 mg BID (n=5)
CD4+ memory T cells trough RO (%)	0	91	93	>99 (n=4)
LYMPHOCYTE SUBSET CHANGES				
CD4+ β_7 + central memory T cells	97.1	94.8	104.5	114.6*
CD4+ β_7 high effector memory T cells	93.1	88.3	100.7	113.2
β_7 + switched memory B cells	98.1	103.2	105.0*	116.7**

* p<0.05, ** p<0.01 based on Mann-Whitney U test, active vs. placebo

T_{CM} : CD3+CD4+CD45RO+CD27+; T_{EM} : CD3+CD4+CD45RO+CD27-; B_{SM} cells: CD19+CD27+IgD-

Table. Baseline-normalized median of β_7 + lymphocyte subsets and $\alpha_4\beta_7$ RO after treatment with MORF-057 BID for 14 days.

Conclusion: Healthy subjects receiving MORF-057 for a period of 14 days in the top dose group achieved saturation of $\alpha_4\beta_7$ receptors and statistically significant increases in circulating ITG β_7 expressing CD4+ T_{CM} , and B_{SM} lymphocyte subsets. Effects observed were consistent with those reported for biologic inhibitors of the same pathway in patients and establish proof-of-biology for MORF-057.⁴

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P0418

EXPLORATORY ANALYSIS OF FILGOTINIB SAFETY DATA IN A SELECTED POPULATION OF PATIENTS WITH RHEUMATOID ARTHRITIS: DATA FROM FINCH 1-4 AND DARWIN 1-3 STUDIES IN PERSPECTIVE TO INTEGRATED ULCERATIVE COLITIS SAFETY DATA

S. Schreiber¹, M.H. Buch², X. Mariette³, G.R. Burmester⁴, C. Charles-Schoeman⁵, V. Rajendran⁶, N. Verbruggen⁶, A. Cerani⁶, P. Van Hoek⁶, K. Van Beneden⁶, A. Oortwijn⁷, Y. Tanaka⁸, E.G. Favalli⁹, H. Schulze-Koops¹⁰, R. Westhovens¹¹, S. Vermeire¹¹
¹Kiel University, Kiel, Germany, ²University of Manchester and NIHR Manchester Biomedical Research Centre, Manchester, United Kingdom, ³Université Paris-Saclay, Assistance Publique - Hôpitaux de Paris, Le Kremlin Bicêtre, France, ⁴Charité – Universitätsmedizin Berlin, Berlin, Germany, ⁵David Geffen School of Medicine, UCLA, Los Angeles, United States, ⁶Galapagos NV, Mechelen, Belgium, ⁷Galapagos NV, Leiden, Netherlands, ⁸University of Occupational and Environmental Health, Kitakyushu, Japan, ⁹University of Milan, ASST Gaetano Pini - CTO Institute, Milano, Italy, ¹⁰Ludwig-Maximilians-University Munich, Munich, Germany, ¹¹University Hospitals Leuven, Leuven, Belgium

Contact E-Mail Address: Alessandra.Oortwijn@glpg.com

Introduction: Filgotinib (FIL) is generally well tolerated in patients with ulcerative colitis (UC), independent of dose, disease history, prior biologic failure, and age group^{1,2}.

Data from the ORAL-SURVEILLANCE study (NCT02092467)³ suggested that, in patients with active rheumatoid arthritis (RA) aged ≥50 years with ≥1 cardiovascular (CV) risk factor, the pan-JAK inhibitor tofacitinib has a higher risk of major adverse cardiovascular events (MACE) and malignancies compared with TNF inhibitors. It is unclear whether a preferential JAK1 inhibitor, such as FIL, may also increase the risk of these events in patients with active UC.

Aims & Methods: In absence of sufficient data from a high-risk UC population, we report an exploratory analysis of adverse events of special interest (AESI) using integrated FIL RA data from Phase 2 (NCT01668641, NCT01894516), Phase 3 (NCT02889796, NCT02873936, NCT02886728), and long-term extension (LTE) studies: DARWIN 3 Phase 2 LTE, NCT02065700; FINCH 4 Phase 3 LTE, NCT03025308, in a patient population at higher-risk for CV events (aged ≥50 years with ≥1 CV risk factor).

Population CV risk factors similar to ORAL-SURVEILLANCE were selected, including: a history of dyslipidemia, diabetes or CV disease, hypertension, ischemic vascular conditions, peripheral vascular disease, extra-articular manifestations of RA, or current smokers. Censored exposure-adjusted incidence rates (EAIR)/100 patient-years of exposure for MACE, venous thromboembolism (VTE), malignancies excluding nonmelanoma skin cancer (NMSC), NMSC, (serious) infections, and deaths were determined. The analysis set included data available through January 2022 for DARWIN 3 and FINCH 4 LTEs.

Results: Overall, the higher-risk population included 1484 patients, mean age 62.1 years (536 [36.1%] aged ≥65 years), 291 (22.5%) were current smokers, and 904 (60.9%) received background methotrexate (MTX); baseline (BL) MTX was higher in the FIL100 vs FIL200 group (66.6 vs 54.6%) and other BL demographics were balanced.

In this population, numerically higher EAIRs for malignancies (excluding NMSC), NMSC, serious infections, and deaths were observed for patients receiving FIL200; 95% confidence intervals (CI) overlapped with the FIL100 dose (Table).

For MACE, incidence was numerically lower in the FIL200 versus FIL100 group, and for VTE incidence was the same in both dose groups, with overlapping 95% CIs.

EAIR per 100 PYE (95% CI) n (%)	Filgotinib 100 mg q.d. (PYE=1849.7) (N=692)	Filgotinib 200 mg q.d. (PYE=2803.7) (N=870)
MACE*	0.6 (0.3, 1.1) 11 (1.6)	0.5 (0.3, 0.9) 14 (1.6)
Myocardial infarction	0.2 (0.1, 0.6) 4 (0.6)	0.1 (0.0, 0.3) 3 (0.3)
VTE*	0.2 (0.1, 0.6) 4 (0.6)	0.2 (0.1, 0.5) 6 (0.7)
Malignancies (excluding NMSC)	1.0 (0.6, 1.5) 18 (2.6)	1.2 (0.8, 1.7) 33 (3.8)
NMSC	0.3 (0.1, 0.7) 6 (0.9)	0.6 (0.4, 1.0) 18 (2.1)
Serious infections	2.6 (1.9, 3.4) 47 (6.8)	2.9 (2.3, 3.6) 81 (9.3)
Infections	35.9 (32.4, 39.8) 367 (53.0)	38.8 (35.6, 42.1) 555 (63.8)
TEAEs leading to death	0.8 (0.5, 1.3) 15 (2.2)	1.4 (1.0, 1.9) 39 (4.5)

*Positively adjudicated MACE/VTE (adjudication cut-off for higher-risk population: 30 November 2021), VTE (deep venous thrombosis/pulmonary embolism). AESI, adverse event of special interest; CI, confidence interval; CV, cardiovascular; EAIR, exposure-adjusted incidence rate; MACE, major adverse cardiovascular event; NMSC, nonmelanoma skin cancer; PYE, patient-years of exposure; q.d., once daily; RA, rheumatoid arthritis; VTE, venous thromboembolism.

Table. EAIR and frequency of treatment emergent AESI in a selected population of patients with RA (≥50 years old, ≥1 CV risk)

Conclusion: In absence of data in a higher-risk UC population, exploratory analysis of safety events in the RA population at higher risk of CV events may inform the safety of FIL in UC. In this RA population, the incidence rate of MACE, VTE and malignancies was similar with both doses. A numerically higher incidence of NMSC, serious infections and deaths was observed in the high dose group versus the low dose group. The ongoing LTE and real-world studies in RA and UC will continue to investigate the safety of FIL in these populations.

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VR is an employee and shareholder of Galapagos NV.

NV is an employee of Galapagos NV.

AC is an employee of Galapagos NV.

PVH is a paid consultant for Galapagos NV.

KVB is an employee and shareholder of Galapagos NV.

AO is an employee and shareholder of Galapagos NV.

YT has received speaking fees and/or honoraria from Abbvie, AstraZeneca, Boehringer-Ingelheim, Bristol-Myers, Chugai, Daiichi-Sankyo, Eisai, Eli Lilly, Gilead, GlaxoSmithKline, Mitsubishi-Tanabe, and Pfizer, and received research grants from Abbvie, Asahi-Kasei, Boehringer-Ingelheim, Chugai, Daiichi-Sankyo, Eisai, and Takeda.

EGF has received consulting/speaking fees from AbbVie, Bristol-Myers Squibb, Celltrion, Galapagos, Janssen, Lilly, MSD, Novartis, Pfizer, and UCB.

HSK has received honoraria for consulting and lectures from Abbvie, Galapagos, Lilly, and Pfizer.

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P0419

EFFECTIVENESS AND SAFETY OF SWITCHING FROM ADALIMUMAB REFERENCE TO BIOSIMILAR IN PATIENTS WITH INFLAMMATORY BOWEL DISEASE: THE ADA-SWITCH STUDY

M.J. Casanova¹, M. Chaparro Sanchez¹, Ó. Nantes², P. Varela³, M. Vela-González⁴, M. Rivero⁵, O. Sierra-Gabarda⁶, S. Riestra⁷, M. Barreiro-de Acosta⁸, M.d.M. Martín-Rodríguez⁹, C.J. Gargallo-Puyuelo¹⁰, C. Reygosa¹¹, R. Muñoz-Pérez¹², I. García de la Filia-Molina¹³, A. Núñez-Ortiz¹⁴, L. Kolle¹⁵, M. Calafat¹⁶, J.M. Huguet¹⁷, E. Iglesias-Flores¹⁸, T.J. Martínez-Pérez¹⁹, O. Bosch²⁰, J.M. Duque-Alcorta²¹, S. Frago-Larramona²², M. Sánchez-Azofra²³, M. Van Domselaar²⁴, V.M. González-Cosano²⁵, L. Bujanda²⁶, S. Rubio², A. Mancebo³, B. Castro⁵, S. García-López⁶, R. de Francisco⁷, L. Nieto⁸, V. Laredo¹⁰, A. Gutiérrez-Casbas¹², F. Mesonero¹³, E. Leo-Carnerero¹⁴, F. Cañete¹⁶, L. Ruiz¹⁷, B. Gros¹⁸, M. del Moral-Martínez¹⁹, C. Rodríguez², J.P. Gisbert¹, on behalf of the ADA-SWITCH Study Group

¹Hospital Universitario de La Princesa, IIS-Princesa, UAM and CIBERehd, Gastroenterology Unit, Madrid, Spain, ²Hospital Universitario de Navarra, Instituto de Investigación Sanitaria de Navarra (IdiSNA), Gastroenterology Unit, Pamplona, Spain, ³Hospital Universitario de Cabueñes, Gastroenterology Unit, Gijón, Spain, ⁴Hospital Universitario Nuestra Señora de la Candelaria, Gastroenterology Unit, Santa Cruz de Tenerife, Spain, ⁵Hospital Universitario Marqués de Valdecilla and IDIVAL, Gastroenterology Unit, Santander, Spain, ⁶Hospital Universitario Miguel Servet, Gastroenterology Unit, Zaragoza, Spain, ⁷Hospital Universitario Central de Asturias, Instituto de Investigación Sanitaria del Principado de Asturias (ISPA), Gastroenterology Unit, Oviedo, Spain, ⁸Hospital Clínico Universitario de Santiago de Compostela, Gastroenterology Unit, Santiago de Compostela, Spain, ⁹Hospital Universitario Virgen de las Nieves, Granada, Spain, ¹⁰Hospital Clínico Lozano Blesa, IIS Aragón, and CIBEREHD,

Gastroenterology Unit, Zaragoza, Spain, ¹¹Hospital Universitario de Canarias, Gastroenterology Unit, La Laguna, Spain, ¹²Hospital General Universitario Dr. Balmis and CIBEREHD, Gastroenterology Unit, Alicante, Spain, ¹³Hospital Universitario Ramón y Cajal, Gastroenterology Unit, Madrid, Spain, ¹⁴Hospital Universitario Virgen del Rocío, Gastroenterology Unit, Sevilla, Spain, ¹⁵Hospital General de La Palma, Gastroenterology Unit, Santa Cruz de Tenerife, Spain, ¹⁶Hospital Universitario Germans Trias i Pujol and CIBEREHD, Gastroenterology Unit, Badalona, Spain, ¹⁷Consorcio Hospital General Universitario de Valencia, Gastroenterology Unit, Valencia, Spain, ¹⁸Hospital Universitario Reina Sofía and Instituto Maimónides de Investigación Biomédica de Córdoba (IMIBIC), Gastroenterology Unit, Córdoba, Spain, ¹⁹Hospital Virgen de La Luz, Gastroenterology Unit, Cuenca, Spain, ²⁰Fundación Jiménez Díaz, Gastroenterology Unit, Madrid, Spain, ²¹Hospital Universitario San Agustín, Gastroenterology Unit, Avilés, Spain, ²²Hospital Santa Bárbara, Gastroenterology Unit, Soria, Spain, ²³Hospital Universitario La Paz, Gastroenterology Unit, Madrid, Spain, ²⁴Hospital Universitario de Torrejón, Gastroenterology Unit, Madrid, Spain, ²⁵Hospital de Montilla, Gastroenterology Unit, Córdoba, Spain, ²⁶Hospital Universitario de Donostia, Instituto Biodonostia, Universidad del País Vasco (UPV/EHU) and CIBEREHD, Gastroenterology Unit, Donostia, Spain

Contact E-Mail Address: mjcasanova.g@gmail.com

Introduction: The effectiveness and safety of switching from adalimumab reference to biosimilar in patients with inflammatory bowel disease (IBD) has been barely studied.

Aims & Methods: Aims: The aims of the present study were:

1. To compare persistence on adalimumab treatment over time in IBD patients who maintained adalimumab reference [non-switch cohort (NC)] vs. those who switched from adalimumab reference to adalimumab biosimilar [switch cohort (SC)];
2. To compare loss of effectiveness of adalimumab treatment in the NC vs. SC;
3. To identify factors associated with discontinuation of adalimumab therapy;
4. To identify the factors associated with relapse in both cohorts; and,
5. To evaluate the safety of both strategies.

Methods: Retrospective, observational, multicenter study conducted at 26 Spanish sites. Patients under adalimumab reference who were in clinical remission at standard dose of adalimumab reference, and in whom adalimumab was the first anti-TNF administered, were included. Clinical remission was defined as a Harvey-Bradshaw index ≤ 4 points in Crohn's disease, a partial Mayo score ≤ 2 in ulcerative colitis, and the absence of fistula drainage despite gentle finger compression in perianal disease. The follow-up time was at least 6 months since start of study observation period. The Kaplan-Meier with log-rank test was used to evaluate the cumulative incidence of treatment discontinuation. Cox regression model was used to investigate factors potentially associated with treatment discontinuation.

Results: A total of 505 patients were included (45% women, 87% Crohn's disease): 229 in the SC and 276 in the NC. The median follow-up was 12 months in the SC and 23 months in the NC ($p < 0.01$). The incidence rate of adalimumab discontinuation was 10% [95% confidence interval (95%CI)=6-14%], and 7% (95%CI=5-10%) per patient-year in the SC and in the NC, respectively ($p = 0.035$). The probability of maintaining adalimumab was 92% at 12 months and 77% at 24 months in the SC, and 97% at 12 months and 86% at 24 months in the NC.

In the multivariable analysis, the switch to adalimumab biosimilar, adjusted for the level of C-reactive protein at baseline, was not associated with therapy discontinuation. 18% of the patients relapsed in the SC vs. 21% in

the NC. The incidence of relapse was 17% (95%CI=13-23%) in the SC, and 12% (95%CI=10-16%) per patient-year in the NC ($p=0.04$). The cumulative incidence of relapse was 11% at 12 months and 38% at 24 months in the SC, and 11% at 12 months and 22% at 24 months in the NC. In the multi-variable analysis, the switch to adalimumab biosimilar (adjusted by type of IBD) was associated with a higher risk of relapse ($HR=1.5$, 95%CI=1.008-2.36). Four percent of the patients had adverse events in the SC vs. 8% in the NC ($p>0.05$).

Conclusion: The incidence rate of relapse was slightly higher in the SC; however, this fact had no impact on persistence on the drug. Switching from adalimumab reference to adalimumab biosimilar was safe.

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Martín-Rodríguez, M.M.Hospital Universitario Virgen de las Nieves, Granada.

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ANTI-INFLAMMATORY AND BARRIER STABILIZING EFFECTS OF A HERBAL COMBINATION MEDICINE OF MYRRH, COFFEE CHARCOAL AND CHAMOMILE FLOWER EXTRACT IN A MULTI-COMPONENT CELL MODEL OF THE INFLAMED INTESTINAL MUCOSA

L. Schiller^{1,2}, B. Lipowicz², C. Vissienon^{1,2}

¹Leipzig University/Medical Faculty, Institute of Medical Physics and Biophysics, Leipzig, Germany, ²Repha GmbH Biologische Arzneimittel, Langenhagen, Germany

Contact E-Mail Address: cica.vissienon@uni-leipzig.de

Introduction: Myrrhinil-Intest®, a herbal medicinal product consisting of myrrh (*Commiphora myrrha* (Nees) Engl.), coffee charcoal (*Coffea arabica* L.) and chamomile flower dry extract (*Matricaria chamomilla* L.), has been used for decades to treat various gastrointestinal diseases. Recent clinical studies suggest its use in remission maintenance therapy of ulcerative colitis and led to its inclusion as a complementary therapeutic option in the German S3-Guideline Ulcerative Colitis. The underlying pharmacological mechanisms have not yet been fully elucidated.

Aims & Methods: Aim of the present study was to assess the influence of the individual components of Myrrhinil-Intest® and their threefold combination on inflammatory cross-talk between immune and intestinal epithelial cells as well as resulting intestinal barrier impairments using a complex co-culture cell model. To model the intestinal mucosa, epithelial cell like Caco-2 and goblet cell like HT29-MTX cells were differentiated on transwell inserts and inflammatory stimulation was realized by co-cultivation with LPS-activated human macrophages for 48 h.

At the same time treatment with different concentrations of the plant extracts (0.1-500 µg/mL) or budesonide (0.1 µM) as positive control was performed. Barrier function was evaluated by measurements of transepithelial electrical resistance (TER). Secretion of cytokines (IL6, TNF) as well as chemokines (IL8, MCP-1) and lipid mediator PGE₂ was quantified by ELISA.

Results: The individual plant extracts and their combined application showed concentration-dependent inhibitory effects on the release of pro-inflammatory mediators from stimulated cells to a varying extent with myrrh extract being most effective component. TER of inflamed monolayers was restored to baseline level upon treatment with myrrh, coffee charcoal and the ternary combination. The effects were comparable to treatment with budesonide. Synergistic and additive interactions were observed after combined application of all three plant extracts.

Conclusion: Thus, the herbal components of Myrrhinil-Intest® inhibited the inflammatory communication between immune and intestinal epithelial cells and counteracted the intestinal barrier impairment. In addition, synergistic and additive pharmacological interactions of the single components aid the overall effect and reinforce the use of their combined application in IBD therapy.

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P0421

USTEKINUMAB IMPROVES HEALTH-RELATED QUALITY OF LIFE IN PATIENTS WITH MODERATE-TO-SEVERE CROHN'S DISEASE: RESULTS UP TO WEEK 104 OF THE STARDUST TRIAL

L. Peyrin-Biroulet¹, S. Vermeire², G.R. D'Haens³, J. Panés⁴, A. Dignass⁵, F. Magro^{6,7}, M. Nazar⁸, M. Le Bars⁹, M. Lahaye¹⁰, L. Ni¹¹, I. Bravatà¹², D.R. Gaya¹³, S. Danese¹⁴

¹University Hospital of Nancy, University of Lorraine, INSERM U 1256 NGERE and Hepato-Gastroenterology, Houdemont, France, ²University Hospitals Leuven, Gastroenterology and Hepatology, Leuven, Belgium, ³University of Amsterdam, Academic Medical Center, Amsterdam, Netherlands, ⁴Hospital Clinic of Barcelona, IDIBAPS, CIBERehd, Gastroenterology, Barcelona, Spain, ⁵Agaplesion Markus Hospital, Goethe University, Medicine I, Frankfurt/ Main, Germany, ⁶Institute for Molecular and Cell Biology, Faculty of Medicine University of Porto, Pharmacology & Therapeutics, Porto, Portugal, ⁷Hospital de São João, Gastroenterology, Porto, Portugal, ⁸Janssen-Cilag Polska Sp. z o.o., Warsaw, Poland, ⁹Janssen-Cilag, Issy Les Moulineaux, France, ¹⁰Janssen-Cilag BV, Breda, Netherlands, ¹¹Janssen-Cilag Russia, Moscow, Russian Federation, ¹²Janssen-Cilag, Milan, Italy, ¹³Glasgow Royal Infirmary, Gastroenterology, Glasgow, United Kingdom, ¹⁴IRCCS Ospedale San Raffaele and University Vita-Salute San Raffaele, Gastroenterology and Endoscopy, Milan, Italy

Contact E-Mail Address: peyrinbiroulet@gmail.com

Introduction: STARDUST is a phase 3b randomized trial comparing two treatment strategies with ustekinumab (UST) in patients (pts) with Crohn's disease (CD): treat-to-target (T2T) using early endoscopic assessment vs standard of care (SoC).

The primary endpoint, safety, and efficacy data of STARDUST from Week (W)48 and the long-term extension (LTE; W48–W104) have been published previously.^{1,2}

Here, we describe results from the LTE period for health-related quality of life (HRQoL) measures and the effect of UST on work productivity and activity impairment at W104, comparing T2T and SoC.

Aims & Methods: Adult pts with moderate–severe active CD, received iv, weight-based UST ~6mg/kg at W0; then sc UST 90mg at W8. At W16, CD Activity Index (CAI) responders (≥70-point reduction in CAI) were randomized 1:1 to either T2T or SoC and received sc UST 90mg, every 12W/8W (up to 4W in the T2T arm) as per the protocol. From W48, pts entering LTE could continue to receive sc UST up to W104 with further protocol-guided dose adjustment (de-escalation/escalation).

This analysis assessed changes from baseline (BL) in the following HRQoL measures at W104: Inflammatory Bowel Disease Questionnaire (IBDQ), EuroQoL 5-Dimension 5-Level (EQ-5D-5L), Functional Assessment of Chronic Illness Therapy-Fatigue (FACIT-F) tools, Hospital Anxiety and Depression Scale (HADS-A and -D), the Work Productivity and Activity Impairment (WPAI) questionnaire and time lost from work. Percentage of pts with IBDQ response (an increase of ≥16 points in IBDQ score from BL) and remission (IBDQ score ≥170) at W104 are also presented. Results are presented as observed and shown only for pts entering LTE (modified randomized analysis set).

Results: Of 440 pts randomized to T2T or SoC at W16, 74 discontinued before W48. Of the remaining 366 pts completing W48, 43 discontinued and did not enter LTE. At W48, 323 pts (T2T, n=147; SoC, n=176) entered LTE and 82.3% and 80.1% of pts in T2T and SoC arms, respectively, completed 104W of treatment. At W104, similar percentages of pts in T2T and SoC arms had an IBDQ response (89.4% and 84.8%, respectively) and remission (76.1% and 71.2%, respectively). Comparable changes from BL in IBDQ, EQ-5D-5L (visual analogue scale and index score), FACIT-F, HADS-A and -D and WPAI were seen in both arms at W104; percentages of pts with WPAI 7-point improvement from BL per domain were also similar (Table 1).

	T2T			SoC		
HRQoL ^a	BL ^b , mean (95% CI), n	W104 ^b , mean (95% CI), n	Change from BL, mean (95% CI), n	BL ^b , mean (95% CI), n	W104 ^b , mean (95% CI), n	Change from BL, mean (95% CI), n
IBDQ	128.4 (122.9; 133.9), n=146	187.3 (181.9; 192.8), n=113	56.4 (50.0; 62.8), n=113	128.2 (122.9; 133.4), n=173	180.2 (174.9; 185.5), n=129	52.5 (46.2; 58.8), n=129
EQ-5D-5L VAS	54.7 (51.6; 57.9), n=146	80.0 (77.2; 82.8), n=113	24.4 (20.7; 28.2), n=113	57.5 (54.6; 60.4), n=174	76.9 (74.0; 79.9), n=132	19.3 (15.5; 23.2), n=132
EQ-5D-5L Index	0.672 (0.640; 0.704), n=145	0.864 (0.836; 0.891), n=111	0.171 (0.138; 0.203), n=111	0.675 (0.645; 0.705), n=173	0.849 (0.824; 0.873), n=129	0.168 (0.131; 0.205), n=129
FACIT-F	28.4 (26.5; 30.3), n=147	41.6 (39.9; 43.3), n=114	12.7 (10.7; 14.6), n=114	27.2 (25.4; 28.9), n=176	40.4 (38.7; 42.1), n=135	13.1 (11.1; 15.0), n=135
HADS-A	7.9 (7.2; 8.6), n=145	4.7 (3.9; 5.4), n=110	-2.8 (-3.6; -2.1), n=110	8.1 (7.5; 8.7), n=173	4.7 (4.0; 5.4), n=129	-3.5 (-4.2; -2.8), n=129
HADS-D	6.8 (6.1; 7.5), n=145	3.4 (2.6; 4.1), n=110	-3.0 (-3.7; -2.2), n=110	6.6 (6.0; 7.2), n=173	3.7 (3.0; 4.3), n=129	-3.0 (-3.7; -2.3), n=129
WPAI ^a	BL ^b , mean (95% CI), n	W104 ^b , mean (95% CI), n	Change from BL, mean (95% CI), n	BL ^b , mean (95% CI), n	W104 ^b , mean (95% CI), n	Change from BL, mean (95% CI), n
Absenteeism	23.1 (15.0; 31.2), n=71	3.0 (-0.5; 6.4), n=42	-15.5 (-26.0; -5.0), n=42	19.6 (12.9; 26.3), n=89	8.0 (2.5; 13.5), n=51	-7.8 (-16.0; 0.5), n=51
Presenteeism	44.8 (38.5; 51.1), n=81	12.1 (6.8; 17.4), n=53	-28.7 (-37.6; -19.7), n=53	47.6 (41.6; 53.6), n=96	17.7 (11.9; 23.5), n=60	-28.3 (-36.3; -20.3), n=60
Work productivity loss	54.4 (46.8; 62.0), n=67	16.0 (8.9; 23.1), n=41	-31.9 (-43.5; -20.4), n=41	50.0 (43.0; 56.9), n=79	19.7 (11.6; 27.7), n=43	-25.6 (-36.3; -14.9), n=43
Activity impairment	51.1 (46.9; 55.4), n=142	14.7 (10.6; 18.8), n=110	-32.8 (-38.5; -27.2), n=110	50.1 (46.0; 54.2), n=171	19.1 (15.3; 22.9), n=130	-30.1 (-35.1; -25.1), n=130
WPAI 7-point improvement from BL ^{a,c}	W104 n/N (%), (95% CI)		W104 n/N (%), (95% CI)			
Absenteeism	15/42 (35.7), (21.6; 52.0)		17/51 (33.3), (24.9; 45.0)			
Presenteeism	39/53 (73.6), (59.7; 84.7)		46/60 (76.7), (66.2; 82.9)			
Work productivity loss	31/41 (75.6), (59.7; 87.6)		32/43 (74.4), (64.4; 83.8)			
Activity impairment	87/110 (79.1), (70.3; 86.3)		101/130 (77.7), (72.6; 83.4)			

The mRAS includes all patients who entered the LTE period (from W48 to W104).

^aData analysed as observed. ^bAbsolute value. ^cWPAI 7-point improvement is defined as a decrease of 7 points per domain.

Only patients with non-missing baseline value and at least one non-missing post-baseline value during the main treatment period are included in the analysis. N at baseline and at W104 is the number of subjects with a non-missing value for the parameter at the specified time point. N for change from baseline is the number of subjects with non-missing values at both baseline and W104 time point.

BL, baseline; CI, confidence interval; EQ-5D-5L, EuroQoL 5-Dimension 5-Level; FACIT-F, Functional Assessment of Chronic Illness Therapy-Fatigue; HADS-A (-D), Hospital Anxiety and Depression Scale – Anxiety subscale (- Depression subscale); HRQoL, Health-Related Quality of Life; IBDQ, Inflammatory Bowel Disease Questionnaire; LTE, long-term extension; mRAS, modified randomized analysis set; SoC, standard of care; T2T, treat to target; VAS, visual analogue scale; W, week; WPAI, Work Productivity and Activity Impairment.

Table 1. Changes from BL in HRQoL and WPAI measures at W104 (mRAS)

At W104, pts on average lost 2.2 and 2.3 fewer days from work due to CD vs BL in T2T and SoC arms, respectively. At W104, 60.9% and 68.7% in T2T and SoC arms were in employment vs 61.6% and 63.4% at BL, respectively.

Conclusion: STARDUST LTE is the first UST efficacy study to use an algorithm-driven dose adjustment. Over 80% of pts responding to induction and receiving maintenance treatment with UST from both T2T and SoC arms achieved IBDQ response at the end of 2 years of follow-up.

Both treatment strategies improved HRQoL (including fatigue, depression and anxiety scales). Work productivity improvements and reduced time lost from work were maintained up to W104 in pts with CD.

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M. Lahaye is an employee of Janssen-Cilag B.V., and has restricted stocks.

L. Ni is an employee of Janssen-Cilag Russia, and has restricted stocks.

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P0422

SAFETY OF COVID-19 VACCINE IN PATIENTS WITH INFLAMMATORY BOWEL DISEASE: DATA OF A NATIONAL STUDY (ESCAPE-IBD)

A. Todeschini¹, A. Contaldo², F.S. Macaluso³, F. Facciotti⁴, F. Castiglione⁵, O.M. Nardone⁶, R. Spagnuolo⁷, P. Doldo⁸, G. Riguccio⁹, F.S. Conforti¹⁰, C. Vignano¹¹, M. Ascolani¹², G. Bodini¹³, M. Milla¹⁴, G. Scardino¹⁵, M. Venero¹⁶, F. Desideri¹⁷, M. Mannino¹⁸, G. Rizzo¹⁹, A. Di Leo²⁰, A. Orlando²⁰, M.R.D. Principi²¹
¹IRCCS Sacro Cuore Don Calabria, IBD UNIT, Negrar di Valpolicella, Italy, ²IRCCS S. De Bellis, U.O. Gastroenterologia 2, Castellana Grotte, Italy, ³Villa Sofia-Cervello Hospital, IBD Unit, Palermo (Pa), Italy, ⁴IEO, Experimental oncology, Milano MI, Italy, ⁵Federico II University, Naples, Italy, ⁶University of Naples Federico II, Gastroenterology, Naples, Italy, ⁷Università \, Catanzaro, Italy, ⁸Policlinico Mater Domini Div. di Gastroenterologia, CATANZARO (ref. Prof. F. Luzzi), Catanzaro, Italy, ⁹Ospedale Santa Maria del Prato, UOSD Malattie Infiammatorie Croniche Intestinali, Feltre, Italy, ¹⁰Ospedale Policlinico di Milano, Unità Operativa di Gastroenterologia ed Endoscopia, Milano, Italy, ¹¹University of Milano-Bicocca, Department of Medicine and Surgery, Monza, Italy, ¹²Ospedale Ca' Foncello, UOC Gastroenterologia, Treviso, Italy, ¹³Policlinico San Martino, Department of Internal Medicine, Genova, Italy, ¹⁴Azienda Ospedaliero Universitaria Careggi, Firenze Oncologia e, Firenze, Italy, ¹⁵Ospedale Valduce, Dipartimento di Gastroenterologia, Como, Italy, ¹⁶IRCCS Policlinico San Matteo, Università degli studi di Pavia, Clinica medica 1, Pavia, Italy, ¹⁷Ospedale Di Bolzano, Gastroenterology, Bolzano, Italy, ¹⁸Villa Sofia-Cervello Hospital, IBD Unit, Palermo, Italy, ¹⁹Section of gastroenterology, DETO, University of Bari, Dr., Bari, Italy, ²⁰Villa Sofia Cervello, IBD Unit, Palermo, Italy, ²¹Policlinico di Bari, Bari, Italy

Contact E-Mail Address: ale_tode@hotmail.com

Introduction: Vaccination is the most effective method to prevent and control the SARS-CoV-2 infection. Recommendations consider patients with inflammatory bowel disease (IBD), Crohn's disease (CD) and ulcerative colitis (UC), a high-priority population to COVID-19 vaccine administration. There were a lot of concerns about vaccination safety in the setting of biological and immunomodulatory drugs.

The purpose of this study was to present data on safety about anti-SARS-CoV-2 vaccination in a cohort of IBD patients. These are data of an ongoing multicenter study assessing effectiveness and safety of COVID-19

vaccines in patients with IBD treated with immunomodulatory or biological drugs (ESCAPE-IBD) sponsored by the Italian Group for the study of Inflammatory Bowel Disease (IG-IBD - ClinicalTrials.gov Identifier: NCT04769258).

Aims & Methods: Anti-SARS-CoV-2 vaccination was administrated to 809 IBD patients. Afterwards completed vaccination, telephone or in-person interviews were conducted from February to July 2021 by gastroenterologists from referral center to report local and/or systemic adverse events (AEs) related to vaccination. Data on medical history and treatment was collected from electronic health records. Of these 809, 346 patients were surveyed on the pandemic burden and the main reason for hesitancy in Covid-19 vaccination. Chi-square test was used to compare categorical variables. Logistic regression was used to assess the relationship between disease-related characteristics and the onset of AEs.

Results: 809 patients, 456 CD and 353 UC, regularly followed in IBD unit, were enrolled. All patients received a complete SARS-CoV-2 vaccination cycle. Most of them (68%) were in biological or immunomodulatory therapy. About 45% of patients had at least one side effect, following the first dose (10%), the second (15%) or both doses (20%). Local pain at site of injection (24%), fatigue (33%) and fever (30%) were the three most common AEs. Flares of the underlying IBD were not reported. The vast majority of AE were mild and lasted only a few days. No serious AEs were reported and no patient was hospitalized. Logistic regression analysis revealed that female gender ($p<0.001$), younger age ($p=0.001$), seroconversion ($p=0.002$) and comorbidity ($p<0.001$) were significantly associated with the occurrence of AEs.

Furthermore the survey showed that the pandemic did not affect IBD at all in 37.5%, and a lot in 9.2% of participants. The majority (95%) of patients welcomed the possibility of getting vaccinated; only 7% feared the vaccine's influence on the course of the IBD. The main concerns were the possibility of adverse effects (33%) and the failure to achieve immunity (17%), few for the type of vaccine (3%) and for the need to a further booster (6%). Almost all patients (99%) felt safer to have vaccinated at their IBD reference center.

Conclusion: The short-term vaccine reactions experienced in this cohort of IBD patients were mostly self-limiting, including local pain at the injection site, fatigue and fever. We found a high acceptance rate and a good safety profile of SARS-CoV-2 vaccination in our cohort.

Disclosure: Nothing to disclose.

P0423

THE PERSISTENCE OF ANTI-SPIKE ANTIBODIES FOLLOWING TWO SARS-COV-2 VACCINES IN PATIENTS WITH INFLAMMATORY BOWEL- AND JOINT DISEASES ON IMMUNOSUPPRESSIVE THERAPY COMPARED TO HEALTHY CONTROLS – A PROSPECTIVE COHORT STUDY

K.K. Jørgensen¹, I.E. Christensen^{2,3}, I. Jyssum^{2,3}, A.T. Tveter², J. Sexton², T. Tran⁴, S. Mjaaland⁵, G. Kro⁶, T.K. Kvien^{2,3}, D. Warren⁶, J. Jahnsen^{3,1}, L.A. Munthe^{4,7}, E.A. Haavardsholm^{2,3}, J.T. Vaage^{4,3}, G. Grødeland^{4,3}, F. Lund-Johansen⁴, S.W. Syversen², G. Lovik Goll², S.A. Provan²

¹Akershus University Hospital, Dept. of Gastroenterology, Lørenskog, Norway, ²Diakonhjemmet Hospital, Division of Rheumatology and Research, Oslo, Norway, ³University of Oslo, Institute of Clinical Medicine, Oslo, Norway, ⁴Oslo University Hospital, Dept. of Immunology, Oslo, Norway, ⁵Norwegian Institute of Public Health, Oslo, Norway, ⁶Oslo University Hospital, Dept. of Medical Biochemistry, Oslo, Norway, ⁷University of Oslo, KG Jebsen Centre for B cell Malignancies, Oslo, Norway

Contact E-Mail Address: Kristin.Kaasen.Jorgensen@ahus.no

Introduction: Limited data is available regarding long-term effectiveness of SARS-CoV-2 vaccines in patients with immune-mediated inflammatory diseases (IMIDs) on immunosuppressive therapy. Whether the persistence of vaccine-induced humoral immunity differs between IMID patients and the general public is currently unknown.

Aims & Methods: IMID patients on immunosuppressive medication and healthy controls were enrolled in the prospective, observational Nor-vaC study. Serum samples were collected at two time points following two dose SARS-CoV-2 vaccination (first assessment within 6–48 days and second within 49–123 days). Sera were analysed for antibodies binding the receptor-binding domain (RBD) of the SARS-CoV-2 Spike protein. Anti-RBD <200 BAU/ml were defined as low levels. The estimated percent reduction in anti-RBD standardised to 30 days was calculated and factors associated with reduction were identified in multivariable regression models.

The aims of the study were to compare the persistence of anti-Spike antibodies following two SARS-CoV-2 vaccine doses between IMID patients and healthy controls, and to identify predictors of antibody decline.

Results: A total of 1097 patients (190 Crohn's disease, 129 ulcerative colitis, 400 rheumatoid arthritis, 189 psoriatic arthritis, 189 spondyloarthritis) (median age 54 years [IQR 43–64]; 56% women) and 133 controls (age 45 years [35–56]; 83% women) provided blood samples within the defined intervals (median 19 days [IQR 15–24] and 97 days [86–105] after second vaccine dose). Of the patients, 464 used tumor necrosis factor inhibitor (TNFi) monotherapy, 259 TNFi + metabolite inhibitor(s), 212 methotrexate monotherapy, 42 interleukin inhibitors, 34 vedolizumab, 29 rituximab, and 23 janus kinase inhibitors. Antibody levels were significantly lower in patients compared to controls at both assessments, with median anti-RBD 1468 BAU/ml [IQR 500–5062] in patients and 5514 BAU/ml [2528–9580] in controls ($p<0.0001$) and 298 BAU/ml [IQR 79–500] in patients and 715 BAU/ml [28–2870] in controls ($p<0.0001$), at first and second assessment respectively. At the second assessment, anti-RBD antibody levels decreased below 200 BAU/ml in 452 (41%) patients and in 1 (0.8%) control ($p<0.0001$) (Table). The percentage change in anti-RBD levels were -86 % in patients and -77 % in controls ($p<0.0001$). In the multivariable regression analyses, patients had a greater decline in anti-RBD levels compared to controls β -3.7 (95% CI -6.0, -1.4) ($p<0.001$). Use of TNFi in mono- or combination therapy was associated with the greatest decline compared to controls, β -6.1 (95% CI -8.1, -4.1) and β -6.4 (-8.4, -4.2) respectively ($p<0.001$).

Conclusion: Within four months after the second vaccine dose, anti-Spike antibody levels declined considerably in both IMID patients and controls. Patients had lower antibody levels at the first assessment and a more

pronounced decline compared to controls, and were consequently more likely to have low antibody levels four months after the second vaccine dose. Our results support that IMID patients lose humoral protection and need additional vaccine doses sooner than healthy individuals.

Anti-RBD antibodies (BAU/ml)	Controls (n=133)		Patients (n=1097)	
	1 st assessment	2 nd assessment	1 st assessment	2 nd assessment
<5, n (%)	0	0	18 (1.6)	54 (5)
5-19, n (%)	0	0	4 (0.4)	60 (5)
20-199, n (%)	0	1 (1)	40 (4)	338 (31)
200-1999, n (%)	25 (19)	89 (67)	548 (50)	558 (51)
2000-8999, n (%)	71 (53)	40 (30)	398 (36)	82 (7.5)
≥ 9000, n (%)	37 (28)	3 (2)	89 (8)	5 (0.5)

Table. Serological response in patients and controls.

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P0424

HOW IS THE CLINICAL COURSE AND DRUG TOXICITY IN LATE-ONSET IBD PATIENTS?

L. Karahan¹, F. Akyuz², B. Çavuş², İ.V. Şenkal², Z. İstemihan², K. Nuriyev², S. Kaymakoglu², F. Besiçik², K. Demir², A. Cifcibasi Ormeci²

¹Istanbul University Faculty of Medicine, Istanbul, Turkey, ²Istanbul University Istanbul Faculty of Medicine, Gastroenterohepatology, Istanbul, Turkey

Contact E-Mail Address: filizakyuz@hotmail.com

Introduction: Inflammatory Bowel Diseases (IBD) rate has increased over the years. Compared to those who started at an early age, the course of the disease and treatment response remain uncertain in this age group.

Aims & Methods: Aims: We aimed to evaluate the disease course, treatment response and prognosis of late and early-onset patients with IBD.

Material and Method: In this study, the files of 1060 patients diagnosed with IBD and followed for more than 6 months were retrospectively evaluated in last 5 years. Thirty-nine patients (3.6%) with late-onset (≥60 years) were included in the study. As the control group, 50 early-onset patients with similar demographic findings with the late-onset patient group were included.

Demographic features, treatment-related side effects and toxicities, mortality rates, complication development, disease activity, endoscopic and clinical remission were compared between the early and late-onset groups. SCCAI and CDAI scores were used for clinical remission. Endoscopic activity was evaluated by Mayo and SES-CD scores.

Results: The mean age of the patients at the time of diagnosis was 49.2±17.5 years, and 53 (59.6%) were male. The mean age of late-onset patients at diagnosis was 66.3±5.5 years, and the mean age of early-onset patients at diagnosis was 35.8±10.7 years. Twenty-five (64.1%) of 39 late-onset patients were UC, 14 (35.9%) CD; Of 50 early-onset patients, 28 (56.0%) were UC and 22 (44.0%) CD.

The mean follow-up time of the late-onset patients was 75.1±53.1 months, and the mean follow-up period of the early-onset patients was 103.9±38.5 months. Clinical (94% vs. 86.8%) and endoscopic remission rates (49% vs. 33.3%) and AZT toxicity (28% vs 20.5%) were similar in early and late-onset patients, respectively.

Mortality rate in late-onset IBD (33.3% vs. 2%, OR: 24.5, CI: 3-197.8; p=0.001) and complication rate in late-onset UC were higher (32% vs. 7.1%, OR: 6.1, CI: 1.1-32.3; p=0.024) than in the early-onset patients. Although the development of malignancy was higher in the late-onset patient group than in the early-onset patients, it was not statistically significant (15.4% vs. 6%, p>0.05).

Age of onset (years)	Crohn's Disease			Ulcerative Colitis		
	<60	≥60	p	<60	≥60	p
AZT toxicity, n (%)	6 (27.3)	3 (21.4)	0.506	8 (28.6)	5 (20)	0.345
Biologic side effect, n (%)	5 (22.7)	1 (7.1)	0.228	3 (10.7)	1 (4)	0.350
AZT use, n (%)	22 (100)	11 (78.6)	0.051	19 (67.9)	11 (44)	0.070
Complication, n (%)	11 (50)	3 (21.4)	0.085	2 (7.1)	8 (32)	0.024
Mortality, n (%)	0 (0)	3 (21.4)	0.051	1 (3.6)	10 (40)	0.001
Biologic use, n (%)	15 (68.2)	5 (35.7)	0.058	10 (35.7)	4 (16)	0.094
Intestinal malignancy, n (%)	0 (0)	1 (7.1)	0.389	0 (0)	1 (4)	0.472
Extraintestinal malignancy, n (%)	0 (0)	1 (7.1)	0.389	3 (10.7)	5 (20)	0.288

Table: Clinical features of two groups

Conclusion: Clinical course and drug toxicity were similar in both groups. The mortality rate is higher in late-onset patients. The rate of development of malignancy is higher in the late-onset age group. Therefore, malignancy follow-up is important in this patient group.

Disclosure: Nothing to disclose.

P0425

HEAD-TO-HEAD PHARMACOKINETIC ANALYSIS OF INFlixIMAB MONO- VS COMBINATION THERAPY IN PAEDIATRIC CROHN'S DISEASE

R.J. Colman^{1,2}, S.A. Vuijk³, R. Mathôt⁴, J. Van Limbergen⁵, P. Minar^{2,6}, L. de Ridder³, G.R. D'Haens¹

¹Amsterdam UMC, Gastroenterology, Amsterdam, Netherlands, ²Cincinnati Children's Hospital Medical Center, Gastroenterology, Hepatology and Nutrition, Cincinnati, United States, ³Erasmus MC Sophia Children's Hospital, Paediatric Gastroenterology, Rotterdam, Netherlands, ⁴Amsterdam UMC, University of Amsterdam, Pharmacy, Amsterdam, Netherlands, ⁵Amsterdam UMC - Emma Children's Hospital, Paediatric Gastroenterology and Nutrition, Amsterdam, Netherlands, ⁶University of Cincinnati, Pediatrics, School of Medicine, Cincinnati, United States

Contact E-Mail Address: colman.rj@gmail.com

Introduction: Post hoc analysis of the SONIC trial found superior efficacy of standard dosing infliximab (IFX) combined with azathioprine (combo) compared to IFX monotherapy (mono) in adults with active CD, with more favorable pharmacokinetics (PK) on combo treatment (1).

Currently, many paediatric centers are increasingly using mono IFX with proactive therapeutic drug monitoring (pTDM) to minimise toxicity risks associated with thiopurine use.

The aim of this study was to evaluate whether combo has PK benefits over pTDM mono IFX, comparing drug exposure expressed as area under concentration curve (AUC), trough concentrations (TL) and IFX clearance (CL) between combo and pTDM mono IFX treated patients.

Aims & Methods: This PK analysis included CD patients who had drug concentrations measured as part of two prospective studies. Combo patients received labeled IFX (5mg/kg at 0, 2 and 6 wks followed by every 8 wks) with immunomodulator (IMM) in the TISKids study (2). In contrast, the mono patients received IFX in the observational REFINE study where pTDM was standard of care (3).

Inclusion criteria for the PK analysis were a weighted Paediatric CD Activity Index (wPCDAI) >40, age 3-17 years and body weight (BW) >10kg at baseline. Combo TL (Sanquin, ELISA) and mono TL (LabCorp, ECLIA) were assessed at week 6, 14 and 22 at trough (dose 3, 4 and 5). ECLIA is a drug-tolerant assay for antibodies to IFX (ATI) detection while the Sanquin ELISA is drug-sensitive (ATI was tested if IFX <3 µg/mL). A population PK model was built using a combined dataset from both cohorts with non-linear mixed effects modeling software using stepwise covariate modeling (objective function value >10.83, $P < 0.001$). IFX CL, AUC, TL and ATI were compared between the two groups using Wilcoxon Rank tests.

Results: The combined cohort consisted of 80 patients (64% combo), 52.5% female, median age 14 (IQR 11-16). The PK analysis included 264 TL and 92 peak concentrations. At baseline, the mono group had a higher wPCDAI 70 (62.5-80) vs 59 (47.5-70; $P < 0.01$), more prednisone use (79% vs 4%, $P < 0.01$) and lower serum albumin 2.9 g/dl (2.5-3.3) vs 3.7 (3.3-4.0; $P < 0.01$). IFX starting dose was 6.2mg/kg (5.3-7.8) vs 5.1 (5.0-5.3; $P < 0.01$) in mono vs combo.

A 2-compartment PK model with a negative correlation between albumin and CL and positive correlations between BW, erythrocyte sedimentation rate (ESR) and CL as well as BW and V1 adequately described the observed concentration data. For a patient with BW 65 kg, average CL and central volume of distribution (V1) were 0.39 L/d and 5.5 L, with corresponding interpatient variability of 31% and 28%. The use of IMM did not explain the interpatient variability in CL.

Moreover, there was no difference in median combo CL 0.29L/d (0.23-0.35) vs 0.30(0.23-0.40) mono CL ($P = 0.45$). There was also no significant difference between induction exposure ($AUC_{infusion1-4}$) 75,876µg*h/ml (60,719-96,168) combo vs 75,518(62,521-96,520; $P = 0.81$) mono, infusion-4 TL

4.4µg/ml (2.3-7.7) vs 4.7(2.4-8.5; $P = 0.77$) and infusion-5 TL 5.6µg/ml (3.2-8.8) vs 4.8(1.8-9.6; $P = 0.41$). While not a PK covariate of CL, 1 mono patient discontinued IFX due to ATI. No combo patients had ATI detected. There was higher CL during steroid use (most stopped by infusion-3), but there were no differences in CL or TLs at infusion-4 or 5 by steroid exposure. There was no difference in change of wPCDAI over time.

Conclusion: This study suggests that there are no PK differences (TL and CL) between mono- and combo therapy in newly IFX started paediatric CD patients, though steroids were initially used during IFX induction without IMM. As clinical outcomes and ATI were more difficult to compare due to heterogeneous study designs, head-to-head clinical trials of early optimised dosing vs combo therapy are needed to further assess efficacy.

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P0426

PREDICTORS OF NON-RESPONSE TO STEROIDS IN SEVERE ACUTE ULCERATIVE COLITIS: A SINGLE-CENTRE RETROSPECTIVE STUDY

V. Karpavičiūtė¹, G. Kiudelis², J. Kupcinskas², L. Kupcinskas²

¹Lithuanian University of Health Sciences, Kaunas, Lithuania,

²Lithuanian University of Health Sciences, Department of Gastroenterology, Kaunas, Lithuania

Contact E-Mail Address: vita.karpaviciute.0116@gmail.com

Introduction: Acute severe ulcerative colitis (ASUC) is a life-threatening condition that requires immediate hospitalization. The early identification of patients who are unlikely to benefit from intravenous corticosteroids (IVS) therapy is one of the main concerns in the management of ASUC.

Aims & Methods: This study aimed to determine early predictors of failure to corticosteroids in patients with ASUC. We performed a retrospective analysis of 121 patients admitted with ASUC to a single gastroenterology centre (Hospital of Lithuanian University of Health Sciences Kaunas Clinics) during 2010-2020. ASUC was defined by the Truelove & Witts criteria. Patients' demographic and clinical data on the disease and the results of laboratory (lowest and highest) and instrumental examinations were collected. Albumin and C-reactive protein (CRP) levels were recorded at baseline, on the 3rd day of hospitalization, and on the 3rd day after IVS initiation.

Results: 119 patients initially received IVS; 2 patients underwent emergency colectomy on the first day. Sixty-four (53%) were females, with a median age of 33 (IQR 27-49) years. 70 (59%) patients were successfully treated with IVS, while 49 (41%) fail to respond to steroid therapy: 40 (34%) patients received second-line rescue therapy (26 with cyclosporine, 14 with infliximab), 15 (12%) patients underwent surgery during hospitalization, while colectomy rate increased to 16% at follow-up (median duration of 47 (23-88) months). 30 day-mortality rate was 1.6%.

The presence of cytomegalovirus (CMV) infection was associated with an increased risk of steroid resistance: CMV DNR in plasma was detected in 13 (27%) patients in steroid-resistant group vs. 7 (10%) in steroid-responsive group ($p = 0.018$).

Comparing these two groups, other factors predicting steroid resistance were newly diagnosed ulcerative colitis (less than a year ago, $p = 0.024$), the presence of high endoscopic activity (Mayo 3, $p = 0.003$), the use of prednisolone prior to admission ($p = 0.004$) and previous treatment with biological agents ($p = 0.017$).

Other factors, such as the presence of *Clostridium difficile* infection, previous treatment with azathioprine did not differ significantly between groups. Comparing the laboratory findings, the strongest predictor of corticosteroids responsiveness was the CRP/albumin ratio at day 3 after IVS initiation (median value was 0.52 (0.19-0.92) in steroid-responsive group vs. 1.26 (0.61-2.98) in steroid-resistant group, $p<0.001$).

Also, the CRP/albumin ratio differed significantly between groups already at baseline ($p=0.031$), while day 1 CRP or albumin alone were relatively poor markers ($p=0.073$ and $p=0.081$, respectively).

Conclusion: High CRP/albumin ratio at day 3 after steroid initiation may be a good prognostic criterium for identifying patients who may not respond to steroid therapy in hospital. Previous use of prednisolone or biologic therapy, cytomegalovirus infection, newly diagnosed ulcerative colitis, and high endoscopic activity also associated with non-responsiveness to steroids in ASUC.

Disclosure: Nothing to disclose.

P0427

EFFECTIVENESS, SAFETY, AND DRUG SUSTAINABILITY OF BIOLOGICS IN ELDERLY PATIENTS WITH INFLAMMATORY BOWEL DISEASE: A SINGLE CENTER RETROSPECTIVE STUDY

G. Hahn^{1,2}, J.-F. LeBlanc¹, P.A. Golovics³, P. Wetwittayakhleng^{1,4}, A. Qatomah¹, A. Wang¹, L. Boodaghians¹, J. Kiow⁵, M. Al Ali¹, G. Wild¹, W. Afif¹, A. Bitton¹, P.L. Lakatos^{1,6}, T. Bessissow¹
¹McGill University Health Center, Division of Gastroenterology - IBD Centre, Montreal, Canada, ²Universidade Federal do Rio Grande do Sul, School of Medicine, Graduate Course Sciences in Gastroenterology and Hepatology, Porto Alegre, Brazil, ³Medical Centre, Hungarian Defence Forces, Budapest, Hungary, ⁴Prince of Songkla University, Unit of Gastroenterology and Hepatology, Division of Internal Medicine, Faculty of Medicine, Songkhla, Thailand, ⁵Centre Hospitalier de l'Université de Montréal (CHUM), Department of Gastroenterology, Montreal, Canada, ⁶Semmelweis University, 1st Department of Medicine, Budapest, Hungary

Contact E-Mail Address: gustavodhahn@gmail.com

Introduction: Biologic therapy resulted in a significant positive impact on the management of inflammatory bowel disease (IBD) however data on the efficacy and side effects of these therapies in the elderly is scant.

Aims & Methods: To evaluate retrospectively the drug sustainability, effectiveness, and safety of the biologic therapies in the elderly IBD population. Consecutive elderly (≥ 60 years old) IBD patients, treated with biologics (infliximab [IFX], adalimumab [ADA], vedolizumab [VDZ], ustekinumab [UST]) followed at the McGill University Inflammatory Bowel Diseases Center were included between January 2000 and 2020.

Efficacy was measured by clinical scores at 3, 6-9 and 12-18 months after initiation of the biologic therapy. Patients completing induction therapy were included. Adverse events (AE) or serious adverse events (SAE) were collected during and within three months of stopping of the biologic therapy.

Results: We identified a total of 147 elderly patients with IBD treated with biologics during the study period, including 109 with Crohn's disease (CD) and 38 with ulcerative colitis (UC). Patients received the following biologics: IFX (28.5%), ADAL (38.7%), VDZ (15.6%), UST (17%). The mean duration of biologic treatment was 157.5 (SD= 148) weeks. Parallel steroid therapy was given in 34% at baseline, 19% at 3 months, 16.3% at 6-9 months and 6.5% at 12-18 months.

The remission rates at 3, 6-9 and 12-18 month were not significantly different among biological therapies. Kaplan-Meier analysis did not show statistical difference for drug sustainability ($p=0.195$), time to adverse event

($p=0.158$) or infection rates ($p=0.973$) between the four biologics studied. The most common AEs that led to drug discontinuation were loss of response, infusion/injection reaction and infection.

Conclusion: Current biologics were not different regarding drug sustainability, effectiveness, and safety in the elderly IBD population. Therefore, we are not able to suggest a preferred sequencing order among biologics.

Disclosure: Nothing to disclose.

P0428

IMPACT OF CONCOMITANT THIOPURINE ON THE EFFICACY AND SAFETY OF FILGOTINIB TREATMENT IN PATIENTS WITH ULCERATIVE COLITIS: POST HOC ANALYSIS OF THE PHASE 2B/3 SELECTION STUDY

K. Watanabe¹, L. Peyrin-Biroulet², S. Danese³, K. Emoto⁴, Y. Fujitani⁴, F.-O. Le-Brun⁵, A. Oortwijn⁶, T. Ueno⁴, J.O. Lindsay⁷, G. Rogler⁸, T. Hibi⁹

¹Center for Inflammatory Bowel Disease, Division of Internal Medicine, Hyogo College of Medicine, Hyogo, Japan,

²University Hospital of Nancy, University of Lorraine, Nancy, France,

³IBD Center, Humanitas Research Hospital, Milan, Italy,

⁴Gilead Sciences K.K., Tokyo, Japan, ⁵Galapagos GmbH, Basel, Switzerland,

⁶Galapagos NV, Leiden, Netherlands, ⁷Centre for Immunobiology, Blizard Institute, Barts and the London School of Medicine, Queen Mary University of London, London, United Kingdom,

⁸University Hospital of Zurich, University of Zurich, Zurich, Switzerland, ⁹Center for Advanced IBD Research and Treatment, Kitasato Institute Hospital, Kitasato University, Tokyo, Japan

Contact E-Mail Address: ke-watanabe@hyo-med.ac.jp

Introduction: Thiopurines (azathioprine [AZA], 6-mercaptopurine [MP]) and other immunomodulators (IM) are used in the treatment of ulcerative colitis (UC). Filgotinib (FIL) is a once-daily, oral, Janus kinase 1 preferential inhibitor approved in Europe and Japan for the treatment of UC.

The efficacy and safety of FIL in adults (18-75 years) with moderately to severely active UC was evaluated in the phase 2b/3 randomized, double-blind, placebo (PBO)-controlled SELECTION study (NCT02914522).¹

Aims & Methods: This *post hoc* analysis aimed to assess the impact of protocol-accepted concomitant thiopurine use on the efficacy and safety of FIL treatment in SELECTION. Patients, including those already receiving IM, were randomized (2:2:1) in two cohorts (A: biologic-naïve; B: biologic-experienced) to receive FIL 200 mg (n=507), FIL 100 mg (n=562) or PBO (n=279) for 11 weeks (induction).

At week 10, patients achieving clinical remission (Mayo endoscopic subscore ≤ 1 , rectal bleed [RB] subscore 0 and stool frequency subscore ≤ 1) or Mayo Clinic Score (MCS) response (≥ 3 -point and 30% reduction in MCS from baseline with a ≥ 1 -point decrease in RB subscore or an absolute RB subscore of ≤ 1) to FIL (n=664) were re-randomized to continue assigned FIL or PBO for 47 weeks (maintenance). IM dose had to be stable until week 10; no IM dosing guidance was given for maintenance.

We assessed efficacy and safety data at weeks 10 and 58 in patients with (+IM, includes AZA [81.8%], MP [10.8%] or methotrexate [7.4%]; n=352) or without (-IM; n=996) concomitant IM.

Results: At week 10, clinical remission was achieved by a similar proportion of patients treated with FIL 200 mg with or without concomitant IM in both cohorts A (+IM, 26.0% [non-stratified risk difference vs PBO (RD), 6.5% (95% CI: -11.2-24.2)]; -IM, 26.2% [RD, 12.6% (95% CI: 2.3-22.9)]) and B (+IM, 11.3% [RD, 1.9% (95% CI: -13.3-17.1)]; -IM, 11.5% [RD, 8.8% (95% CI: 2.7-14.8)]).

Proportion of patients achieving MCS response at week 10 was also similar across these subgroups in both cohort A (+IM, 65.8% [RD, 14.5% (95% CI: -6.1–35.2)]; -IM, 66.9% [RD, 22.1% (95% CI: 9.1–35.1)]) and B (+IM, 61.3% [RD, 39.4% (95% CI: 18.3–60.6)]; -IM, 50.5% [RD, 34.1% (95% CI: 23.6–44.6)]).

At week 58, clinical remission rates for patients receiving FIL 200 mg were similar in patients with or without concomitant IM (+IM, 39.6% [RD, 28.5% (95% CI: 8.0–49.0)]; -IM, 36.3% [RD, 25.0% (95% CI: 13.3–36.8)]). The proportion of patients achieving MCS response at week 58 with FIL 200 mg was also similar across these subgroups (+IM, 62.3% [RD, 21.5% (95% CI: -3.9–47.0)]; -IM, 68.5% [38.9% (95% CI: 24.9–53.0)]).

Over 58 weeks, the proportion of patients receiving FIL 200 mg who experienced adverse events was similar with or without concomitant IM (Table). There were two deaths in patients receiving FIL 200 mg, one each in the +IM and -IM groups; neither was considered related to treatment.

Induction	FIL 200 mg				FIL 100 mg				PBO	
Maintenance	FIL 200 mg		PBO		FIL 100 mg		PBO		PBO	
AEs, n (%)	+IM (n=57)	-IM (n=145)	+IM (n=28)	-IM (n=71)	+IM (n=44)	-IM (n=135)	+IM (n=25)	-IM (n=66)	+IM (n=30)	-IM (n=63)
Any AE	34 (63.0)	101 (68.2)	20 (74.1)	39 (54.2)	31 (70.5)	77 (57.0)	12 (50.0)	48 (71.6)	22 (73.3)	35 (55.6)
Any SAE	4 (7.4)	5 (3.4)	0 (0.0)	0 (0.0)	2 (4.5)	6 (4.4)	1 (4.2)	6 (9.0)	2 (6.7)	2 (3.2)
Any infections and infections	13 (24.1)	58 (39.2)	9 (33.3)	16 (22.2)	14 (31.8)	32 (23.7)	5 (20.8)	22 (32.8)	11 (36.7)	10 (15.9)
Any serious infections	1 (1.9)	1 (0.7)	0 (0.0)	0 (0.0)	1 (2.3)	2 (1.5)	0 (0.0)	2 (3.0)	0 (0.0)	1 (1.6)
Any herpes zoster	1 (1.9)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (4.2)	0 (0.0)	0 (0.0)	0 (0.0)
Any pulmonary embolism	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

+IM includes azathioprine, 6-mercaptopurine or methotrexate.
 AE, adverse event; FIL, filgotinib; IM, immunomodulator; PBO, placebo; SAE, serious adverse event.

Table. Summary of treatment emergent AEs at week 58.

Conclusion: Concomitant treatment with IM, predominantly the thiopurine AZA, had no clear impact on the efficacy and safety of FIL in the SELECTION study.

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P0429
 HISTOLOGICAL FEATURES OF JOINT INFLAMMATION IN INFLAMMATORY BOWEL DISEASE PATIENTS WITH PERIPHERAL ARTHRITIS

D. Pugliese¹, S. Alivernini², L. Parisio³, G. Privitera⁴, S. Perniola², B. Tolusso², A. Gasbarrini⁵, E. Gremese², L. Guidi⁶, A. Armuzzi⁷
¹Fondazione Policlinico Universitario “A. Gemelli” IRCCS, CEMAD – IBD UNIT - Unità Operativa Complessa di Medicina Interna e Gastroenterologia, Dipartimento di Scienze Mediche e Chirurgiche, Rome, Italy, ²IRCCS Fondazione Policlinico “A. Gemelli”, Immunology Research Core Facility – Gemelli Science and Technology Park (GSTeP), Division of Rheumatology, Università Cattolica del Sacro Cuore, Roma, Italy, ³IRCCS Fondazione Policlinico “A. Gemelli”, CEMAD – IBD UNIT - Unità Operativa Complessa di Medicina Interna e Gastroenterologia, Dipartimento di Scienze Mediche e Chirurgiche, Roma, Italy, ⁴Università Cattolica del Sacro Cuore, Rome, Italy, ⁵Fondazione Policlinico Universitario Gemelli IRCCS, Università Cattolica, Internal Medicine, Gastroenterology and Liver Diseases, Rome, Italy, ⁶Policlinico A. Gemelli, Rome, Italy, ⁷humanitas, IBD Unit, Milan, Italy

Contact E-Mail Address: lparisio11@gmail.com
Introduction: Up to 50% of patients with Inflammatory Bowel Disease (IBD) experience at least one extraintestinal manifestation during their life among whom musculoskeletal manifestations (arthralgia and arthritis) are the most common

Aims & Methods: This study aims to explore the role of synovial histological assessment in the therapeutic management of IBD patients with clinical signs of peripheral articular involvement. A retrospective study enrolling consecutive IBD patients receiving TNF α inhibitor, with concomitant joint involvement was performed from April 2015 to October 2020. At baseline, each patient underwent synovial-tissue (ST) biopsy for the semi-quantitative assessment of synovitis degree through H&E-based Krenn score (KSS) by trained pathologist, blinded to clinical characteristics. Clinical IBD activity was evaluated with Harvey Bradshaw Index for Crohn's disease (CD), and Partial Mayo Score for Ulcerative colitis (UC).

Based on ST findings, 4 different therapeutic interventions were done:

1. Addition of a conventional disease modifying antirheumatic drug (DMARD);
2. Switch to another anti-TNF α ;
3. Swap to other biological class or,
4. Addition of a second biological drug. Patients were followed in an out-patients clinical setting to record treatment response within 12 months.

Results: 46 IBD patients (31 CD; 15 UC) with median age of 46 years [IQR 35-53 years] and a median of disease duration of 8 years [IQR 4-16 years] were included. At enrollment all patients showed clinical signs of peripheral arthritis.

Overall, 31 patients (67%) had at least histologically proven low-grade synovitis (J_h+), defined as a KSS ≥ 2 . IBD patients were stratified based on baseline ST (J_h+ / J_h-) and IBD activity (B+/B-) as follows: B- J_h+ (22 patients), B+ J_h+ (9 patients) and B- J_h- (15 patients) respectively. The rate of B- J_h+ patients under anti-TNF α and paradoxical arthritis was 82%.

Considering the whole cohort, 12(54%) IBD patients added a DMARD among whom 33% achieved joint remission at 12 months while one patient swapped to other biological class, resulting in joint remission.

In the B+ J_h+ group, 4(44%) patients maintained the baseline therapy, resulting in no joint remission while one patient added a second biological drug, achieving joint remission. In the B- J_h- group, 7(46%) patients added a cDMARD of whom 39% achieved articular remission; conversely, 4 (27%) patients did not modify the baseline therapy of whom 75% achieved joint remission. Finally, the persistence on the therapeutic strategy was 60% at the median follow-up of 42.5 months (IQR 23.5-57.2).

Conclusion: The semiquantitative evaluation of synovial inflammation is a useful tool which might help physicians to better address therapeutic intervention, especially for IBD patients with mild/remission bowel activity or paradoxically developed arthritis

Disclosure: Nothing to disclose.

P0430

THE IMPACT OF SARS-COV-2 PANDEMIC IN PATIENTS WITH INFLAMMATORY BOWEL DISEASE: A SYSTEMATIC REVIEW OF CLINICAL DATA

K. Shaban¹, M. Mohamed²

¹Royal Blackburn, Blackburn, United Kingdom, ²Royal Liverpool, Gastroenterology, Liverpool, United Kingdom

Contact E-Mail Address: dr.mohamedab93@gmail.com

Introduction: Coronavirus disease 2019 (COVID-19) and its consequences on individuals with inflammatory bowel diseases (IBD) are not yet fully understood despite the fact that evidence on this topic are rapidly evolving.

Aims & Methods: This comprehensive study of clinical data aims to enhance the gastroenterologists' ability to manage inflammatory bowel disease during these Covid-19 pandemic dominated times.

Until November 2021, a thorough search of PubMed and Embase for published data served as the primary source for the examined research, which was solely composed of English-language sources. Additionally, websites

of gastroenterology societies and organizations dedicated to inflammatory bowel disease (IBD) were searched for consensus statements and recommendations for patients and clinicians (IBD).

The information sources, the search strategy, and the eligibility criteria of the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statements were followed

Results: There are 1560 publications on this subject, including 30 randomized controlled trials, including 64,259 patients with inflammatory bowel disease (IBD). There are twenty-four studies (n = 51,920) that examined the effect of COVID 19 on inflammatory bowel disease (IBD) management. Crohn's disease affected 52.9% of patients, ulcerative colitis affected 42.0%, and indeterminate colitis affected 5.1%.

These trials showed that the use of corticosteroids, azathioprine, or mesalamine was related to adverse outcomes, but the use of anti-TNFs was linked to improved outcomes.

Seven randomized controlled trials evaluated the safety and efficacy of the COVID-19 vaccine in inflammatory bowel disease (IBD) patients and found that vaccination was extremely effective, with a seroconversion rate of 96.49% and no significant increase in adverse outcomes when compared to the general population.

Conclusion: Patients with inflammatory bowel disease (IBD) are at an increased risk of severe COVID-19 infection. There is a substantial influence on the management of inflammatory bowel disease (IBD) patients during the pandemic, as certain IBD drugs have been connected with a worsening of outcomes. Although the COVID vaccine has been shown to be effective, additional research is needed to determine the long-term consequences of COVID 19 infection and vaccination.

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P0431

A PILOT FEASIBILITY STUDY OF A NOVEL WHOLE-FOOD, SULPHIDE-REDUCING (5-SURE) DIET STRATEGY FOR THE TREATMENT OF SYMPTOMS IN PATIENTS WITH AN ULCERATIVE-COLITIS POUCH

Z. Ardalan¹, C.K. Yao², M. Sparrow¹, P.R. Gibson³

¹Alfred Health, Gastroenterology, Melbourne, Australia,

²Monash University, Department of Gastroenterology, Melbourne, Australia, ³Alfred Hospital Dept. of Gastroenterology, Dept. of Gastroenterology, Melbourne, Australia

Contact E-Mail Address: chu.yao@monash.edu

Introduction: There is an unmet need for dietary therapies that target physiological and pathogenic mechanisms underlying symptoms of a poorly functioning ileo-anal pouch and in pouchitis to improve clinical outcomes in these patients. A novel whole-food diet was recently developed called 'the 5-strategies to a SULphide REDucing' (the 5-SURE) diet that theoretically reduces pouch water content and corrects imbalances in pouch microbial metabolite production, namely less toxic hydrogen sulphide (H₂S), more carbohydrate fermentation^{1,2}. Tolerability of this diet requires assessment.

Aims & Methods: This pilot study aimed to assess tolerability of a 5-SURE diet in patients with an ileoanal pouch and its effects on pouch microbial metabolic activities and clinical indices. Patients with an ulcerative colitis (UC) pouch on stable pouch therapies received dietary counselling to (i) increase oligosaccharide intake whilst (ii) restricting osmotically-active carbohydrates, (iii) reduce total & (iv) animal protein and (v) minimise sulphate/sulphite preservatives over 5 weeks. Tolerability and acceptability were assessed using a 100mm visual analogue scale and a Diet Satisfaction Questionnaire³ at the end of 5 weeks. Changes in faecal metabolites (faecal SCFA, branched-chain fatty acids (BCFA), pH and ammonia), clinical indices (clinical pouch disease activity index and pouch obstructed defecation symptom scores) including faecal calprotectin were also measured at baseline and post-intervention. Faecal BCFA was used as a proxy for faecal H₂S in the absence of reliable measurements.

Results: Of the 12 patients (6 men, mean age 55 years) enrolled, one with a known anastomotic stricture withdrew following partial bowel obstruction. Median tolerability scores were high (78[IQR:21-93]), with 82% patients reporting excellent tolerability and high diet satisfaction scores (mean±SD:38±4/total score 50) at week 5. Overall adherence was excellent in 8/11 (73%). The 5-SURE diet did not alter faecal SCFA, pH or ammonia (Table 1) but successfully decreased faecal BCFA excretion by 14% (p=0.03). Faecal BCFA:SCFA ratio fell by median [IQR] of 60[11-80%] (p=0.02), but these were no longer significant after correction for multiple comparisons. Moreover, improvements in clinical PDAI scores were observed in 8/11 (73%) after 5 weeks, with trends for improved pouch obstructed defecation scores (p=0.03) and pouch frequency (p=0.09). No changes in faecal calprotectin were detected in the overall group at week 5 (p=0.72) but there was a tendency for calprotectin to fall (p=0.07) when patients with high baseline calprotectin (>1500µg/g) were excluded.

	Baseline	Week 5	p-value
Faecal short-chain fatty acid, µmol/g	106.8 ± 23.1	105.6 ± 29.2	0.32
Faecal branched-chain fatty acids, µmol/g	0.56 ± 0.53	0.33 ± 0.30	0.03
Faecal ammonia, µmol/g	22.7 ± 8.6	19.5 ± 8.5	0.12
Faecal pH	6.0 ± 0.3	6.1 ± 0.3	0.25
Clinical indices			
Clinical PDAI scores	3 ± 1	2 ± 1	0.06
Pouch emptying frequency, n	7 [5-8]	5 [5-6]	0.09
Pouch obstructed defecation score	6 [4-8]	4 [3-4]	0.04
Faecal calprotectin, µg/g	292 [176-527]	205 [148-310]	0.72

Values are shown as mean± SD or median [IQR]

Table 1. Changes in pouch microbial fermentation markers and clinical indices following 5 weeks of a 5-SURE diet.

Conclusion: The novel 5-SURE diet was highly tolerated and acceptable, with the potential to promote a more favourable microbial metabolite profile within the pouch. Signals for symptom improvement and inflammation were detected in a proportion of UC-pouch patients but larger, randomised controlled studies are needed.

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P0432

FROM INTRAVENOUS TO SUBCUTANEOUS INFLIXIMAB – A TRANSITION LEADING TO CHANGES?

M.J. Temido¹, A.E.P. Silva¹, M. João², R. Pimentel¹, C. Correia¹, S. Lopes¹, S. Mendes¹, P. Narra Figueiredo¹, F. Silva Portela¹

¹Centro Hospitalar e Universitário de Coimbra, Gastroenterology, Coimbra, Portugal, ²Portuguese Oncology Institute of Coimbra, Gastroenterology, Coimbra, Portugal

Contact E-Mail Address: mariajosetemido@hotmail.com

Introduction: A new subcutaneous (sc) formulation of Infliximab has recently been approved. The transition from intravenous (iv) to sc infliximab can reduce costs and improve patients' convenience, but prospective data about pharmacokinetics and immunogenicity is limited. This formulation may lead to more stable plasmatic levels of IFX and, as a consequence, to less formation of anti-drug antibodies.

Aims & Methods: We aim to compare symptomatic and analytic efficacy and tolerability of sc IFX and to assess whether the formulation results in higher plasmatic levels of IFX (IFXpl). A prospective single center cohort study was performed. Patients with either CD or UC, aged 18 years or older, stable clinically, undergoing maintenance therapy with iv IFX (5mg/kg every 7-8 weeks) for more than 6 months were switched.

The administrations of sc IFX were 120mg every 2 weeks. A clinical and analytical evaluation was performed at day 0 (d0) and at weeks 2 (w2), 8 (w8) and 16 (w16) after the initiation. IFXpl and anti-drug antibodies were also measured at these time points.

Results: 36 patients (24 with CD and 12 with UC) were included. 50% of patients were concomitantly taking azathioprine (aza). All the patients maintained clinical remission (CR). C-reactive protein and FCP maintained approximately the same values in d0, w2, w8 and w16. Median IFXpl at d0, w2, w8 and w16 were respectively 4.9±3.2, 9.7±3.8, 20±4.8 and 19.76±8ug/mL. A statistically significant difference between IFXpl at different time points was found (d0 Vs w2 and w2 Vs w8). Aza led to a statistically significant difference in the IFXpl on d0, but not on w2, w8 or w16. Greater body weight was statistically associated with lower IFXpl on w2 and w16, but not on d0 or w16, both in the univariate and in the multivariate analysis. No patient developed anti-drug antibodies. No severe drug adverse effects were documented. Three patients developed infusion site reactions. Two patients developed arthralgias of undetermined significance. One patient returned to iv Infliximab for personal choice.

Conclusion: Transition from iv to sc showed no signs of loss of CR. Biological markers were similar before and after the transition. Aza influences iv IFXpl, but not sc ones. Body weight influences IFXpl. IFXpl are w2 are still lower than expected considering the results at w8.

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The other authors report no conflict of interest.

P0433

PSYCHOLOGICAL INTERVENTIONS IMPROVE OUTCOMES IN INFLAMMATORY DIGESTIVE SYSTEM DISEASES. A META-ANALYSIS

B. Fogarasi¹, B. Teutsch¹, E. Tari¹, L. Szabó¹, D.S. Veres², A.S. Bognár¹, D. Dohos^{3,4}, B. Erőss¹, M.F. Juhász^{3,5}, K. Ocskay⁶, P. Hegyi¹

¹Centre for Translational Medicine, Semmelweis University, 1085 Budapest, Üllői út 26, Hungary, Budapest, Hungary, ²Department of Biophysics and Radiation Biology, Semmelweis University, Budapest, Hungary, ³Heim Pál National Pediatric Institute, Budapest, Budapest, Hungary, ⁴Institute for Translational Medicine, University of Pécs, Medical School, Department of Medicine, Pécs, Hungary, ⁵Institute for Translational Medicine, Medical School, University of Pécs, Pécs, Hungary, ⁶Faculty of Medicine, University of Pécs, Institute for Translational Medicine, Vértesboglár, Hungary

Contact E-Mail Address: fogarasi.beatrix@gmail.com

Introduction: Inflammatory digestive system diseases can have a severe effect on the physical and mental health of the patients. Moreover, psychosocial factors can modify the behaviour linked to disease and influence treatment.

Aims & Methods: The aim of our systematic review and meta-analysis is to evaluate the efficacy and safety of psychological interventions in patients suffering from inflammatory digestive system diseases. The systematic search was conducted in three major databases (MEDLINE, CENTRAL, EMBASE) for various psychological interventions applied for all digestive system diseases.

Only randomized controlled trials were eligible. Anxiety and depression were assessed right after the last intervention provided to the patients. Due to the differences in the questionnaires used, the Hedges' g method was used to calculate the pooled effect size with 95% confidence interval (CI). Subgroup analysis was conducted for diseases assessed by at least 3 studies. Our protocol was prospectively registered on PROSPERO (CRD42021282965).

Results: The systematic search yielded a total of 13212 articles, resulting in 60 eligible RCTs for the qualitative synthesis. 39 studies were conducted in patients with inflammatory bowel disease (IBD). Further studies included patients with gastroesophageal reflux disease, peptic ulcer, hepatitis, cirrhosis, pancreatitis and cystic fibrosis. Interventions included Cognitive Behavioral Therapy, Psychotherapy, Hypnosis, stress reduction, psychoeducation and psychological nursing.

Psychological interventions proved to have a medium to large effect on depressive symptoms measured at the end of the intervention ($g = -0.68$; CI: 1.11 to -0.25); $I^2 = 91\%$; CI: 89%-94%), while in the IBD subgroup a small to medium effect was observed (-0.40 ; CI: -0.78 to -0.02). Symptoms of anxiety were also significantly reduced; in overall a large effect was seen ($g = -0.86$; CI: -1.29 to -0.42), while in the IBD subgroup a small to medium effect was detected (-0.36 ; CI: -0.60 to -0.12).

Conclusion: Psychological interventions effectively reduce depressive symptoms and anxiety in inflammatory digestive system disease and are effective in IBD patients. Further studies are needed to assess the efficacy of certain psychological interventions in all gastroenterological inflammatory diseases for more detailed recommendations.

Disclosure: Nothing to disclose.

P0434

LINKING LOCATION SPECIFIC GENE EXPRESSION PATTERNS TO POTENTIAL VEDOLIZUMAB OUTCOMES IN CROHN'S DISEASE PATIENTS

B. Regí¹, I. Tagarro², A. Lagarda¹, T. Letosa², J. Aparicio², M. Coma¹, C. Montoto Otero², J. Manye^{3,4}, E. Domenech Morra^{3,5,6}

¹Anaxomics Biotech, Barcelona, Spain, ²Takeda, Medical Department, Madrid, Spain, ³IBD Research Group, Germans Trias i Pujol Research Institute (IGTP), Badalona, Catalonia, Spain, ⁴Centro de Investigación Biomédica en Red Sobre Enfermedades Hepático-Digestivas (CIBEREHD), Madrid, Spain, ⁵Centro de Investigación Biomédica en Red Sobre Enfermedades Hepático-digestivas (CIBEREHD), Madrid, Spain, ⁶Germans Trias i Pujol University Hospital, Gastroenterology Department, Badalona, Catalonia, Spain

Contact E-Mail Address: vedo415@anaxomics.com

Introduction: Crohn's disease (CD) and ulcerative colitis (UC) are chronic immune-mediated bowel diseases (IBD), often treated with immunomodulators and anti-inflammatory antibody-based biological drugs. Among the spectrum of approved treatments is vedolizumab (VDZ), a gut-selective anti-lymphocyte trafficking (GSALT) humanised monoclonal antibody which binds $\alpha 4\beta 7$ integrin expressed on circulating lymphocytes, selectively preventing their migration into the gut mucosa and thus reducing inflammation.

As there is evidence suggesting that biologic drugs, and particularly VDZ, may be more effective in CD patients with colonic involvement vs. CD patients with ileal-only disease location, there is a need to understand the mechanisms underlying these differences.

To explore the potential impact of CD disease location on VDZ outcomes, we explored publicly available gene-expression data. The objective was to address the question whether disease location alters mucosal immune responses, and/or trafficking patterns in a way that could lead to a differential response to VDZ in different intestinal segments.

Aims & Methods: Patients' gene-expression data were collected from the publicly available dataset GSE16879, which includes sixty patients with active IBD, (19 with colonic CD and 18 with ileal CD), and a control group of 12 CD patients (6 with colonic involvement and 6 with ileal involvement) who underwent endoscopy for polyp screening.

Results: The analysis of publicly available gene-expression data has identified a potential impact of disease location on a set of key proteins involved in neutrophil, monocyte and eosinophil migration, as well as neutrophil chemoattraction. Specifically, genes such as ANXA1, VCAM1, ICAM1 and CCL24 show different expression patterns depending on the locations of disease. A lower constitutive expression of VCAM1, ICAM1, CCL24 adhesion and migration proteins coupled with higher expression of ANXA1, which have been observed to play a protective role in IBD, have been observed in colonic CD. Together, these results may suggest a higher efficacy of VDZ in CD in colonic segments vs. ileal locations.

Conclusion: Our results suggest a potential increased response to VDZ in the colon when compared to the ileum, likely due to gut regional-specific chemoattractant gene expression profiles.

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P0435

CROHN'S DISEASE (CD): THE PREDICTIVE VALUE OF MONTREAL CLINICAL PATTERNS, AND BIOLOGICAL TREATMENT IN A LATIN AMERICAN IBD REFERENCE CENTER

A.M. Sambuelli¹, P. Tirado¹, S. Huernos², S.M. Negreira¹, A. Gil², M.J. Rohwain², S. Goncalves², I. Candel²

¹IBD Section - Bonorino Udaondo Gastroenterology Hospital, Gastroenterology, Buenos Aires, Argentina, ²Bonorino Udaondo Gastroenterology Hospital, IBD Section Gastroenterology, Buenos Aires, Argentina

Contact E-Mail Address: alicia.sambuelli@gmail.com

Introduction: CD is a potentially disabling condition, with a high rate of complications and surgical requirements. Biological treatments have revolutionized CD management, but their efficacy and predictive factors have been reported variable in different casuistic, influenced by genetic, phenotypic, and socioeconomic conditions, which should be locally analyzed worldwide.

Aims & Methods: To describe by a retrospective study in a Latin American IBD reference center, clinical features of CD casuistic, predictive Montreal patterns for surgical risk, and efficacy of biologics and immunosuppressants. Surgical risk of Montreal classification groups, as well as, biological and immunomodulator (IMM) treatment (thiopurines) in the prevention of first major surgery were estimated.

Clinical patterns were evaluated as predictive factors at the basal time (up to 90 days from the debut) in:

Age at diagnosis (A) A1:≤16yrs, A2:17-40, A3:>40,

Behavior (B): nonstricturing nonpenetrating (B1), stricturing (B2), penetrating (B3), perianal disease modifier (p),

Location (L): L1:ileal, L2: colonic, L3: ileocolonic, L4: upper G.I.

Incidence rates of surgery and preventive treatment efficacy were estimated by a Cox regression model.

Results: 598 CD pts (M 313, F 285) with mentioned available data, CD median duration 13.9 yr (IQR 7.1-21.2) were analyzed.

Montreal patterns A1: n 93 (15.6%), A2:n 335 (56.0%), A3:n 170 (28.4%), B1:n 523 (87.5%), B2:n 52 (8.7%), B3:n 23 (3.8%) L1:52 (8.7%),L2:n 368 (61.5%), L3:n 176 (29.4%), L4:iUGI: n 2 (0.33%) and L4 combined with L1, L2, L3: n 47 (7.9%), Perianal disease (p) n 286 (47.8%).

Major surgery was performed in 304/598 pts (50.8%). Globally, 264/598 patients (44.1%) received biologics in any time (45 only induction and 219 patients also maintenance), ≥ two biologics: 12.7%, Anti-TNFs > 90% (access reasons).

Before first surgery, biologics were indicated in 202 pts, 34 of them received only induction and 168 induction plus maintenance.

Kaplan Meier estimates: major surgery incidence rate: 5.1 per 100 person/ yrs., median survival without surgery: 14.2 yrs. Significant variables of Cox model for surgical risk were:

B1 HR 1 (reference),

B2 HR 3.03 (95%CI 2.14-4.29, p=0.000),

B3 HR 3.27 (95%CI 2.03-5.29, p=0.000),

L2 HR 1 (reference),

L1 HR 2.025 (95%CI 1.37-2.99, p=0.000),

L3 HR 2.51 (95%CI 1.95-3.23, p=0.000),

A1 HR 1 (reference),

A2 HR 1.48 (95%CI 1.05-2.10, p=0.027),

A3 HR 1.89 (95%CI 1.27-2.83, p=0.002),

Biologics (mainly anti-TNFs used by access reason): only induction HR 1.49 (95%CI 1.005-2.195, p=0.047), induction plus maintenance HR 0.388 (95% CI 0.27-0.55), p=0.000. Non-significant variables involved in the risk for surgery were: gender, perianal complication, and IMM treatment.

Conclusion: In our CD population, we found:

1. Montreal patterns associated with surgical risk (fistulizing and stricturing behaviors), ileal and ileocolonic locations, and A2, but also A3 (debut beyond 40 yrs) which is unusually described,
2. Biologics showed a reduction in surgical risk (as expected induction plus maintenance versus only induction).

Disclosure: No conflict of interest.

P0436

STEROID USE IN A HIGH PROPORTION OF IBD PATIENTS – FIRST RESULTS FROM THE GERMAN COHORT OF THE IBD-DICE STUDY

I. Blumenstein¹, A. Luegering², I. Fischer³, L. Hammer⁴, S. Rath⁴, B. Bokemeyer⁵

¹University Hospital Frankfurt, Medical Clinic 1, Frankfurt, Germany, ²Center for Hepatic Diseases and Gastroenterology, Muenster, Germany, ³Biostatistics Tuebingen, Tuebingen, Germany, ⁴AbbVie Germany GmbH, Medical Department Gastroenterology, Wiesbaden, Germany, ⁵Interdisciplinary Crohn Colitis Centre, Minden, Germany

Contact E-Mail Address: irina.blumenstein@kgu.de

Introduction: Corticosteroids (CS) have been an important therapeutic milestone for treating inflammatory conditions such as inflammatory bowel diseases (IBD). While in some situations, CS use might be unavoidable, steroid excess poses the patient at a significant risk for irreversible side effects [1].

However, the proportion of IBD patients with steroid use in a real-world setting among different geographies and in particular in Germany that face steroid excess remain unclear.

We aim to evaluate the proportion of German IBD patients experiencing steroid use/dependency as well as risk-associated factors on patient and study site level.

Aims & Methods: IBD-DICE was a multicentre, international cross-sectional study to evaluate determinants and consequences of steroid excess in IBD patients. In Germany, a total of 384 IBD patients (53.6% CD, 45.8% UC, 0.5% IBD-U) with quiescent or active disease were consecutively enrolled at 15 IBD-experienced sites from Sep – Dec 2021.

Data on CS use (orally administered prednisolone and/or budesonide) were captured by a web-based steroid assessment tool (SAT) in addition to a patient questionnaire (PQ) to evaluate additionally the patient's perspective on steroids. SAT and PQ data were available for 359 IBD patients. Steroid dependency was defined as more than 1 steroid course within the last 12 months and/or no reduction of steroids within the last 3 months without recurrent disease activity.

Results: The majority of the 384 documented patients presented with quiescent (36.5%, n = 140/384) or mild (35.4%, n = 136/384) disease activity rather than moderate (23.4%, n = 90/384) or severe disease activity (4.7%, n = 18/384). Of all patients, 35.9% (n=138/384) received oral steroids (prednisolone/budesonide) over the past 12 months. CS use was higher in UC patients (43.2%, n=76/176) than in CD (29.1%, n=60/206; p = 0.004, Chi-square test) (2/2 IBD-U patients received CS).

Notably, 58.0% (n = 80/138) of all patients on CS had received more than 1 course of CS (prednisolone/budesonide) and/or could not taper CS within 3 months after CS initiation and were therefore deemed steroid-dependent (table 1).

In other words, 20.8% (n = 80/384) of all documented patients were steroid-dependent. Interestingly, when patients were asked for their CS use, 82.5% (n = 296/359) as opposed to the above mentioned 35.9% (reported by investigator in SAT) disclosed CS use over the past 12 months.

Parameter % (n)	IBD patients (n = 384) (documented via SAT by physician)
CS use (prednisolone/budesonide)	35.9 (138/384)
CS dependency	20.8 (80/384)

Table 1. Steroid use over the past 12 months in IBD patients of the German IBD-DICE cohort

Conclusion: We found that in our German cohort, steroid use as assessed by the physician occurred in 35.9% of all patients and steroid dependency in 58.0% of the documented IBD patients with CS, respectively. There might be a discordance between patient and physician reported CS use. These data suggest that routine monitoring of CS use might increase awareness for steroid burden in IBD patients.

References:

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P0437

INDUCTION AND MAINTENANCE TREATMENT WITH RISANKIZUMAB LEADS TO SYMPTOMATIC RELIEF IN PATIENTS WITH MODERATE TO SEVERE CROHN'S DISEASE

E. Louis¹, J. Torres², J. Lindsay³, S. Schreiber⁴, R. Ungaro⁵, L.V. Jonaitis⁶, K. Kligys⁷, S. Van Haaren⁷, E. Neimark⁷, J. Zambrano⁷, Y. Zhang⁷, G.R. D'Haens⁸

¹University Hospital CHU of Liège, Gastroenterology, Liège, Belgium, ²Hospital Beatriz Ângelo, Gastroenterology, Lisbon, Portugal, ³Digestive Disorders Clinical Academic Unit, Barts & The London School of Medicine, Digestive Diseases, London, United Kingdom, ⁴University Hospital Schleswig-Holstein, Internal Medicine I, Kiel, Germany, ⁵Icahn School of Medicine at Mount Sinai, Gastroenterology, New York, United States, ⁶Lithuanian University of Health Sciences, Gastroenterology, Kaunas, Lithuania, ⁷AbbVie Inc., North Chicago, United States, ⁸AMC Amsterdam Inflammatory Bowel Disease Centre, Amsterdam, Netherlands

Contact E-Mail Address: edouard.louis@uliege.be

Introduction: STRIDE II guidelines identify symptom relief as important short and intermediate treatment goals. The most burdensome symptoms reported by patients with Crohn's disease (CD) are abdominal pain (AP) and increased stool frequency (SF). Risankizumab (RZB) was shown to be well-tolerated and superior to placebo (PBO) for inducing and maintaining clinical remission and endoscopic response in patients with moderate-to-severe CD.^{1,2}

This post-hoc analysis examined improvements in the patient reported outcomes (PROs) of AP score (APS) and SF with RZB induction and maintenance dosing and their correlation with endoscopic outcomes.

Aims & Methods: PROs using pooled data from the ADVANCE/MOTIVATE induction studies¹ for the PBO and RZB 600 mg intravenous (IV) treatment groups, and data from the RZB withdrawal (PBO subcutaneous [SC]) and

ADVANCE + MOTIVATE														
% Patients Achieving Endpoint														
[95% CI]														
P-value														
Endpoint	PBO	RZB 600 mg IV	PBO	RZB 600 mg IV	PBO	RZB 600 mg IV								
	Week 4	Week 4	Week 8	Week 8	Week 12	Week 12								
Decrease in APS from BL	59.4	71.7	63.8	75.9	58.8	76.9								
	[54.3, 64.5]	[67.9, 75.6]	[58.9, 68.8]	[72.2, 79.6]	[53.8, 63.9]	[73.2, 80.5]								
		P<0.001		P<0.001		P<0.001								
Decrease in SF from BL	65.7	81.6	63.5	84.1	58	85.4								
	[60.9, 70.6]	[78.3, 84.9]	[58.6, 68.5]	[80.9, 87.2]	[52.9, 63.1]	[82.4, 88.4]								
		P<0.001		P<0.001		P<0.001								
AP =0 in patients with APS ≥1 at Baseline	2.6	5.6	3.2	11.5	6.4	17.9								
	[0.9, 4.3]	[3.6, 7.6]	[1.3, 5.0]	[8.7, 14.3]	[3.8, 8.9]	[14.5, 21.2]								
		P=0.052		P<0.001		P<0.001								
SF ≤1 in patients with SF >2.8 at Baseline	4.8	9.8	6	18.2	11.6	26.1								
	[2.5, 7.1]	[7.1, 12.5]	[3.4, 8.5]	[14.7, 21.6]	[8.2, 15.1]	[22.2, 30.0]								
		P=0.004		P<0.001		P<0.001								
FORTIFY														
% Patients Achieving Endpoint														
[95% CI]														
P-value														
Endpoint	Withdrawal (PBO SC)	RZB 360 mg SC	Withdrawal (PBO SC)	RZB 360 mg SC	Withdrawal (PBO SC)	RZB 360 mg SC	Withdrawal (PBO SC)	RZB 360 mg SC	Withdrawal (PBO SC)	RZB 360 mg SC	Withdrawal (PBO SC)	RZB 360 mg SC	Withdrawal (PBO SC)	RZB 360 mg SC
	Week 8	Week 8	Week 16	Week 16	Week 24	Week 24	Week 32	Week 32	Week 40	Week 40	Week 48	Week 48	Week 52	Week 52
APS Remission (APS ≤1)	67.7	75.9	70.1	70.2	61	68.1	54.3	63.1	48.8	61.7	48.8	56	46.3	55.3
	[60.5, 74.8]	[68.8, 82.9]	[63.1, 77.1]	[62.7, 77.8]	[53.5, 68.4]	[60.4, 75.8]	[46.6, 61.9]	[55.2, 71.1]	[41.1, 56.4]	[53.7, 69.7]	[41.1, 56.4]	[47.8, 64.2]	[38.7, 54.0]	[47.1, 63.5]
		P=0.033		P=0.743		P=0.052		P=0.035		P=0.001		p=0.080		P=0.028
SF Remission (SF ≤2.8)	66.5	67.4	64.6	67.4	59.8	63.8	57.3	58.2	51.2	58.2	48.2	53.9	44.5	56
	[59.2, 73.7]	[59.6, 75.1]	[57.3, 72.0]	[59.6, 75.1]	[52.3, 67.3]	[55.9, 71.8]	[49.7, 64.9]	[50.0, 66.3]	[43.6, 58.9]	[50.0, 66.3]	[40.5, 55.8]	[45.7, 62.1]	[36.9, 52.1]	[3.6, 24.3]
		P=0.420		P=0.266		P=0.154		P=0.437		P=0.038		P=0.089		P=0.008
AP =0	..	..	..	..	..	..	..	..	..	..	..	..	18.3	30.6
													[12.4, 24.2]	[23.4, 37.8]
														P=0.009
SF ≤1	..	..	..	..	..	..	..	..	..	..	..	..	28.7	39.0
													[21.7, 35.6]	[31.0, 47.1]
														P=0.006
AP =0 and SF ≤1	..	..	..	..	..	..	..	..	..	..	..	..	14.6	23.4
													[9.2, 20.0]	[16.4, 30.4]
														P=0.021

BL = baseline; Endoscopic remission = SES-CD ≤4 and at least 2-point reduction from baseline; Ulcer-free endoscopy = SES-CD ulcerated surface subscore =0 in patients with subscore ≥1 at baseline; a)Intent-to-treat (ITT) population Includes randomized patients who (ADVANCE/MOTIVATE) received at least one dose of study drug during the 12-Week Induction Period, and had an SES-CD of ≥6 (≥4 for isolated ileal disease) or who (FORTIFY) received IV risankizumab for 12 weeks in the induction study and at least one dose of study drug in FORTIFY sub-study 1 and had an SES-CD of ≥6 (≥4 for isolated ileal disease) at baseline of induction. b)Calculations were based on non-responder imputation with no special data handling for missing data due to COVID-19 pandemic. 95% CI and p-value for adjusted response rate difference compared to PBO calculated according to the Cochran-Mantel-Haenszel test adjusted for strata.

P0437 Table.

360 mg RZB SC treatment groups from the FORTIFY maintenance study², were examined. AP and number of liquid or very soft stools were recorded in a daily diary; AP was rated as none (=0), mild (=1), moderate (=2), or severe (=3). AP remission (AP ≤1) and SF remission (SF ≤2.8) were assessed. Tetrachoric correlations, used to assess the statistical correlation between two dichotomous variables, were applied to measure the association between PROs and achievement of endoscopic remission and ulcer-free endoscopy (see Table footnotes for endpoint definitions) at Weeks 12 and 52.

Results: Significantly more patients receiving 600 mg RZB IV versus PBO reported improvements from baseline (BL) in SF and APS at Weeks 4, 8, and 12 (p-values <0.001). Of patients reporting AP ≥1 at Induction BL, significantly more patients receiving RZB treatment achieved APS =0 at Weeks 8 and 12 compared to PBO (p-values [p] ≤0.001). Similarly, of

patients reporting SF >2.8 at BL, significantly more patients receiving RZB treatment achieved SF ≤1 at Weeks 4, 8 and 12 compared to PBO (p-values ≤0.004). At Week 52 of maintenance, more patients achieved AP remission (p <0.05) and SF remission (p <0.01) with RZB 360 mg SC compared to RZB withdrawal (PBO SC). More patients also achieved complete resolution of symptoms (APS =0 [p =0.05], or SF ≤1 [p =0.006], or AP =0 and SF ≤1 [p =0.02]). AP remission at Week 12 was weakly correlated with endoscopic remission (r=0.19; p <0.001) and ulcer-free endoscopy (r=0.17; p =0.001) at Week 12. Similarly, weak/moderate correlations of SF remission with these endoscopic outcomes were observed at Week 12 (r=0.34 [p <0.001] and r=0.35 [p <0.001], respectively). At Week 52, moderate correlations were observed with endoscopic remission or ulcer-free endoscopy and AP remission (r=0.55 [p <0.001] and r=0.50 [p <0.001]) or SF remission (r=0.59 [p <0.001] and 0.48 [p <0.001]).

Conclusion: CD-related PROs improved with RZB induction therapy, and RZB maintenance dosing led to AP and SF remission. Symptom improvements and endoscopic outcomes were moderately correlated, underscoring the importance of an objective measure to assess disease activity.

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P0438

COMPARATIVE ANALYSIS OF ORIGINATOR VERSUS BIOSIMILAR COUNTERPARTS WHEN TREATING ULCERATIVE COLITIS

M. Thoo¹, C. Ng¹, D. Baldock², P. Robinson², E. Baynton²

¹Ipsos, Kuala Lumpur, Malaysia, ²Ipsos, London, United Kingdom

Contact E-Mail Address: elizabeth.baynton@ipsos.com

Introduction: The aim of this study is to investigate originator and bio-similar (bsx) drug usage in ulcerative colitis (UC) patients, examine if and where differences exist, as well as examine any changes in prescribers' attitudes towards both product types.

Aims & Methods: A multi-centre online medical chart review study of patients with UC was conducted between Jan-Mar and Jul-Sep 2019, 20 and 21 among UK, FR, DE, IT & ES gastroenterologists practicing across hospital and private practices. Recruited from a large access panel, physicians were screened for duration of practice in their specialty and caseload. Respondents completed a 3 part survey; doctor demographics, perceptual questionnaire and patient record forms of their next 4 UC patients seen following receipt of the survey.

Results: The total number of sampled gastroenterologists recruited in this survey, plus the collective total of reported UC patients treated with advanced therapy (biologics/targeted oral therapies) are in Table 1.

Survey Year	2019	2021	2022
Sampled gastroenterologists	287	264	247
Reported UC advanced therapy patients	1637	1601	1566

Table 1. Physician and patient sample size

Reported UC patients treated with adalimumab and infliximab originator products declined over time (% patient share of reported sample - 2019: 41.1%, 2020: 24.6%, 2021: 21.5%) while those treated with bsx versions directionally increased (2019: 29.7%, 2020: 38.9%, 2021: 38.3%). This is in line with changes observed with stated physician access to biologic therapies when treating UC. Access to originator products among sampled gastroenterologists declined from 2019 to 2021 (% sampled physicians citing access - 2019: 96.3%, 2020: 90.5%, 2021: 87.5%), while access to bsx versions directionally increased, surpassing that of the originators in 2020 and 2021 (2019: 91.7%, 2020: 95.7%, 2021: 95.1%).

Disease remission rates among reported bsx treated UC patients increased over time (% patients - 2019: 63.2%, 2020: 67.8%, 2021: 71.0%) but decreased for those treated with originator products (2019: 77.9%, 2020: 75.9%, 2021: 74.1%). Reported bsx treated patients had higher Mayo

scores than originator treated patients in 2019 (Mean: bsx 4.0 vs originator 3.2, respectively; $p \leq 0.01$) but in 2020, Mayo scores of originator treated patients were greater than that of bsx treated patients (2020 Mean: bsx 3.6 vs originator 4.0, $p \leq 0.05$).

Reasons for choosing the originator product for treatment were also different to that of bsx treated patients; in the reported bsx treated cohort, a higher proportion of gastroenterologists cited 'inhibited disease progression' as a reason for choosing a bsx product vs patients reported in the originator treated patient cohort (% patients- bsx 2019: 41.8%, 2020: 41.1%, 2021: 39.8%; originator-2019: 42.8%, 2020: 34.4%, 2021: 32.9%; respectively). 'To induce mucosal healing' was also selected more frequently as a reason for choosing a bsx product vs the originator (bsx vs originator- 2019: 55.8% vs 43.4%; 2020: 46.7% vs 37.6%, 2021: 50% vs 35.4%, respectively; $p \leq 0.01$).

Conclusion: From the sample surveyed, there is evidence of a change in bsx and originator prescribing when treating UC; gastroenterologists cite increasing access to bsx products, which may go some way in influencing levels of familiarity. There is evidence to suggest that gastroenterologists are more likely to prescribe bsx products for efficacy reasons, such as inducing remission and impacting clinical disease scores used to monitor patients' disease e.g., Mayo score. Further investigation using comparator cohort is warranted.

Disclosure: Nothing to disclose.

P0439

USTEKINUMAB PERSISTENCE IN THE TREATMENT OF CROHN'S DISEASE, FISTULIZING CROHN'S DISEASE AND ULCERATIVE COLITIS

B. Bressler¹, J. Jones², T. S.H. In³, T. Lan⁴, C. Iconaru⁴,

J.K. Marshall⁵

¹University of British Columbia, Department of Medicine, Vancouver, Canada, ²Dalhousie University, Department of Medicine, Halifax, Canada, ³Janssen Inc, Toronto, Canada, ⁴IQVIA Solutions Canada Inc., Kirkland, Canada, ⁵McMaster University, Department of Medicine and Farncombe Family Digestive Health Research Institute, Hamilton, Canada

Contact E-Mail Address: marshallj@mcmaster.ca

Introduction: Data on the real-world effectiveness of ustekinumab (UST) in the treatment of inflammatory bowel disease (IBD), including Crohn's disease (CD), fistulizing Crohn's disease (FCD) and ulcerative colitis (UC), are limited. Persistence on therapy is a measure of real-world treatment success. Previous studies of persistence of UST treatment in patients with IBD have been limited by relatively small sample size or relatively short follow-up.

Aims & Methods: The aim of this study was to estimate the persistence of UST treatment among adult patients with CD, FCD or UC, and to identify factors that impact treatment persistence.

Using data from a national patient support program that captures patients treated with UST in Canada, a retrospective study was conducted on adult patients with CD or FCD who initiated UST treatment between January 1, 2017 and July 31, 2021, and adult patients with UC who initiated UST treatment between February 1, 2020 and July 31, 2021. Treatment persistence, defined as time from a patient's first recorded pharmacy fill for UST to discontinuation (gap between two pharmacy fills > 20 weeks) or censoring, was described using the Kaplan-Meier (KM) method. The impact of patient characteristics at index (age group, sex, region, year of treatment initiation, and biologic-naïve status) on persistence was explored by stratified analyses and multivariable Cox proportional hazards models.

Results: 8,724 patients with CD (mean age 46.8 years; 55.2% female; 36.0% biologic-naïve), 276 patients with FCD (mean age 45.4 years; 55.4% female; 20.7% biologic-naïve), and 1,291 patients with UC (mean age 45.9

years; 47.1% female; 24.9% biologic-naïve) were included. Persistence rates for patients with CD were 82.9%, 71.4%, 64.1%, and 59.7% at 1, 2, 3, and 4 years, respectively. Among patients with UC, 76.5% were persistent at 1 year, and 69.5% at 1.5 years. Stratified by prior IBD-indicated biologic experience, biologic-naïve patients had higher persistence than biologic-experienced patients (Table). This difference was significant among patients with CD based on the multivariable Cox regression model (hazard ratio: 0.72; confidence interval: 0.65-0.79).

	Total patients, n	1 year, % (n at risk)	1.5 year, % (n at risk)	2 years, % (n at risk)	3 years, % (n at risk)	4 years, % (n at risk)
Patients with CD	8,724	82.9% (5,476)	76.4% (4,190)	71.4% (2,971)	64.1% (1,248)	59.7% (504)
Biologic-naïve	3,143	87.2% (1,869)	80.6% (1,399)	76.7% (968)	70.6% (376)	66.0% (159)
Biologic-experienced	5,581	80.8% (3,607)	74.2% (2,791)	68.8% (2,003)	61.1% (872)	56.7% (345)
Patients with FCD	276	84.1% (178)	76.8% (133)	70.9% (95)	64.9% (39)	63.1% (14)
Biologic-naïve	57	87.3% (33)	84.1% (25)	76.5% (16)	76.5% (8)	76.5% (6)
Biologic-experienced	219	83.4% (145)	75.1% (108)	69.7% (79)	62.6% (31)	60.3% (8)
Patients with UC	1,291	76.5% (452)	69.5% (125)	-	-	-
Biologic-naïve	322	81.2% (93)	73.1% (30)	-	-	-
Biologic-experienced	969	75.3% (359)	68.5% (95)	-	-	-

Table. KM-derived ustekinumab persistence, by indication and biologic-naïve status

Conclusion: This study reports the long-term real-world persistence of UST in a large population of patients with IBD. Over half of patients with CD were estimated to remain on UST therapy after 4 years of treatment, and biologic-naïve patients with CD was shown to have significantly better persistence than biologic-experienced patients.

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- Tracey S.H. In: employee of Janssen

- Tommy Lan: employee of IQVIA

- Cristian Iconaru: employee of IQVIA

- John K. Marshall: Speaker: AbbVie, Allergan, Amgen, Ferring, Janssen, Lupin, Organon, Pfizer, Pharmascience, Roche, Shire, Takeda, Viartis. Consultant: AbbVie, Alimentiv, Allergan, Amgen, Bausch, BMS, Celltrion, Ferring, Fresenius Kabi, Janssen, Lilly, Lupin, Novartis, Organon, Paladin, Pfizer, Pharmascience, Qu Biologics, Roche, Sandoz, Takeda, Teva, Viartis.

P0440

EFFICACY AND SAFETY OF UPADACITINIB IN PATIENTS WITH MODERATELY TO SEVERELY ACTIVE ULCERATIVE COLITIS RECEIVING 16 WEEKS' EXTENDED INDUCTION TREATMENT FOLLOWED BY 52 WEEKS' MAINTENANCE TREATMENT IN THE U-ACHIEVE/U-ACCOMPLISH TRIALS

R. Panaccione¹, S. Danese², W. Zhou³, J. Klaff³, D. Ilo³, X. Yao⁴, G. Levy⁵, P.D.R. Higgins⁶, E.V. Loftus Jr.⁷, S. Vermeire⁸

¹University of Calgary, Inflammatory Bowel Disease Unit, Division of Gastroenterology and Hepatology, Calgary, Canada, ²IRCCS Ospedale San Raffaele and University Vita-Salute San Raffaele, Gastroenterology and Endoscopy, Milan, Italy, ³AbbVie Inc., Research and Development, North Chicago, United States, ⁴AbbVie Inc., Data & Statistical Sciences, North Chicago, United States, ⁵AbbVie Inc., Pharmacovigilance & Patient Safety, North Chicago, United States, ⁶University of Michigan, Department of Medicine, Division of Gastroenterology, Ann Arbor, United States, ⁷Mayo Clinic, College of Medicine & Science, Division of Gastroenterology and Hepatology, Rochester, United States, ⁸University Hospital Leuven & KU Leuven, Gastroenterology & Hepatology, Leuven, Belgium

Contact E-Mail Address: rpanacci@ucalgary.ca

Introduction: Upadacitinib (UPA) is an oral selective and reversible Janus kinase inhibitor. UPA 45 mg once daily (QD) has demonstrated superior efficacy to placebo and a favorable safety profile following an 8-week induction therapy in patients with moderately to severely active ulcerative colitis (UC) in two double-blinded, randomized induction trials U-ACHIEVE Induction (NCT02819635) and U-ACCOMPLISH (NCT03653026).^{1,2}

Aims & Methods: Patients who did not achieve a clinical response (Adapted Mayo score decrease of ≥ 2 points and $\geq 30\%$ from baseline, plus a ≥ 1 point decrease in rectal bleeding score [RBS] or absolute RBS ≤ 1) following an initial 8 weeks' UPA 45 mg QD treatment in the induction trials were eligible to receive an additional 8-week, open-label extended treatment with UPA 45 mg QD. Patients with a clinical response following completion of the extended induction (Week 16) were re-randomized 1:1 to UPA 15 mg QD or UPA 30 mg QD in the U-ACHIEVE Maintenance trial (NCT02819635).

This analysis evaluated the efficacy and safety of UPA following extended induction treatment (UPA 45 mg QD for 16 weeks) and subsequent maintenance treatment (UPA 15 mg QD or UPA 30 mg QD for 52 weeks).

Results: Of the patients who received UPA 45 mg QD in the induction trials, 125 did not achieve a clinical response at 8 weeks and received a further 8 weeks' induction treatment. At Week 16, 73/125 (58.4%) subsequently responded and were re-randomized to maintenance UPA 15 mg QD or UPA 30 mg QD. Among 16-week responders who entered the maintenance trial, a greater proportion of patients who received UPA 30 mg QD vs UPA 15 mg QD achieved the primary endpoint of clinical remission at 52 weeks (43.6% vs 26.5%, respectively), and the secondary endpoints of clinical response (78.1% vs 49.1%, respectively) and endoscopic improvement (51.3% vs 34.3%, respectively) at 52 weeks (Table).

A similar pattern was seen across all clinical, endoscopic, and histologic endpoints (Table). At Week 52, the proportions of patients with serious adverse events (AEs) were 2.9% with UPA 15 mg QD and 10.0% with UPA 30 mg QD. Selected AEs of special interest with UPA 15 mg QD and UPA 30 mg QD included serious infection (2.9% vs 5.0% of patients, respectively), herpes zoster (0% vs 5.0%, respectively), adjudicated major adverse cardiovascular events (0% vs 2.5%, respectively), and non-melanoma skin cancer (NMSC; 0% vs 2.5%, respectively). No adjudicated venous thromboembolic events or cases of malignancy excluding NMSC were reported with either UPA dose.

Conclusion: Extended induction treatment for an additional 8 weeks with UPA 45 mg QD induced a response in over half of patients with UC who did not achieve a response after 8 weeks. The benefit of maintenance therapy in delayed responders was demonstrated with both UPA doses, although UPA 30 mg QD provided a greater benefit than UPA 15 mg QD. UPA was well tolerated with no new safety signals and selected AEs of special interest were reported infrequently with both maintenance doses.

Primary and key secondary endpoints, %	UPA 45 mg QD at Week 16 (induction) ^a (N=125)	UPA 15 mg QD at Week 52 (maintenance) ^b (N=34)	UPA 30 mg QD at Week 52 (maintenance) ^b (N=39)
Primary endpoint: Clinical remission ^c	5.6	26.5	43.6
Clinical response at end of induction ^d	58.4	N/A	N/A
Maintenance of clinical response ^e	N/A	(N=25) 49.1	(N=32) 78.1
No abdominal pain	40.0	38.2	48.7
No bowel urgency	30.4	32.4	59.0
Endoscopic improvement ^f	14.3	34.3	51.3
Endoscopic remission ^f	4.9	12.2	17.9
Histologic-endoscopic mucosal improvement ^g	11.0	21.9	41.0
Mucosal healing ^h	3.4	12.0	12.8
Among patients who achieved clinical remission at the end of induction:		(N=3)	(N=4)
Clinical remission ^c	N/A	0	100
Clinical remission ^c and corticosteroid free for ≥90 days immediately prior to Week 52	N/A	0	100
Among patients who achieved endoscopic improvement at the end of induction:		(N=7)	(N=9)
Endoscopic improvement ^f	N/A	42.9	66.7

Data are presented for the ITT population comprising patients who achieved a clinical response with 16-week UPA 45 mg QD induction therapy and were re-randomized to receive UPA 15 mg or 30 mg QD maintenance therapy.

^aTwo patients were excluded from analysis owing to site non-compliance as prespecified in the statistical analysis plan.

^bIncluded patients who had completed, or had the potential to complete, 52 weeks' maintenance treatment.

^cPer Adapted Mayo score ≤2; stool frequency subscore ≤1 and not greater than induction baseline, RBS=0, and ES ≤1.

^dInduction therapy (UPA 45 mg QD): Clinical response, defined as a decrease in Adapted Mayo score ≥2 and ≥30% from induction baseline, plus a decrease in RBS ≥1 or an absolute RBS ≤1, at Week 16. Maintenance therapy (UPA 15 mg or 30 mg, QD): Maintenance of clinical response at Week 52 among patients who achieved clinical response at the end of the 16-week induction therapy.

^eES ≤1.

^fES=0.

^gES ≤1 and Geboes score ≤3.1.

^hES=0 and Geboes score <2.

ES, endoscopic subscore; ITT, intent-to-treat; N/A, not applicable; QD, once daily; RBS, rectal bleeding subscore; UPA, upadacitinib.

Table.

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- Danese S, et al. J Crohns Colitis 2021;15(Suppl. 1):S022–4.

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P0441

AN ANALYSIS OF HIGHER SECONDARY EFFICACY FAILURE RATES AMONG ULCERATIVE COLITIS PATIENTS WHEN COMPARING THE EU TO THE US

L. Fendrick¹, P. Zimmerman¹
¹Spherix Global Insights, Gastroenterology, Exton, United States

Contact E-Mail Address: paul.zimmerman@spherixglobalinsights.com

Introduction: This retrospective analysis of gastroenterologist-provided patient records for ulcerative colitis (UC) compares patients who recently switched advanced therapies due to secondary efficacy failure in the European Union (EU) and United States (US) with a discussion of continued higher prescribing rates for tumor necrosis factor inhibitors (TNFi) in the EU.

Aims & Methods: In August-September 2021, Spherix conducted a retrospective EU (France, Germany, Italy, Spain, and the United Kingdom) patient chart audit of 717 patients with UC who had switched from one biologic/JAK inhibitor agent to another in the previous four months. 289 EU gastroenterologists submitted this patient-level data, including the therapy patients were switched from and the reasons for that switch to have taken place, via a GDPR and HIPAA-compliant audit form.

In July-September 2021, Spherix conducted a retrospective US patient chart audit of 629 patients with UC who had switched from one biologic/JAK inhibitor agent to another in the previous four months. 196 US gastroenterologists submitted this patient-level data, a process identical to the method used in the EU. The aim is to profile differences between the EU5 and US in secondary efficacy failure rates in relation to TNFi prescribing levels in both regions.

Results: Secondary efficacy failure was the primary reason for switching therapies for 29% of EU UC patients, making it the leading reason for switching in the EU. In the US, secondary efficacy failure was indicated as

the primary reason for switching in 16% of UC patients, falling third on the list of reasons for switching. The past four years of EU UC switching patient chart data show that secondary efficacy has been the leading primary reason for switching (2018- 32%, 2019- 36%, 2020- 28%, 2021- 29%). However, in the US, these rates have decreased over the same period (2018- 23%, 2019- 25%, 2020- 18%, 2021- 16%).

Coinciding with these differences, TNFi prescribing for UC has remained high in the EU5, due to the availability of biosimilars for both infliximab and adalimumab. 96% of EU patients who switched due to secondary efficacy failure were switched from a TNFi (2018- 97%, 2019- 89%, 2020- 95%, 2021- 96%). In the US, TNFi prescribing relative to other classes of therapy has declined. In 2021, 79% of US patients who switched due to secondary efficacy failure were switched from a TNFi (2018- 96%, 2019- 89%, 2020- 87%, 2021- 79%).

Conclusion: Switching therapies due to secondary efficacy failure has remained high, along with the rates of switching from TNFi therapies in the EU. In contrast, the US, with less TNFi prescribing in the absence of an adalimumab biosimilar, also has notably less therapy switching due to secondary efficacy failure. Further analysis of the potential impact of TNFi therapies on secondary efficacy failure is recommended with potential impacts on both the US and EU UC markets.

References: 2021 Spherix Global Insights Real World Dynamix Switching EU5 Report

2021 Spherix Global Insights Real World Dynamix Switching US Report

Disclosure: Spherix Global Insights is a privately owned market research organization and both authors are employees of Spherix Global Insights.

P0442

LONG-TERM TREATMENT PERSISTENCE WITH INFLIXIMAB IN PATIENTS WITH INFLAMMATORY BOWEL DISEASE: A REAL-WORLD STUDY

M.G. Gonçalves¹, T. Carvalho¹, J.P. Monteiro Almeida Pereira², A. Guimarães¹, P. Antunes¹, B.M. Gonçalves¹, J.B. Soares¹, A. Rebelo¹, R. Gonçalves¹

¹Braga Hospital, Gastroenterology, Braga, Portugal, ²Unidade Local de Saúde de Matosinhos, Gastroenterologia, Águeda, Portugal

Contact E-Mail Address: margaridagoncalves21@gmail.com

Introduction: Infliximab was one of the first biologic treatment options for patients with inflammatory bowel disease (IBD). Long-term outcome studies of anti-TNF therapy with an observation time longer than 5 years are limited.

Aims & Methods: The authors intend to assess length of treatment persistence with Infliximab and also identify independent predictors for treatment failure. This was a single-center and retrospective study that included patients who received infliximab (either on induction or maintenance regimen), as first biologic therapy, between 2012 and 2015. Kaplan-Meier analysis with log-rank test was used to describe treatment persistence. With multi-variable Cox regression analysis, independent predictors for treatment persistence were investigated.

Results: During the study period 176 patients were included (134 with Crohn's disease, 40 with ulcerative colitis and 2 with unclassified IBD) with a mean age at diagnosis of 27.7±12.2 years. Sex distribution was balanced (51.7% female vs 48.3% male). Median time from diagnosis to infliximab was 38 months (IQ 16-94.5) and the median time of follow-up (until suspension or last visit) was 13.2 years (IQ 10.2-18.2).

At the end of follow-up 79 patients (44.9%) were still on Infliximab, with a median treatment persistence of 8.1 years (IQ 4.9-12.9). The main reasons for discontinuation were treatment failure (53.6%) and side effects (30.9%). Female gender, longer duration of disease and the presence of

immunomodulator at the beginning of Infliximab were identified as independent predictors on Cox Regression (OR 1.74, p=0.013, OR 0.98, p<0.001 and OR 1.75, p=0.30, respectively). These independent predictors remain valid in the sub-analysis of patients with Crohn's disease.

Conclusion: Treatment persistence with Infliximab in inflammatory bowel diseases was limited, mainly due to treatment failure and side effects. Gender, duration of disease prior biological therapy and immunomodulator influence infliximab treatment persistence.

Disclosure: Nothing to disclose.

P0443

QINGDAI (QD) FOR PATIENTS WITH ACTIVE ULCERATIVE COLITIS: A RETROSPECTIVE ISRAELI NATIONAL EXPERIENCE

U. Kopylov¹, N. Salomon¹, E. Zittan², E. Shachar¹, A. Lahat¹, A. Eliakim³, B. Weiss⁴, A. Shitrit⁵, B. Koslowsky⁶, L. Saban², N. Maharshak⁷, N. Tamir⁸, E. Ritter⁹, A. Hirsch¹⁰, I. Dotan¹¹, S. Ben-Horin¹², H. Yanai⁸

¹Sheba Medical Center Hospital - Tel Hashomer, Ramat Gan, Israel,

²Emek Medical Center, Gastroenterology, Afula, Israel, ³Sheba

Medical Center, Gastroenterology, Ramat Gan, Israel, ⁴Sheba

Medical Center, Pediatric Gastroenterology, Ramat Gan, Israel,

⁵Shaare Zedek Medical Center, IBD and Pregnancy Unit, Jerusalem,

Israel, ⁶Shaare-Zedek Medical Center, Gastroenterology,

Jerusalem, Israel, ⁷Tel Aviv Medical Center, Gastroenterology and

Liver Diseases, Tel Aviv, Israel, ⁸Rabin Medical Center, Division of

Gastroenterology, Petah Tikva, Israel, ⁹Tel Aviv Sourasky Medical

Center, IBD Center, Gastroenterology and Liver Diseases, Tel Aviv,

Israel, ¹⁰Tel Aviv Medical Center, Kiryat Ono, Israel, ¹¹Rabin Medical

Center, Director, Division of Gastroenterology, Petah Tikva, Israel,

¹²University of Tel Aviv, Sheba Medical Center, Gastroenterology,

Tel Hashomer, Israel

Contact E-Mail Address: Nironsl@gmail.com

Introduction: QingDai (QD) is a herbal extract used in traditional Chinese medicine. QD has been shown to be effective for ulcerative colitis (UC) in randomized controlled trials and retrospective reports from Japan. However, experience with QD for UC in the West is extremely limited. We aimed to describe the effectiveness and safety of QD in a national cohort of patients with UC followed at tertiary referral centers.

Aims & Methods: A retrospective study. We included adult patients who received QD for active UC (simple colitis clinical activity index (SCCAI)≥3) between January 2018 and January 2022 at five participating centers. A majority of patients received QD in a combination with curcumin. Clinical, biochemical and endoscopic data were retrieved from patients' medical records.

The primary outcome was clinical response at the end of induction (up to 16 weeks from the start of the treatment). Clinical response was defined as an improvement of SCCAI≥ 3 points; clinical remission as SCCAI≤2. C-reactive protein (CRP), fecal calprotectin (FC) levels and endoscopic Mayo score before and after treatment were compared when available. Starting corticosteroid or biologic treatment, hospitalization due to disease exacerbation, colectomy, discontinuation of treatment due to an adverse event or missing follow-up data were considered treatment failures.

Results: A total of 82 patients were included [median age-32, interquartile ratio (IQR)-23-41], 47 (57.3%) female; disease extent- 16 (20.5%)-proctitis, 28 (35.9%)- left-sided, 34 (43.6%) – pancolitis]. Forty one (54.7%) patients were biologics naïve, 10 (12.9%) failed ≥ 3 biologics or small molecules. Median SCCAI was 6 (5-9), CRP- 5 (2-17) mg/L, fecal calprotectin levels – 698 (320 -1190) mg/g and endoscopic Mayo score- 2. At treatment onset, 27 (41.5%) were treated with corticosteroids and 28 (34.1%) with a bio-

logic or small molecule. The initial QD dose was 1 g/d in 68 (82.9%) and 2g /d in 14 (17.1%) of the patients. QD was initiated in combination with curcumin in 77 (95.1%) of the patients.

Last induction follow-up occurred after 8 (8-12) weeks. At the end of induction, 64 (78%) responded to treatment, including 52 (63.4%) that achieved clinical remission. At the end of induction, median SCCAI was 2 (1-3) ($p<0.001$), CRP-2 (1-5) mg/L ($p=0.003$, 22 patients with paired measurements), FC levels -75 (12-139, 35 patients) mg/g ($p<0.001$) and median endoscopic Mayo score -1 (0-2) ($p=0.03$, 12 patients). Two (2.3%) patients experienced headaches and 5 (6.1%) – mild liver function elevations that resolved spontaneously or following QD discontinuation (2 patients).

Conclusion: In this multicenter retrospective cohort, QD treatment (frequently combined with curcumin) was effective for induction of clinical response and remission in 78% of patients, including biologic-experienced patients. All adverse events were mild and resolved either spontaneously or after QD discontinuation.

Our results suggest QD as a potential effective and safe agent for induction of response and remission in patients with active UC.

Disclosure: Nothing to disclose.

P0444

SWITCH FROM INTRAVENOUS TO SUB-CUTANEOUS INFLIXIMAB IN INFLAMMATORY BOWEL DISEASE: WHICH CONSEQUENCES FROM A PHARMACOKINETIC PERSPECTIVE?

C. Tron¹, B. Franck¹, M.-C. Verdier¹, F. Lemaître¹, G. Bouguen²
¹Rennes University Hospital, Pharmacology Department, Rennes, France, ²CHU Pontchaillou, Service des Maladies de l'Appareil Digestif, Rennes, France

Contact E-Mail Address: guillaume.bouguen@chu-rennes.fr

Introduction: Therapeutic drug monitoring (TDM) of infliximab is routinely performed in many centers to optimize treatment response in patient with inflammatory bowel disease (IBD). While the pharmacokinetic of intravenous formulation (IV) has been extensively described and therapeutic range have been reported, few data are available regarding the actual infliximab exposure reached with the new subcutaneous formulation (SC).

Aims & Methods: The aim of this work was to compare exposures in patients switched from IV to SC infliximab.

A retrospective monocentric study was conducted in stable patients with IBD switched from IV to SC infliximab between March 2021 and February 2022 in the Gastroenterology department of Rennes University Hospital. Paired-trough concentrations (C₀) measured

i) after the last IV injection and;

ii) at steady state after initiation of SC injections, were collected from routine TDM.

All infliximab concentrations measurements were centralized in the same laboratory. It allowed estimating the exposure reflected by the area under the curve of concentrations of infliximab versus time (AUC). Exposure between to administrations (AUC_{0-8weeks}) and exposure normalized to eight weeks (AUC_{0-8weeks}) were derived using population pharmacokinetics modelling [1,2].

Results: A total of 119 patients were switched from infliximab IV to SC during the study period. The patient self-administrates SC infliximab at home, so visits to the hospital are less frequent. Eventually, concentrations at steady state after switch (> 2 months after the switch) were available for seven-five patients at the time of the data analysis. SC dosage was 120 mg/2 weeks (n=65) or /1 week (n=10). Median [range] of C₀ were 4.7 µg/mL [<0.2 -19.4] for IV and 20.8 µg/mL [<0.2 -64.1] for SC ($p<0.0001$). AUC_{0-8weeks} were also different between both formulations (32378 µg.h/mL [11364-59409] for IV and 8010 µg.h/mL [3320-11400] for SC, $p<0.0001$). However, median

AUC_{0-8weeks} were similar before and after the switch (33333 µg.h/mL [17857-91314] for IV and 32451 µg.h/mL [12279-84181] for SC, $p=0.3$). A poor correlation was observed between IV/SC C₀ ($r^2=0.08$, $p=0.01$) and IV/SC AUC_{0-8weeks} ($r^2=0.11$, $p=0.002$). Both formulations displayed an high inter-patient variability of C₀ (Coefficients of variation: 69.5 % for IV and 53.8 % for SC).

Conclusion: This study provides useful data to interpret TDM results in the era of SC infliximab. Intravenous therapeutic range based on C₀ should not be applied to SC infliximab. While globally exposures (AUC_{0-8weeks}) are similar between the two formulations, they may unpredictably change after the switch from an individual perspective. Further study are required to precise the target range of concentrations of SC infliximab.

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P0445

SAFETY OF TOFACITINIB IN THE TREATMENT OF ULCERATIVE COLITIS:

I. Rodríguez Mendiluze¹, N. Hervás Palacios¹, A. Arrubla Gamboa¹, P. Salmón Olavarría¹, A. Elosua González², S. Rubio Iturria¹, Ó. Nantes Castillejo¹, E. Amorena Muro¹, M. Vicuña Arregui¹, C. Rodríguez Gutierrez¹

¹Hospital Universitario Navarra, Pamplona, Spain, ²Hospital García Orcoyen, Gastroenterology and Hepatology, Pamplona, Spain

Contact E-Mail Address: irenita.rm@gmail.com

Introduction: Tofacitinib (TF) is a partially selective JAK inhibitor with anti-inflammatory and immunomodulatory effect approved by the EMA in 2018 in moderate-severe UC. Minor side effects have been described and there are two alerts for venous thromboembolic phenomena in patients >50 years with rheumatoid arthritis and doses of 10 mg/12 hours and for risk of malignancies and infections.

Aims & Methods: Retrospective analysis of UC patients treated with TF in our center from April 2018 to November 2021. Safety and adverse effects are analyzed.

Results: Seventy-one patients (45% female) were included. Median age 48 years (18-83) with 16% >60 years. 12 patients smokers (16%), 3 diabetics (4%), 11 with AHT (15%), 13 with dyslipidemia (18%) and 8 with BMI >30 (12%). History of ischemic heart disease in 4 patients (6%) and thromboembolic phenomena in 2 (1 venous thrombosis associated with PICC and 1 pulmonary thromboembolism in the context of sepsis). Previous neoplasms in 5 cases (7%): 1 breast cancer, 1 melanoma, 1 thyroid and 2 non-melanoma skin cancers. Side effects were observed in 11 patients (15.5%), including digestive intolerance, pruritus, lymphopenia, herpes zoster, renal failure and dyslipidemia. Adverse effects were the reason for definitive discontinuation of the drug in 4 patients, temporary discontinuation in 3 and dose reduction in 2 patients. There was no secondary mortality.

Conclusion: - In our series, Tofacitinib shows an acceptable safety profile.

- The prevalence of side effects is low but may condition drug withdrawal.

- No thromboembolic phenomena or cardiovascular events were detected in our series.

Disclosure: None.

P0446

EFFICACY AND SAFETY OF USTEKINUMAB IN ASIAN PATIENTS WITH MODERATELY TO SEVERELY ACTIVE ULCERATIVE COLITIS: A SUBPOPULATION ANALYSIS OF UNIFI LONG-TERM EXTENSION THROUGH 3 YEARS

T. Hisamatsu¹, H.J. Kim², S. Motoya³, Y. Suzuki⁴, Y. Ohnishi⁵, C.W. Marano⁶, Y. Imai⁷, C. Saadoun⁸, J. Zhuo⁹, S. Kawamura⁸
¹Kyorin University School of Medicine, Department of Gastroenterology and Hepatology, Tokyo, Japan, ²Kyung Hee University College of Medicine, Center for Crohn's and Colitis, Department of Gastroenterology, Seoul, Korea (Republic of), ³Sapporo-Kosei General Hospital, IBD Center, Hokkaido Prefectural Welfare Federation of Agricultural Cooperative, Hokkaido, Japan, ⁴Toho University Sakura Medical Center, Division of Gastroenterology and Hepatology, Department of Internal Medicine, Sakura, Japan, ⁵Shizuoka Medical Center, Division of Gastroenterology, Shizuoka, Japan, ⁶Janssen Research & Development, LLC, Spring House, United States, ⁷Janssen Pharmaceutical K.K., Tokyo, Japan, ⁸Janssen Pharmaceuticals Asia Pacific, Singapore, Singapore, ⁹Janssen China Research & Development, Shanghai, China

Contact E-Mail Address: yasuo-suzuki@sakura.med.toho-u.ac.jp

Introduction: Ustekinumab (UST) is approved for treatment of moderately to severely active ulcerative colitis (UC) in many countries, including Asia. However, the long-term efficacy and safety in an Asian population still remain unclear.

This analysis is aimed to assess the efficacy and safety of UST in the Asian subpopulation in the UNIFI long-term extension (LTE).

Aims & Methods: UNIFI, a Phase 3, randomized, double-blind, placebo-controlled trial consisting of an 8-week induction study and a 44-week re-randomized withdrawal maintenance study with a 4-year LTE, evaluated UST in patients with moderately to severely active UC. In this report, all patients who continued into the LTE were followed up to 3 years (Week 152). The patients on the placebo arm were discontinued when the study was unblinded after Week 44. Efficacy was evaluated using symptomatic remission (defined as a Mayo stool frequency subscore of 0 or 1 and a rectal bleeding subscore of 0). All adverse events (AEs) were summarized for long-term safety assessment.

Results: A total of 87 randomized patients in maintenance were treated in the LTE with either subcutaneous (SC) placebo (n=34 [39.1%]), UST 90 mg SC every 12 weeks (n=24 [27.6%]), or UST 90 mg SC every 8 weeks (n=29 [33.3%]). Of the 53 randomized patients who were treated with UST, 31 (58.5%) and 28 (52.8%) patients were in symptomatic remission at Week 44 and Week 152 in the combined UST group, respectively (Table 1). Of note, all patients who achieved symptomatic remission were corticosteroid-free (Table 1).

The average duration of follow up from Week 0 through the final safety visit was 138.9 weeks and 88.0 weeks in the combined UST and placebo groups, respectively. Among the combined UST group (n=69), safety events (per hundred patient-years) from maintenance Week 0 through final safety visit included: AEs, 240.9; serious AEs, 10.9; infections, 99.3; and serious infections, 2.2. Among the placebo group (n=34), safety events (per hundred patient-years) from maintenance Week 0 to the final safety visit included: AEs, 314.6; serious AEs, 7.0; infections, 125.2; and serious infections, 1.7. Non-melanoma skin cancers (per hundred patient-years) were 0.5 in the combined UST group and 0.0 in the placebo group. No deaths were reported and 9 (22.0%) patients discontinued UST (due to AEs [n=2; 9.1%], lack of efficacy [n=3; 7.3%], no improvement in UC disease activity 16 weeks after dose adjustment [n=1; 2.4%], and other [n=3; 13.6%]) during LTE.

	Week 44 – UST 90 mg SC			Week 152 – UST 90 mg SC		
	q12w ^a (n=24)	q8w ^a (n=29)	Combined (n=53)	q12w ^a (n=24)	q8w ^a (n=29)	Combined (n=53)
Symptomatic remission ^{b,c,d}	66.7 (16/24)	51.7 (15/29)	58.5 (31/53)	62.5 (15/24)	44.8 (13/29)	52.8 (28/53)
Symptomatic remission and not receiving CS ^{b,c,e,f}	66.7 (16/24)	51.7 (15/29)	58.5 (31/53)	62.5 (15/24)	44.8 (13/29)	52.8 (28/53)

All data are presented as % (n/N). Combined UST 90 mg data (n=53) include UST 90 mg SC q12w (n=24) and 90 mg SC q8w (n=29).
 AE, adverse event; CS, corticosteroid; q8w, every 8 weeks; q12w, every 12 weeks; SC, subcutaneous; UC, ulcerative colitis; UST, ustekinumab.
^aRandomized group at maintenance Week 0 regardless of whether patients had a dose adjustment during the long-term extension.
^bSymptomatic remission is defined as a stool frequency subscore of 0 or 1 and a rectal bleeding subscore of 0.
^cPatients who had both stool frequency and rectal bleeding subscores missing at a visit were considered not to be in symptomatic remission for that visit.
^dPatients who had an ostomy or colectomy, or discontinued study drug due to lack of therapeutic effect or due to an AE of worsening of UC prior to the designated visit were considered not to be in symptomatic remission.
^ePatients who had a missing value in corticosteroid use had their last value carried forward.
^fPatients who had a prohibited change in UC medication, on ostomy or colectomy, or used a rescue medication after clinical flare, or discontinued study agent due to lack of therapeutic effect or due to an AE of worsening of UC prior to the Week 44 visit were considered not to be in symptomatic remission.

Table 1. Key clinical efficacy in Asian patients randomized in maintenance who were treated during the long-term extension.

Conclusion: Long-term efficacy and safety of UST in an Asian subpopulation with moderately to severely active UC were confirmed in this study. Symptomatic remission was maintained without any new safety findings in Asian patients through 3 years. Overall, the safety and efficacy profiles of UST in an Asian subpopulation are consistent with the overall study population previously reported.

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Carine Saadoun, MD and Shiho Kawamura, PhD report employment with Janssen Pharmaceuticals Asia Pacific, Singapore, Singapore, a wholly owned subsidiary of Johnson & Johnson, and stock ownership in Johnson & Johnson.

Jianmin Zhuo, MS reports employment with Janssen China Research & Development, Shanghai, China, a wholly owned subsidiary of Johnson & Johnson, and stock ownership in Johnson & Johnson.

P0447

LIVE VACCINES IN CHILDREN EXPOSED TO BIOLOGICAL AGENTS FOR IBD IN UTERO AND/OR DURING BREASTFEEDING: ARE THEY SAFE? RESULTS FROM THE DUMBO REGISTRY OF GETECCU

M. Chaparro Sanchez¹, M. García Donday¹, S. Rubio², C. Calviño Suarez³, A. Nuñez Ortiz⁴, M. Figueira⁵, S. Marín Pedrosa⁶, M. Rivero⁷, A. Fernández-Clotet⁸, L. Madero⁹, M.T. Diz-Lois Palomares¹⁰, I. Pérez-Martínez¹¹, A. Ruiz-Cerulla¹², M. Arroyo¹³, M. Piqueras¹⁴, C. Suárez Ferrer¹⁵, M. Aguas¹⁶, M. Calvo Moya¹⁷, I. Guerra¹⁸, P. López Serrano¹⁹, J.M. Vázquez Morón²⁰, L. Arias García²¹, M.J. Casanova¹, J.M. Huguet²², G. Valldosera Gomis²³, B. Zúñiga de Mora-Figueroa²⁴, R. Armesto²⁵, M.P. Martínez Montiel²⁶, I. Rodríguez-Lago²⁷, P. Sendra Rumbau²⁸, R. Camargo Camero²⁹, D. Hervías Cruz³⁰, G. Molina Arriero³¹, C. Tardillo Marín³², M.Á. De Jorge Turrión³³, R. Vicente Lidón³⁴, L. Bujanda Fernández de Piérola³⁵, P. Ramírez de la Piscina³⁶, V. Robles Alonso³⁷, L. Ramos³⁸, R. Rodríguez Insa³⁹, M. Van Domselaar⁴⁰, D. Busquets Casals⁴¹, M. Barreiro-de Acosta¹, D. Acosta¹, Y. Brenes¹, S. Hermida¹, P. Parra¹, A. Garre¹, J.P. Gisbert¹, on behalf of DUMBO Study Group
¹Hospital Universitario de La Princesa, IIS-Princesa, Universidad Autónoma de Madrid (UAM) and CIBEREHD, Gastroenterology Unit, Madrid, Spain, ²Hospital Universitario de Navarra, Gastroenterology Unit, Pamplona, Spain, ³Hospital Clínico Universitario de Santiago de Compostela, Gastroenterology Unit, Santiago de Compostela, Spain, ⁴Hospital Universitario Virgen del Rocío, Gastroenterology Unit, Sevilla, Spain, ⁵Xerencia Xestión Integrada de Vigo, SERGAS, Grupo de Investigación de Patología Digestiva, IIS Galicia Sur. SERGAS UVIGO, Gastroenterology Unit, Vigo, Spain, ⁶Hospital Universitario Reina Sofía, Gastroenterology Unit, Córdoba, Spain, ⁷Hospital Universitario Marqués de Valdecilla e IDIVAL, Gastroenterology Unit, Santander, Spain, ⁸Hospital Universitario Clínic i Provincial, Gastroenterology Unit, Barcelona, Spain, ⁹Hospital General Universitario de Alicante, Gastroenterology Unit, Alicante, Spain, ¹⁰Complejo Hospitalario Universitario de A Coruña, Gastroenterology Unit, A Coruña, Spain, ¹¹Hospital Universitario Central de Asturias e Instituto de Investigación Sanitaria del Principado de Asturias (ISPA), Gastroenterology Unit, Oviedo, Spain, ¹²Hospital Universitario de Bellvitge, Gastroenterology Unit, Barcelona, Spain, ¹³Hospital Clínico Universitario Lozano Blesa, Fundación del Instituto de Investigación Sanitaria de Aragón (IIS Aragón) and CIBEREHD, Gastroenterology Unit, Zaragoza, Spain, ¹⁴Consorci Sanitari de Terrassa (CST), Gastroenterology Unit, Barcelona, Spain, ¹⁵Hospital Universitario La Paz, Gastroenterology Unit, Madrid, Spain, ¹⁶Hospital Universitario y Politécnico La Fe and CIBEREHD, Gastroenterology Unit, Valencia, Spain, ¹⁷Hospital Universitario Puerta de Hierro Majadahonda, Gastroenterology Unit, Madrid, Spain, ¹⁸Hospital Universitario de Fuenlabrada e Instituto de Investigación Hospital Universitario La Paz (IdiPAZ), Gastroenterology Unit, Madrid, Spain, ¹⁹Hospital Universitario Fundación Alcorcón, Gastroenterology Unit, Madrid, Spain, ²⁰Hospital Universitario Juan Ramón Jiménez, Gastroenterology Unit, Huelva, Spain, ²¹Hospital Universitario de Burgos, Gastroenterology Unit, Burgos, Spain, ²²Hospital General Universitario de Valencia, Gastroenterology Unit, Valencia, Spain, ²³Hospital Universitario Joan XXIII, Gastroenterology Unit,

Tarragona, Spain, ²⁴Hospital Clínico Universitario San Cecilio, Gastroenterology Unit, Granada, Spain, ²⁵Complejo Hospitalario Universitario de Ourense, Gastroenterology Unit, Ourense, Spain, ²⁶Hospital Universitario 12 de Octubre, Gastroenterology Unit, Madrid, Spain, ²⁷Hospital Universitario de Galdakao, Instituto de Investigación Sanitaria Biocruces Bizkaia, Gastroenterology Unit, Galdakao, Spain, ²⁸Hospital Universitario Son Espases, Gastroenterology Unit, Mallorca, Spain, ²⁹Hospital Universitario Virgen de La Victoria, Gastroenterology Unit, Málaga, Spain, ³⁰Hospital General Universitario de Ciudad Real, Gastroenterology Unit, Ciudad Real, Spain, ³¹Complejo Hospitalario Universitario de Ferrol, Gastroenterology Unit, Ferrol, Spain, ³²Hospital Universitario Nuestra Señora de Candelaria, Gastroenterology Unit, Tenerife, Spain, ³³Hospital Universitario de Cabueñes, Gastroenterology Unit, Gijón, Spain, ³⁴Hospital Universitario Miguel Servet, Gastroenterology Unit, Zaragoza, Spain, ³⁵Instituto Biodonostia, Universidad del País Vasco (UPV/EHU) and CIBEREHD, Gastroenterology Unit, San Sebastián, Spain, ³⁶Hospital Universitario de Araba, Gastroenterology Unit, Vitoria, Spain, ³⁷Hospital Vall d'Hebrón, Gastroenterology Unit, Barcelona, Spain, ³⁸Hospital Universitario de Canarias, Gastroenterology Unit, Santa Cruz de Tenerife, Spain, ³⁹Hospital General Universitario de Castellón, Gastroenterology Unit, Castellon, Spain, ⁴⁰Hospital Universitario de Torrejón, Universidad Francisco de Vitoria, Gastroenterology Unit, Madrid, Spain, ⁴¹Hospital Universitari Dr Josep Trueta, Gastroenterology Unit, Girona, Spain

Contact E-Mail Address: mariachs2005@gmail.com

Introduction: Biological drugs used for inflammatory bowel disease (IBD) are detected in breast milk at a concentration below 10% of the maternal serum concentration and have therefore been considered as permitted drugs. However, warnings have recently been published regarding vaccination with live agents in children whose mothers receive infliximab during lactation.

Aims & Methods: To assess the risk of serious adverse events related to the administration of live vaccines in children exposed to biological drugs *in utero* and/or whose mothers were receiving biological agents during lactation.

Children born to IBD mothers from DUMBO registry were included. DUMBO is a prospective, observational and multicentre registry, which enrolls pregnant women with IBD over 5 years in 70 centres in Spain¹.

Data on treatment during gestation, type of lactation, breastfeeding, end-date of breastfeeding, maternal treatments during breastfeeding, and serious adverse events in children from birth are being prospectively included contacting with the mothers every-3-months.

Following the Spanish immunization calendar, rotavirus vaccine is (voluntarily) administered at 2, 4 and 6 months (3rd dose only with Rotateq¹); measles, mumps and rubella (MMR) at 12 months and 3-4 years of age; and varicella at 15 months and 3-4 years of age.

Results: 526 newborns were included (51% female). 56% of the mothers had Crohn's disease. 10% of the children were premature, and 10% had low birth weight. 29% were born by C-section. 198 children (38%) had been exposed to biologics during pregnancy (28% to anti-TNF, 2% to vedolizumab, and 8% to ustekinumab).

Of the children exposed to biologics, 88% were exposed during the 2nd trimester, and 73% during the 3rd trimester. The median follow-up of children from birth (still ongoing) was 12 months at the time of data analysis (IQR=6-18 months).

The percentage of children who had been vaccinated according to the recommended schedule was above 95% at all visits up to 24 months of follow-up. Of the children who had been exposed *in utero* to biologics during the 3rd trimester of gestation, 65 (47%) had already received the 1st dose

of rotavirus, 61 (44%) the 2nd dose, and 19 (14%) the 3rd dose; 63 (45%) the first dose of MMR; and 42 (30%) the 1st dose of varicella vaccine. No serious adverse event was observed in children associated with the administration of these vaccines. From birth, 73% of infants were breastfed (55% exclusively breastfed). The percentage of breastfed children was 49% at 6 months, 33% at 12 months, 28% at 18 months, and 18% at 24 months. During breastfeeding, 23% of the mothers were under biological therapy: 17% anti-TNF agents, 4% ustekinumab, and 2% vedolizumab. From children breastfed at least until month 6 and whose mothers were under biologics, 40 (60%) received the 1st and 2nd dose of rotavirus vaccine, and 11 (17%) the 3rd dose.

From children breastfed at least until month 12 and whose mothers were under biologics, 35 (97%) received the 1st dose of MMR vaccine; and from children breastfed at least until month 15 and whose mothers were under biologics, 21 (84%) received the 1st dose of varicella vaccine. No serious adverse event related to live vaccine was reported in our cohort.

Conclusion: Administration of live virus vaccines from 12 months of age in children born to IBD mothers and exposed to biological drugs *in utero* and/or during breastfeeding seems safe and should not be recommended against vaccination or breastfeeding. Rotavirus vaccine (under 6 months of age) appears to be equally safe in these children.

References: ¹Chaparro M, et al. The safety of drugs for inflammatory bowel disease during pregnancy and breastfeeding: the DUMBO registry study protocol of GETECCU. *Therap Adv Gastroenterol*. 2021

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P0448

THE CONTRIBUTION OF THE POLYMORPHISM OF THE ABCB1 GENE IN RESPONSE TO TREATMENT IN TUNISIAN INFLAMMATORY BOWEL DISEASE PATIENTS

F. Zine El Abidine¹, N. Elleuch¹, H. Ouaja², A. Omezzine², W. Dahmani¹, W. Ben Ameur¹, R. Hassine², A. Moussa², H. Jaziri¹, A. Ben Slama¹, M. Ksiaa¹, A. Brahemi¹, S. Ajmi¹, A. Hammami¹, A. Jmaa¹, A. Bouslama²

¹Sahloul Hospital, Gastro-Enterology, Sousse, Tunisia, ²Sahloul Hospital, Biochemistry Department, Sousse, Tunisia

Contact E-Mail Address: fatma.zinelabidine@gmail.com

Introduction: Corticosteroids (CS) are the most commonly prescribed first-line drugs, for the induction of remission in moderate to severe Crohn's disease (CD) or Ulcerative Colitis (UC) relapse. However, CS dependency and refractoriness are a significant clinical problem associated with numerous side effects.

Despite intensive research, CS still generate a challenge for personalized medicine by causing resistance or dependence in a significant proportion of patients. Identification of molecular markers of CS response is of paramount importance. The ABCB1 gene codes for P-glycoprotein, a transporter involved in the metabolism of CS.

Aims & Methods: The aim of this study is to investigate the contribution of polymorphisms of the ABCB1 gene to response to CS therapy in IBD patients.

Ninety-five patients with moderate to severe CD or UC who had been treated with a first course of corticosteroid therapy with a minimum follow up of 3 months, between January 2005 and December 2020 were retrospectively reviewed at Sahloul Hospital of Sousse in Tunisia and were genotyped. DNA was extracted from blood samples. Three of the most frequent Single nucleotide polymorphisms (SNP) of the ABCB1 gene were genotyped: C1236T, G2677T/A, and C3435T.

Patients were evaluated and classified as dependent, resistant, or responsive to CS therapy. Resistant or dependent patients were classified as non-responders.

The relation between CS therapy response and the genetic polymorphisms considered was examined using univariate and multivariate analysis.

Results: Fifty-nine CD (62.1%) and 36 UC (37.9%) were enrolled in our study. The mean age was 38.7 +/- 12.7 years with extremes [18-81]. At 3 months, 58 patients (61.1%) were classified as responder to CS therapy and 37 patients (38.9%) were classified as non-responders to CS therapy including 25 CS refractoriness (26.3%) and 12 CS dependency (12.6%). CT and TT genotypes of the C1236T polymorphism of the ABCB1 gene were associated with a non-response to corticosteroid therapy (64.9% vs 43.1%, p=0.038) in univariate analysis. The C1236T polymorphism was also associated with risk of CS resistance (68% vs. 41.3%, p= 0.037). No polymorphism was associated with risk of CS dependence (p=0.335).

In multivariate analysis, the C1236T polymorphism of the ABCB1 gene was associated with a risk of non-response to CS therapy (OR= 2.518 95% CI [1.100-6.328]; p=0.04) and with a risk of refractoriness to CS therapy (OR= 2.99; IC95% [1,164-8,423] ; p=0,038).

Conclusion: Our study showed that the polymorphism C1236T of the ABCB1 gene was associated with a risk of non-response to CS therapy and CS refractoriness.

A genetic study of the polymorphisms of other genes involved in the pharmacogenetics of CS would allow individualization of treatment and optimization of management by proposing an algorithm for predicting IBD patients at risk of non-response to CS.

Disclosure: Nothing to disclose

P0449

SAFETY AND EFFICACY OF AUTOLOGOUS HEMATOPOIETIC STEM CELL TRANSPLANTATION FOR REFRACTORY CROHN'S DISEASE AFTER CYCLOPHOSPHAMIDE-FREE MOBILIZATION: PRELIMINARY RESULTS

A. Giordano¹, M. Rovira², R. Barastegui¹, P. Marín², N. Martínez², F. Fernández-Avilés², M. Suárez-Lledó², A. Doménech², I. Ordás^{1,3}, A. Fernández-Clotet^{1,3}, B. Caballol Oliva^{1,3}, M. Gallego^{1,3}, A. Vara¹, M.C. Masamunt^{1,3}, A. Giner¹, A.M. Corraliza³, J. Panés^{1,3}, A. Salas³, E. Ricart^{1,3}

¹Hospital Clínic de Barcelona, Gastroenterology Department - Inflammatory Bowel Disease Unit, Barcelona, Spain, ²Hospital Clínic de Barcelona. ICMHO. IDIBAPS. Institut Josep Carreras, BMT Unit, Hematology Department, Barcelona, Spain, ³Institut d'Investigacions Biomèdiques August Pi i Sunyer, Barcelona. CIBER-EHD, Barcelona, Spain

Contact E-Mail Address: dr.antoniogiordano@gmail.com

Introduction: Autologous hematopoietic stem cell transplantation [AH-SCT] is a therapeutic option for patients with refractory Crohn's disease [CD]. Although the safety of the procedure has been improved over the last decade, AH-SCT is still burdened by high adverse event rate due to chemotherapy toxicity and immunosuppression.

Aims & Methods: The aim of this study was to evaluate the safety and efficacy of AH-SCT by using a cyclophosphamide (Cy)-free mobilization regimen followed by a standard conditioning approach.

A prospective observational study was conducted at Hospital Clínic of Barcelona in refractory CD patients undergoing AHSCT. Outpatient regimen with G-CSF 12-16 µg/kg/daily for 5 days was used for mobilization. Patients who failed to achieve >2x10⁶ CD34⁺ cells received Plerixafor 240 µg/d (1-2 doses). For conditioning, Cy and ATG were administered according to standard protocols. After transplant, patients were followed-up at regular intervals. Colonoscopy and/or magnetic resonance imaging were performed at baseline and at weeks 26, 52, 104 after AHSCT. Crohn's Disease Activity Index (CDAI) and SES-CD were used for clinical and endoscopic disease assessment.

Results: From June 2017 to April 2022, 14 refractory CD patients were enrolled (9F, median age 40 yr, median CDAI 204, median SES-CD 13); all of them achieved successful mobilization (median collected CD34⁺ cells 7.7x10⁶±2.8) and were transplanted. Patients were followed-up during a median of 106 months [range 0-236 months]. No SAEs or CD worsening were observed during mobilization. The proportion of patients in clinical remission (CDAI<150) was 71% at 6 months, 50% at 1 yr and 60% at 2 yr. Median SES-CD was 6 at 6 months and 9 at 1 yr. The proportion of patients who restarted CD therapy for clinical relapse and/or endoscopic/radiological activity was 14% at 6 months, 30% at 1 yr and 40% at 2 yrs. AEs and SAEs during and after conditioning were comparable to previous series, being neutropenic fever the most frequently observed (54%). Colectomy due to refractory severe relapse was needed in one patient at 70 weeks from transplant.

Conclusion: Cy-freemobilization is feasible and safe in refractory CD patients undergoing AHSCT but early relapse is observed in a significant proportion of patients. While representing an improvement on safety, studies exploring early reintroduction of drugs to decrease relapse rate after transplant are warranted.

Disclosure: Nothing to disclose.

P0450

SWITCHING FROM AN INTENSIFIED REGIMEN OF INFLIXIMAB TO A SUBCUTANEOUS STANDARD DOSE IN ADULTS WITH INFLAMMATORY BOWEL DISEASE: OUR EXPERIENCE IN A TERTIARY HOSPITAL

I. Chivato Martín Falquina¹, B. Vicente González², L. Arias García³, N. Revilla Cuesta², R.M. Saiz Chumillas⁴, B. Sicilia Aladrén⁵

¹Hospital Universitario Burgos, Gastroenterology, Burgos, Spain,

²Hospital Universitario de Burgos, Hospital Pharmacy, Burgos,

Spain, ³Hospital Universitario de Burgos, Inflammatory Bowel

Disease Unit, Burgos, Spain, ⁴Hospital Universitario de Burgos,

Gastroenterology, Burgos, Spain, ⁵H Universitario de Burgos,

Inflammatory Bowel Disease Unit, Burgos, Spain

Contact E-Mail Address: bsicilia4@gmail.com

Introduction: Intravenous (IV) infliximab is a first line treatment for moderate or severe flare of inflammatory bowel disease. Recently a new formulation of infliximab with subcutaneous (SC) administration has been developed and approved for this indication.

Aims & Methods: From March 2021, 14 patients diagnosed with inflammatory bowel disease (Crohn's disease-CD- or ulcerative colitis-UC), in clinical remission for at least 6 months with IV infliximab who had needed previous intensification, either because of a reactive therapeutic drug monitoring and loss of response, or because of a proactive drug monitoring (trough levels <3µg/ml), were switched to SC infliximab.

We analyzed retrospectively from the start of SC infliximab until week 8 and 24 after switch, fecal calprotectin levels (FC), C reactive protein (CRP), concomitant treatment, trough levels, treatment adherence, need for intensification or relapse, and adverse events.

Results: Four patients (28.57%) were diagnosed with CD, ten (71.4%) were diagnosed with UC. Patient's baseline characteristics are described in table. Median duration of IV treatment was 53 months (IQR 33-59). Reasons for starting infliximab were corticoid dependence in 6 patients (42,8%), corticorefractoriness in 6 (42,8%) and topdown strategy in B3 phenotype with Crohn's disease in 2 (14,3%). Reasons for intensification were: loss of response in 5 patients (35,7%), intensified induction in one (7,1%), proactive therapeutic drug monitoring in 8 (57,14%).

Eleven patients (78.57%) were still in an intensified regimen when switched. All patients were in clinical and biochemical remission (FC<150 µg/g and CRP<5 mg/dl) before switch. Twelve patients (86%) were in clinical and biochemical remission with standard infliximab doses, without any differences between CRP and FC levels in week 8 nor 24. 2 patients relapsed. Three patients of the 9 who were in combo therapy (33%) could withdraw immunosuppressors. Median basal infliximab trough levels before switch were **6.98µg/ml** (0.20; 20.10); median trough levels in week 8 after switch were **14.12** (9.86; 37.88) (**p=0.003**); median trough levels in week 24 were **10.49** (1.31; 24.12) (**p>0.05**). There were no adverse events.

Baseline characteristics	N=14
Age (years), median (IQR)	49,5 (38-64)
Weight (kg), median (IQR)	70 (61-80)
Sex (male), n (%)	99,5 (53-262)
Concomitant treatments, n (%)	13 (92,8%)
Corticoids, n(%)	0 (0%)
Topical salicylates, n (%)	10 (71,42%)
Immunomodulators, n (%)	9 (64,28%)
Duration in clinical remission (months), median (IQR)	48 (23-58)
Current intensification when switched, n (%)	11 (78,57%)

Conclusion: In our centre, switching from IV to standard dose SC infliximab maintained clinical and biochemical remission in most patients that previously needed intensified regimen, improving trough levels, without any adverse events, being able to withdraw immunosuppression in 33% of them. These findings provide potential therapeutic insights into SC infliximab as a monotherapy agent for inflammatory bowel disease.

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Disclosure: Nothing to disclose.

P0451

EFFICACY AND SAFETY OF USTEKINUMAB IN ASIAN PATIENTS WITH MODERATELY TO SEVERELY ACTIVE CROHN'S DISEASE: A SUBPOPULATION ANALYSIS OF UNITI/IM-UNITI LONG-TERM EXTENSION THROUGH 5 YEARS

T. Hibi¹, B. Duk Ye², C. Gasink³, Y. Imai⁴, C. Saadoun⁵, J. Zhuo⁶, S. Kawamura⁵

¹*Kitasato University, Kitasato Institute Hospital, Center for Advanced IBD Research and Treatment, Tokyo, Japan*, ²*Asan Medical Center, University of Ulsan College of Medicine, Department of Gastroenterology, Inflammatory Bowel Disease Center, Seoul, Korea (Republic of)*, ³*Janssen Scientific Affairs, LLC, Horsham, United States*, ⁴*Janssen Pharmaceutical K.K., Tokyo, Japan*, ⁵*Janssen Pharmaceuticals Asia Pacific, Singapore, Singapore*, ⁶*Janssen China Research & Development, Shanghai, China*

Contact E-Mail Address: thibi@insti.kitasato-u.ac.jp

Introduction: Ustekinumab (UST) is approved for treatment of moderately to severely active Crohn's disease (CD) in many countries, including Asia. However, the long-term efficacy and safety in Asian populations still remain unclear.

This analysis aimed to assess the efficacy and safety of UST in the Asian UNITI/IM-UNITI subpopulation through 5 years of UST treatment in the long-term extension (LTE).

Aims & Methods: UNITI/IM-UNITI, a Phase 3, randomized, double-blind, placebo-controlled trial consisting of two 8-week induction studies and a 44-week re-randomized withdrawal maintenance study followed by a 4-year LTE, evaluated UST in patients with moderately to severely active CD.

This study analyzed 63 Asian patients who entered the LTE at Week 44 and were followed up to 5 years (Week 252). The patients on the placebo arm were discontinued when the Week 44 data were unblinded.

Clinical remission (defined as CD Activity Index [CDAI] score <150) and clinical response (defined as a reduction in CDAI score ≥100) were assessed for long-term efficacy. All adverse events (AEs) were summarized for long-term safety.

Results: A total of 63 Asian patients (mean age at induction baseline, 34 years; males, 76.2%) entered the LTE and were treated with either subcutaneous (SC) placebo (8 [12.7%]), UST 90 mg SC every 12 weeks (22 [34.9%]), or UST 90 mg SC every 8 weeks (33 [52.4%]) from maintenance Week 0 through Week 252. Of the 55 patients who were treated with UST, 33 (60.0%) were in clinical remission and 45 (81.8%) were in clinical response at Week 44 in the combined UST group (Table 1).

At Week 252, 18 (32.7%) were in clinical remission and 25 (45.5%) were in clinical response in the combined UST group (Table 1). All patients who were in clinical remission were corticosteroid-free at Week 252, except for 1 patient in the UST 90 mg SC every 8 weeks group (Table 1).

The average duration of follow-up from Week 0 through the final safety visit was 208.4 weeks and 90.9 weeks in the combined UST and placebo groups, respectively.

Among the 55 patients in the combined UST group, safety events (per hundred patient-years) from maintenance Week 0 through the final safety visit included: AEs, 267.2; serious AEs, 23.1; infections, 98.4; and serious infections, 4.5. Among the 8 patients in the placebo group, safety events (per hundred patient-years) from maintenance Week 0 through the final safety visit included: AEs, 278.9; serious AEs, 14.3; infections, 71.5; and serious infections, 0. A total of 8 patients (14.5%) discontinued UST due to AEs (all due to a worsening of CD). No deaths or malignancies were reported.

	Week 44 – UST 90 mg SC			Week 252 – UST 90 mg SC		
	q12w ^a (n=22)	q8w ^b (n=33)	Combined (n=55)	q12w ^a (n=22)	q8w ^b (n=33)	Combined (n=55)
Clinical remission ^{c,d}	54.5 (12/22)	63.6 (21/33)	60.0 (33/55)	31.8 (7/22)	33.3 (11/33)	32.7 (18/55)
Clinical remission and not receiving corticosteroids ^{c,d,e}	-	-	-	31.8 (7/22)	30.3 (10/33)	30.9 (17/55)
Clinical response ^{f,g}	86.4 (19/22)	78.8 (26/33)	81.8 (45/55)	54.5 (12/22)	39.4 (13/33)	45.5 (25/55)

Data are presented as % (n/N). Combined UST 90 mg data (n=55) include UST 90 mg SC q12w (n=22) and 90 mg SC q8w (n=33).

-, data not available; AE, adverse event; CD, Crohn's disease; CDAI, Crohn's Disease Activity Index; IV, intravenous; LTE, long-term extension; q8w, every 8 weeks; q12w, every 12 weeks; SC, subcutaneous; UST, ustekinumab.

^aPatients who were in clinical response to UST IV induction dosing who were randomized to receive UST 90 mg q12w SC treatment upon entry into maintenance and did not meet loss of response criteria from Week 8 through Week 32; and includes patients who were not in clinical response to placebo IV induction dosing, received UST 130 mg IV at Week 0, achieved clinical response at Week 8, and initiated UST 90 mg q12w SC.

^bPatients who were in clinical response to UST IV induction dosing and were randomized to receive UST 90 mg q8w SC treatment upon entry into maintenance; patients who were randomized upon entry into maintenance and did meet loss of response criteria from Week 8 through Week 32 and received UST 90 mg q8w SC thereafter; and includes patients who were not in clinical response to UST IV induction dosing, received UST 90 mg SC at Week 0, achieved clinical response at Week 8, and initiated UST 90 mg q8w SC.

^cPatients who had a prohibited CD-related surgery or discontinued study drug due to lack of efficacy or due to an AE indicated to be of worsening CD prior to the designated analysis timepoint are considered not to be in clinical remission, regardless of their CDAI score.

^dPatients who had insufficient data at the designated analysis timepoint are considered not to be in clinical remission.

^ePatients who had a missing value in corticosteroids use at the designated analysis timepoint had their last value carried forward.

^fPatients who had a prohibited CD-related surgery or discontinued study drug due to lack of efficacy or due to an AE indicated to be of worsening CD prior to the designated analysis timepoint are considered not to be in clinical response, regardless of their CDAI score.

^gPatients who had insufficient data at the designated analysis timepoint are considered not to be in clinical response.

Table 1. Clinical efficacy in all Asian patients who entered the LTE.

Conclusion: Long-term efficacy and safety of UST in an Asian subpopulation with moderately to severely active CD were confirmed in this study. Clinical remission and clinical response were maintained without any new safety findings through 5 years. Overall, the safety and efficacy profiles of UST in an Asian subpopulation are consistent with the overall study population previously reported.

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P0452

OPTIMIZING DUAL-TARGETED THERAPIES IN INFLAMMATORY BOWEL DISEASE VIA MULTIPLE MECHANISMS OF ACTION

Z. Feng¹, X. Cao¹, H. Huang², G. Kang², J. Zhao¹, X. Wang¹, Y. Ye¹, L. Liu¹

¹Tianjin Medical University General Hospital, Department of Gastroenterology and Hepatology, Tianjin, China, ²Tianjin University, Department of Biochemical Engineering, School of Chemical Engineering and Technology, Key Laboratory of Systems Bioengineering, Ministry of Education, Tianjin, China

Contact E-Mail Address: fengzelina@163.com

Introduction: More and more studies have focused on dual-targeted therapy on refractory IBD or extraintestinal manifestations these days but till now data on the efficacy and safety of dual-targeted therapy on either Crohn's disease or ulcerative colitis is still exiguous. Moreover, studies on the mechanisms of dual-targeted therapy are rare.

Given that different drug molecules target various action sites in an inflammatory cytokine network in the immune microenvironment, dual-targeted therapy may be counted to reach a complementary strategy for IBD.

Aims & Methods: Through a search of multiple electronic databases by the end of April 15, 2022, emerging data on the safety, effectiveness and current clinical development status of novel targeted drugs on refractory IBD were summarized in this review.

By dividing the therapeutic agents into "Therapeutic Agents Targeting Cellular Signaling Pathways" and "Therapeutic Agents Targeting Leukocyte Trafficking" according to the different therapeutic targets in addition by classing therapeutic agents targeting cellular signaling pathways into "JAK-dependent" and "JAK-independent", the mechanisms of targeted therapy were explored and summarized. Furthermore, 32 studies related to dual-targeted therapy were included in this review, including 2 RCTs, which classified the existing dual-targeted treatments according to mechanisms.

Results: The combination of drugs targeting the JAK-dependent pathway with TNF- α and leukocyte trafficking with TNF- α achieved more clinical and endoscopy remission in patients. The former combination was relatively safe.

Furthermore, the latest RCT demonstrated that the combination with guselkumab and golimumab is more effective than either approach alone. However, it seems impossible from our data to give a clear recommendation on which combination should be used as the now available data are not comparable.

Conclusion: In conclusion, given its efficacy and safety, the combination of drugs targeting the JAK-dependent pathway and TNF- α seem especially attractive. According to in being understanding on the advantages, shortcomings and research prospects of different targeting combinations, the

possible mechanisms of dual-targeted therapies were deduced so as to conceive a theoretical framework for clinical decision-making and further drug development and research on IBD.

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P0453

BURDEN OF BOWEL URGENCY ACROSS SPECIFIC TREATMENT GROUPS AMONG CROHN'S DISEASE PATIENTS – REAL WORLD GLOBAL STUDY ANALYSES

R. Atreya¹, M. Protic², P. Streit³, S. Hartz⁴, H. Knight⁵, S. Barlow⁶, F. Hennessy⁶, T. Hunter Gible⁶

¹University Erlangen-Nuremberg, Medical Department 1, Erlangen, Germany, ²Eli Lilly & Company, IBU, Vernier, Genève, Switzerland, ³Eli Lilly and Company, Vernier, Switzerland, ⁴Eli Lilly and Company, Bracknell, United Kingdom, ⁵Adelphi Real World, Bollington, United Kingdom, ⁶Eli Lilly and Company, Indianapolis, United States

Contact E-Mail Address: raja.atreya@uk-erlangen.de

Introduction: Bowel urgency (BU) is a sudden and immediate need to have a bowel movement, a common symptom in Crohn's disease (CD) patients. The pathophysiology /mechanism of BU in CD is very complex. BU may persist despite treatment for CD and when disease is considered inactive^{1,2}.

This study explored differences in disease burden among CD patients with BU based on their treatment pathway.

Aims & Methods: Data were extracted from the Adelphi Disease Specific Programme for CD³, a point-in-time survey of gastroenterologists (GIs) and patients from Jan 2020-Mar 2021 in Germany, France, Spain, Italy, UK and US. GIs provided patient demographics, clinical characteristics and treatment history. The same patients were invited to complete the Short Inflammatory Bowel Disease Questionnaire (SIBDQ), EQ-5D and Work Productivity and Activity Impairment (WPAI) questionnaire. Three patient subgroups were identified: never received targeted therapy (biologics and JAK inhibitors) (TT-naïve), receiving first TT currently (1L TT) and receiving TT with prior TT use (TT-exp). Within these groups, patients currently experiencing BU, reported by physicians, with current treatment duration >3 months, were included. ANOVA, chi-square and/or Kruskal-Wallis tests were used to compare across groups.

Results: Of the CD patients in the TT-naïve (n=643), 1L TT (n=994) and TT-exp (n=404) groups, 17%, 13% and 15% experienced BU, respectively (Table). 9% of the TT-naïve group were flaring vs. 15% 1L TT and 29% TT-exp patients (p=0.0024). Steroid use was higher in the TT-naïve group (45%) vs. 15% 1L TT and 12% TT-exp (p<0.0001). The patient reported outcome measures indicated substantial and similar quality of life impairment across all patients with BU (Table).

Conclusion: This study confirmed that a substantial proportion of patients with CD across all three groups still experience BU despite receiving treatment. Since BU is known to negatively impact patients' quality of life, there is a therapeutic need to address this symptom.

	TT-naïve N=110	1L TT N=126	TT-exp N=60	p-value
Age, mean (SD)	37.8 (13.1)	40.0 (13.0)	44.7 (14.1)	0.0059*
Sex, male, n (%)	62 (56.4)	59 (46.8)	30 (50.0)	0.3381
BMI, mean (SD)	23.4 (2.9)	24.0 (3.9)	23.9 (3.5)	0.2910
Smoking status	N=103	N=117	N=59	0.5772
Current smoker, n (%)	28 (27.2)	22 (18.8)	14 (23.7)	
Ex-smoker, n (%)	30 (29.1)	44 (37.6)	20 (33.9)	
Never smoked, n (%)	45 (43.7)	51 (43.6)	25 (42.4)	
Flare status: Currently flaring, n (%)	N=103 9 (8.7)	N=115 17 (14.8)	N=58 17 (29.3)	0.0024*
Current treatment: Steroids, n (%)	N=110 50 (45.4)	N=126 19 (15.1)	N=60 7 (11.7)	<0.0001*
SIBDQ ¹ : Total score, mean (SD)	N=53 49.0 (8.5)	N=37 47.9 (14.7)	N=30 45.4 (11.9)	0.3873
EQ-5D: VAS ² , mean (SD)	N=55 76.3 (13.6)	N=39 71.6 (21.0)	N=30 71.8 (13.6)	0.2893
WPAI				
Activity impairment, mean % (SD)	N=53 27.2 (16.2)	N=38 31.1 (27.0)	N=27 29.3 (20.0)	0.6839
Absenteeism ³ , mean % (SD)	N=29 1.1 (4.1)	N=19 11.7 (31.4)	N=17 3.9 (6.7)	0.1247
Presenteeism ³ , mean % (SD)	N=38 24.5 (15.0)	N=21 19.0 (14.1)	N=18 25.0 (14.7)	0.3332
Overall work impairment ³ , mean % (SD)	N=29 26.4 (17.5)	N=17 22.0 (15.6)	N=17 27.9 (16.2)	0.5582

SD – standard deviation; BMI – body mass index; SIBDQ – Short Inflammatory Bowel Disease Questionnaire; VAS – Visual analogue scale; WPAI – Work Productivity and Activity Impairment
¹Scores range from 10 – 70, with higher scores indicating better health related quality of life
²Scores range from 0 – 100, with higher scores indicating better health related quality of life
³Includes working patients only with known data
*statistical significance of $\alpha = 0.05$

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P0454

CHANGES IN QUALITY OF LIFE IN IBD PATIENTS DURING VEDOLIZUMAB THERAPY- RESULTS FROM THE PATIENT SUPPORT PROGRAM IN THREE REFERRAL CENTERS IN SERBIA

A. Sokic Milutinovic^{1,2}, T. Jovicic², O. Latinovic Bosnjak³, S. Markovic^{4,2}, T. Jovicic³, T. Knezevic Ivanovski⁴, I. Jovicic¹

¹University Clinical Center Serbia, Clinic for Gastroenterology and Hepatology, Belgrade, Serbia, ²University of Belgrade - Faculty of Medicine, Belgrade, Serbia, ³Clinical center of Vojvodina, Clinic for Gastroenterology and Hepatology, Novi Sad, Serbia, ⁴University Hospital Zvezdara, Department of Gastroenterology and Hepatology, Belgrade, Serbia

Contact E-Mail Address: asokicmilutinovic@gmail.com

Introduction: Patients with inflammatory bowel disease (IBD) often report impaired quality of life (QoL). Decrease in QoL is seen both in ulcerative colitis (UC) and Crohn disease (CD) patients. Biologic therapy induces remission in a significant number of IBD patients and has been repeatedly associated with improvement of QoL.

Aims & Methods: We conducted an observational study in three referral IBD centers in Serbia. We aimed to assess patients' perception of the effects of vedolizumab (VDZ) therapy on specific symptoms (fatigue, urgency, abdominal pain, weight loss), social interactions and overall QoL, but also to identify reasons for therapy discontinuation in the first 12 months of VDZ therapy.

We included 296 patients (153 males, mean age 50±12) in the study. UC was diagnosed in 184, while remaining 112 had CD. Patients filled a standardized questionnaire at the 1st dose, after 6 and after 12 months of therapy, and answers were given for a 14 day period. Occurrence of symptoms, possibility of interacting socially as planned and QoL were assessed using the 5 grade Likert scale. Patients were offered patient support program (PSP), in which an IBD nurse and an IBD specialist were available twice a week for phone consultations.

Results: Our results revealed that patients were diagnosed with IBD 12.5±9.5 years before starting VDZ therapy. In 153 patients VDZ was introduced as 1st line therapy (40 CD, 113 UC), in 86 as 2nd line (38CD, 48UC), while in 57 patients VDZ was 3rd or 4th line of biologic therapy (34CD, 23UC). After 6 months of therapy in CD patients, QoL was improved (p=0.006) and urgencies were significantly less frequent (p=0.004). In UC patients, a significant decrease in frequency of abdominal pain (p=0.04), urgency (p=0.000) and fatigue (p=0.004) were reported together with increased possibility of participating in social interactions (p=0.008) and a significant increase in QoL (p=0.004).

No significant difference was observed for any of the parameters analyzed between 6 and 12 months of VDZ therapy. After 6 months of VDZ therapy and participation in patient support program, both CD and UC patients reported significant improvement in terms of communication and support from family members (p=0.006 for CD and p=0.021 for UC).

In 27 (9.1%) patients therapy was stopped during the first year, 21 (7%) had loss of response, and 6 moved. Out of 21 patient with loss of response, VDZ was 1st line in 12 and 2nd line therapy in 5 patients.

Conclusion: In patients on biologic therapy with VDZ, both UC and CD, self-perceived QoL as significantly improved after 6 months of therapy. Patients with UC reported significant reduction in frequency of abdominal pain, urgency and fatigue.

On the other hand, patients with CD did not report significant decrease in frequency of symptoms apart from urgencies. We feel that participation in PSP resulted in increased support for IBD patients from family members. PSP could be a valuable tool for empowering IBD patients.

References: In patients on biologic therapy with VDZ, both UC and CD, self-perceived QoL as significantly improved after 6 months of therapy. Patients with UC reported significant reduction in frequency of abdominal pain, urgency and fatigue.

On the other hand, patients with CD did not report significant decrease in frequency of symptoms apart from urgencies. We feel that participation in PSP resulted in increased support for IBD patients from family members. PSP could be a valuable tool for empowering IBD patients.

Disclosure: Nothing to disclose.

P0455

OUTCOMES OF ANTI-TNF TREATMENT IN CROHN'S DISEASE: A REAL LIFE, TERTIARY CENTER EXPERIENCE

I. Ergenc¹, H.T. Kani², Ç. Keklikkiran², Y. Izgi³, H. Salva³, S. Saydam³, S.B. Karakaya⁴, Y. Özen Alahdab², O. Atug²

¹Marmara University, Gastroenterology, Istanbul, Turkey, ²Marmara University, School of Medicine, Gastroenterology, Istanbul, Turkey, ³Marmara University, School of Medicine, Internal Medicine, Istanbul, Turkey, ⁴Marmara University, School of Medicine, Istanbul, Turkey

Contact E-Mail Address: ergencilkay@gmail.com

Introduction: Anti-TNF agents are widely using to both remission induction and maintaining for mild to severe intestinal and extra-intestinal involvements. The effectiveness and safety of these agents were evaluated frequently in clinical trials. Real life experience provides additional information about the treatment in the context of the daily patient care.

Aims & Methods: The aim of this study was to assess the treatment choices, short and long term response, treatment duration and the safety of anti-TNF agents in patients with CD. IBD diagnosis established with clinical, biochemical, endoscopic, and histologic findings.

We enrolled the patients retrospectively who were following up at our IBD specific gastroenterology out-patient clinic between October 2006 and April 2019. Patients who completed induction doses of at least one anti-TNF treatment included to the study. We collected demographic and clinical data from the electronic hospital database and hardcopy patient files.

Primary outcomes of this study are short term and long-term efficacy. Secondary outcomes are the safety of treatments and indications of anti-TNF initiation.

Results: An of 870 CD patients were screened, 236 were exposed to anti-TNF and 200 patients were included for the final analysis. Median follow-up period under anti-TNF treatment was 55 months (range: 4 - 168).

A total of 133 patients were received infliximab, 97 were received adalimumab and 11 were received certolizumab as first-, second- or third-line treatment. Six patients (4.2%) were primary unresponsive (PU) and 15 (10.6%) patients were secondary unresponsive (SU) to infliximab.

Three patients (2.8%) were PU and 14 patients (13.3%) were SU to adalimumab. Two (18%) patients were PU and 1 (9%) patient was SU to certolizumab. Complete response and partial response rates were respectively seen as 51.3% and 43.3% for infliximab users, 59.7% and 36,1% for adalimumab users, 36.4% and 45.5% for certolizumab users.

There was no difference seen between three agents in complete and partial response rates ($p=0.281$). Remaining on the same anti-TNF agent for infliximab and adalimumab at the end of the first year was 64.5 and 87.3% respectively.

Patients who were treated with adalimumab was seen to continue on same agent more common in 1st year when compared to infliximab ($p=0.000$). The most common indication of anti-TNF treatment was fistula formation (47.7%, $n=87$). Complete healing was seen in 20 (15.9 %) patients and partial healing was seen in 43 (34.1%) patients.

However, 63 (50.0%) patients had no response to anti-TNF treatment (Table 1). Perianal disease was seen in 103 (51.5%) patients. In patients with perianal disease, 5 (4.9%) had perianal abscess, 56 (54.4%) had perianal fistula and 42 (40.8%) had both abscess and fistula formation.

Severe allergic reaction was seen in 8 patients with infliximab and in 4 patients with adalimumab exposure. Treatment cessation due to serious adverse reactions was seen in 21 patients who exposed to infliximab and in 11 patients who exposed to adalimumab.

	Infliximab (n=43)	Adalimumab (n=29)	Certolizumab (n=4)
Complete closure	27.9% n=12	6.9% n=2	--
Partial closure	23.3% n=10	6.9% n=2	25% n=1
Improvement in fistula drainage	20.9% n=9	10.3% n=3	--
No response	27.9% n=12	72.4% n=21	75% n=3

Table 1. Fistula response according to anti-TNF agents.

Fisher's Exact Test; value:19,39 $p=0.004$

Conclusion: Two thirds of the patients had response to anti-TNF treatment, no significant difference was seen in between agents. Half of the patients has fistulising disease and fifty percent of them were non-responder.

Disclosure: Nothing to disclose.

P0456

CYTOMEGALOVIRUS INFECTION IN PATIENTS WITH ACTIVE ULCERATIVE COLITIS - A PROSPECTIVE OBSERVATIONAL STUDY

J. Szlak¹, A. Magdziak², A. Mroz³, P. Wieszczy¹, E.S. Zagorowicz¹

¹Maria Skłodowska-Curie National Research Institute of Oncology, Department of Oncological Gastroenterology, Warsaw, Poland,

²Maria Skłodowska-Curie National Research Institute of Oncology, Department of Microbiology, Warsaw, Poland, ³Maria Skłodowska-Curie National Research Institute of Oncology, Department of Pathology and Laboratory Medicine, Warsaw, Poland

Contact E-Mail Address: jakub.szlak@gmail.com

Introduction: The role of cytomegalovirus (CMV) infection and its influence on the course of ulcerative colitis (UC) has been evaluated mostly in retrospective studies with small groups of patients and different definitions of CMV infection.

Aims & Methods: We aimed to prospectively evaluate frequency of CMV infection in hospitalised patients with exacerbation of UC along with subsequent colectomy rate in patients with and without CMV. Frequency of hospitalizations, the need of treatment modification and quality of life were also compared in the two groups.

The study group comprised of consecutive patients admitted to Department of Oncological Gastroenterology between 2016 to 2019 with moderate or severe exacerbation of ulcerative colitis measured by endoscopic and full Mayo score. In every patient tissue samples from colon were subjected to immunohistochemistry (IHC) analysis. Patients were asked to fill in the Inflammatory Bowel Disease Questionnaire (IBDQ).

Follow-up involved out-patients visits, hospitalisations, analysis of available medical records and telephone contact with patients. Relationship between categorical variables was examined with the use of chi-square statistic test or Fisher's exact test depending on the size of subgroups.

Results: The final analysis involved 84 patients who fulfilled the inclusion criteria. The median follow-up in the group was 2,1 years (range 0.3-3.6 years). The CMV IHC result was positive in 16 (19%) cases. Severe endoscopic lesions on index colonoscopy - Mayo score 3 - were more frequent in the CMV IHC positive group as compared in the CMV IHC negative group (81.2% vs 51.5%; $p=0.048$) just as using corticosteroids before the admission (81,2% vs 54.4%; $p=0.015$).

Colectomy was performed in 20 patients (23.8%). There were no difference in colectomy rate between the groups with positive (25%) and negative (23.5%) CMV IHC result($p=1.0$).

Similarly, no significant difference was found in the frequency of hospitalizations and the perceived quality of life in IBDQ. The percentage of patients who subsequently started biological treatment was significantly higher in the CMV IHC negative group than in the group with positive results (58.8% vs 18.8%; $p=0.005$).

Conclusion: Colectomy rate in consecutive patients hospitalized because of UC exacerbation was similar in the group with CMV IHC positive and the group with CMV IHC negative results. Previous steroid treatment and severe colonic mucosal lesions on index endoscopy were more frequent in patients with CMV infection. Routine screening for CMV is not justifiable. Detection of CMV infection in high risk groups and its treatment may prevent escalation of anti-inflammatory treatment.

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P0457

LOW CONCENTRATION OF CITRATE IN AN ADALIMUMAB FORMULATION DOES NOT IMPACT THE INTENSITY OF INJECTION SITE PAIN: EVALUATION FOLLOWING A SINGLE DOSE OF GP2017, A LOW CONCENTRATION ADALIMUMAB BIOSIMILAR VERSUS HIGH CONCENTRATION ADALIMUMAB CITRATE-FREE FORMULATION IN HEALTHY VOLUNTEERS

J.C. Rondon¹, C. Fey², O. von Richter², J. Fan³, F. Furlan², L. Lemke²

¹Clinical Pharmacology of Miami, LLC, Miami, United States, ²Hexal AG (A Sandoz company), Holzkirchen, Germany, ³Sandoz Inc., Princeton Corporate, Princeton, United States

Contact E-Mail Address: fabrizio.furlan@sandoz.com

Introduction: Multiple factors such as formulation, injection process, injection devices and several patient-related factors contribute to injection site pain following subcutaneous (s.c.) administration of a medicine.¹ There are conflicting results regarding the local tolerance of adalimumab (ADL) formulations containing citrate buffer, thereby creating uncertainties among health care professionals as well as patients.^{1,2}

We compared the local tolerance of SDZ-ADL (GP2017), a low-concentration biosimilar ADL (50 mg/ml) with low citrate (1.2 mM), to a high-concentration (100 mg/ml) citrate-free ADL formulation (HC/CF-ADL) in healthy volunteers.

Apart from the difference in citrate concentrations and presence of saline in GP2017, both the study formulations were composed of the same compounds and were dispersed in identical devices (prefilled syringes).

Aims & Methods: A total of 330 subjects were treated in the study; 168 subjects received a single dose of 40 mg/0.8mL s.c. injection of GP2017 and 162 received a single dose of 40 mg/0.4 mL of HC/CF-ADL. The injection site pain (ISP) was evaluated by the subjects using a Visual Analogue Scale (VAS) of 0-100 mm (representing a range from no pain to unbearable pain) immediately after the injection and at 15- minutes and 4-hours post injection on Day 1. VAS scores between 0-4 mm were considered no pain and 5-44 mm as mild pain.³

Time point	Statistics	HC/CF-ADL N=162	SDZ-ADL N=168
Immediately after injection	Mean (SD)	5.2 (7.35)	7.6 (9.89)
	Median	3.0	4.0
	Min-Max	0-50	0-60
15 Minutes post-dose	Mean (SD)	2.8 (3.01)	3.3 (4.27)
	Median	2.0	2.0
	Min-Max	0-18	0-27
4 Hours post-dose	Mean (SD)	2.8 (3.03)	2.5 (2.48)
	Median	2.0	2.0
	Min-Max	0-15	0-13

The scale of pain at the injection site as assessed on the Visual Analogue Scale (0 mm-100 mm) is between 'no pain' and 'unbearable pain'.

HC/CF-ADL, high concentration/citrate free-adalimumab; N= total number of subjects treated; SD, standard deviation; SDZ-ADL, Sandoz adalimumab

Table 1. Injection Site Pain assessed using Visual analogue scale (0-100mm)

Results: The mean scores for both groups were lower than 10 mm at all time points. Immediately after the s.c. injection, the mean [SD] pain VAS score was comparable between study groups (SDZ-ADL group: 7.6 mm [9.89]; HC/CF-ADL group: 5.2 mm [7.35]). Similarly, at 15-minutes and 4-hours post dose, there was no clinically meaningful difference in the mean pain VAS score in both the study groups (Table 1).

Overall, the ISP was considered as mild immediately after injection. The low mean VAS scores at 15 minutes and 4-hours post injection do not suggest of any ISP.

Conclusion: The ISP was comparable following administration of SDZ-ADL or HC/CF-ADL, showing that there is no impact of a low concentration of citrate buffer on ISP.

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Oliver von Richter: Employee of Hexal AG

Jamie Fan: Employee of Sandoz Inc.,

Fabrizio Furlan: Employee of Hexal AG

Lena Lemke: Employee of Hexal AG

P0458

DIAGNOSTIC DELAY AND ECONOMIC BURDEN IN IBD: A SINGLE-CENTRE EXPERIENCE IN PATIENTS TREATED WITH BIOLOGICS

A. Todeschini¹, C. Angelini², R. Tessari², A. Ossato², G. Lunardi³, A. Geccherle¹, T. Zuppin², A. Variola¹

¹IRCCS Sacro Cuore Don Calabria, IBD UNIT, Negrar di Valpolicella, Italy, ²IRCCS Sacro Cuore Don Calabria, Hospital Pharmacy, Negrar di Valpolicella, Italy, ³IRCCS Sacro Cuore Don Calabria, Central Laboratory, Negrar di Valpolicella, Italy

Contact E-Mail Address: ale_tode@hotmail.com

Introduction: Inflammatory bowel diseases (IBDs), Crohn's disease (CD) and ulcerative colitis (UC), are chronic and immune-mediated diseases with a relapsing-remitting trend. The overall incidence of these diseases is increasing. However, it is estimated that more than one third of patients experienced symptoms for more than one year before diagnosis. Delay in IBD diagnosis has several clinical, therapeutic and economic implications. Early diagnosis and proper treatment are the cornerstones for improving the standard of care for these patients.

Aims & Methods: This study aims to evaluate the diagnostic delay in patients with IBD and to analyze the clinical and economic burden of the delay in IBD diagnosis in patients treated with biological drugs. An observational and retrospective study was performed in IBD patients, regularly followed in our IBD Unit. Data regarding delay in IBD diagnosis were assessed through a questionnaire evaluating the disease course. Moreover, data about biologics dispensation were obtained from the medical records in the period 2014-2020.

Results: 606 IBD patients were enrolled. The median delay in IBD diagnosis was 5.0 months (IQR:1.0 11.0); it was statistically lower in UC patients (4 months (IQR: 1.0 12.0)) compared to CD (6 months (IQR: 2.0 12.0)) (p =0.041). Of these 606, 229 patients were treated with biological therapy; in this subgroup 58.9% showed a diagnostic delay. The statistical analysis showed that the diagnostic delay was statistically significant associated with biological drugs (p=0.041).

Conversely, there was no association with surgical treatment. Moreover, it has appeared that the diagnostic delay is associated, with a trend of statistical significance, with need to switch or swap to other biologics (p=0.058).

Regarding economic burden, patients with delayed diagnosis have significantly higher median annual cost of biological therapy than patients without diagnostic delay (€7179.26 vs € 5131.51 $p=0.009$).

Conclusion: The diagnostic delay in IBD represents a challenge with clinical, therapeutic and economic impact.

It's crucial to cooperate with general practitioner and gastroenterologists not dedicated to IBD in order to reduce the diagnostic delay and guarantee an effective, appropriate and early treatment that will improve the patients' quality of life and meanwhile reduce the health care system costs.

Disclosure: Nothing to disclose.

P0459

COMPARATIVE OUTCOMES AND SAFETY OF BUDESONIDE-MMX VERSUS PREDNISOLONE FOR ULCERATIVE COLITIS AND POSSIBLE GENETICAL PREDICTORS OF SIDE-EFFECTS

T. Resál¹, K. Mangó², P. Bacsur³, K. Szántó³, Á. Milassin³, M. Rutka⁴, A. Balint³, S. Zoltán³, K. Farkas³, K. Monostory², T. Molnár⁵

¹University of Szeged, I. st Department of Internal Medicine, Szeged, Hungary, ²Eötvös Loránd University, Budapest, Hungary, ³University of Szeged, Department of Medicine, Szeged, Hungary, ⁴University of Szeged, Department of Internal Medicine, Szeged, Hungary, ⁵University of Szeged, Department of Internal Medicine, Szeged, Hungary

Contact E-Mail Address: resal.tamas@med.u-szeged.hu

Introduction: Budesonide-MMX is an orally administered topically active corticosteroid, with high first-pass metabolism through the cytochrome P450 isoenzymes CYP3A4 and CYP3A5, resulting in a favourable side effect profile. Nevertheless, a number of patients treated with budesonide-MMX faced with systemic steroid side effects. CYP3A5*3 and CYP3A4*22 genotypes result in decreased, while CYP3A5*1 and CYP3A4*1B genotypes result in increased expression.

As increased metabolism result in higher degradation of the budesonide-MMX, it may potentially cause lower efficacy. Budesonide-MMX homogeneously releases the active drug along the whole colon, resulting in wider range of usage in mild-to moderate UC.

Aims & Methods: We aimed to compare the safety profile of the budesonide-MMX with orally administered methylprednisolone focusing on endocrine, mineral, bone and lipid metabolism and change in body composition.

Our second goal was to assess difference in the efficacy of disease extents of UC, in addition, how the different CYP genotypes affect the efficacy and safety profile of the treatment.

This was an observational prospective cohort study conducted at our tertiary center. Inclusion criteria was mild to moderate IBD. Oral budesonide-MMX 9 mg was administered until 8 weeks, and oral methylprednisolone (tapered by 4 mg per week from a maximum dose of 1 mg/bwkg) over an 8-to 12-week period. Blood tests were obtained and body composition was measured at inclusion and after 8 weeks of the therapy.

Electrolytes, cholesterol, triglyceride, CRP, beta-crosslap, leukocyte and serum hormone levels (cortisol, dehydroepiandrosterone [DHEA], DHEA-sulfate, osteocalcin) were monitored to follow metabolic and hormonal changes. In addition, CYP450 (CYP3A5 and CYP3A4) enzyme genotypes were assessed in the budesonide group.

Results: In total, 58 IBD patients were included in our prospective cohort study, 19 patients (68.4% UC) received orally administered methylprednisolone and 39 UC patients budesonide-MMX. In total, 31.6% UC patients had pancolitis, and 50% of the CD patients had colonic disease. In both groups the clinical indices decreased following the treatment regimen ($p<0.05$). Budesonide-MMX is effective in all extents of UC ($p<0.05$). Follow-

ing the budesonide-MMX treatment, the cortisol ($p<0.001$), DHEA ($p<0.05$) and DHEAS ($p<0.001$) levels decreased, while cholesterol increased ($p<0.001$). No further significant difference was observed. DHEA was lower in the methylprednisolone group ($p<0.001$) compared to budesonide-MMX, while beta-crosslap ($p<0.05$), weight gain ($p<0.05$), and increase in BMI was higher ($p<0.05$).

In the budesonide-MMX group no adverse event was observed, while in the methylprednisolone group 3 patients (15.7 %) developed Cushingoid appearance. 3 patients have CYP3A5*1/*3 genotype, and 16 have CYP3A5*3/*3, and no significant difference was observed among them. Only 1 patient have CYP3A4*1B genotype, while the rest have CYP3A4*1, hence, no statistics could be performed.

Conclusion: Budesonide-MMX is an effective treatment in mild-to moderate UC, regardless of the extensions. In addition, as budesonide have systemic steroid effects, the administration of the drug should be with more precaution, even though it has been shown to be safer than methylprednisolone. Due to the small number of patients and genetic homogeneity, further data is required to assess the role of CYP genotypes.

Disclosure: Nothing to disclose.

P0460

EFFECTS OF AN ESTABLISHED SPECIALIST INFLAMMATORY BOWEL DISEASE NURSING SERVICE ON PATIENT OUTCOMES, QUALITY OF CARE AND HEALTHCARE COSTS

N. Yu¹, K. Wu¹, T. Samyue¹, S. Fry¹, A. Stanley¹, A. Ross¹, R. Malcolm¹, W. Connell^{1,2}, E. Wright^{1,2}, N.S. Ding^{1,2}, O. Niewiadomski¹, M. Lust¹, J. Schulberg^{1,2}, E. Flanagan^{1,2}, M.A. Kamm^{1,2}, C. Basnayake^{1,2}

¹St Vincent's Hospital Melbourne, Gastroenterology, Melbourne, Australia, ²The University of Melbourne, Medicine, Melbourne, Australia

Contact E-Mail Address: natalieyu24@gmail.com

Introduction: Inflammatory bowel diseases (IBD) are complex chronic gastrointestinal conditions that are best managed by a multidisciplinary team in a dedicated IBD service. Within this team, specialist IBD nurses play a critical role in supporting the delivery of high quality patient care. Despite this, few studies have examined the impact of an IBD nurse service on patient outcomes, particularly in the modern biologic era.

Aims & Methods: Our study aimed to evaluate the effects of our IBD nursing service on patient outcomes, quality of care and healthcare costs. We performed a retrospective audit of all IBD nurse encounters with patients, documented over a 12-month period from 1 October 2020 to 30 September 2021 at a tertiary referral centre. The IBD unit employs 3.2 full time equivalent specialist IBD nurses, including a nurse practitioner, who support a team of 13 IBD subspecialist gastroenterologists. Each IBD nurse encounter was classified in terms of the context in which it occurred, activity performed and outcome it led to.

All encounters were assigned to one context, but some encounters were assigned to multiple activities and outcomes. An economic analysis was performed to estimate cost savings to the health service.

Results: There were 2537 IBD nurse encounters (53% female, median age 38 years, 70% Crohn's disease, 77% on biologic drug therapy) with 682 patients (median 3 encounters each). 41% of encounters were IBD nurse-initiated contacts with patients, 34% were patient-initiated contacts with the IBD nurse helpline (26% via email, 8% via phone), 21% were therapeutic drug monitoring follow-up contacts with patients, 3% were gastroenterologist or doctor-initiated contacts with IBD nurses and 1% were patient contacts through the IBD nurse practitioner outpatient clinic. IBD nurse contacts most commonly involved clinical assessments (66%), providing

education, counselling or updates about the patient's disease, investigations or therapy (47%) and reviewing investigation results (38%). Many encounters involved biologics-related activities (30%), organising investigations (30%) and preventive care assessments (20%).

A gastroenterologist was consulted for advice in 35% of contacts. Interventions by the IBD nurses led to the avoidance of 29 emergency department (ED) visits, 1944 outpatient clinic (OPC) visits and 118 general practitioner (GP) visits, representing an estimated AUD \$956,441.32 saved.

After deducting costs of the IBD nurse service, a net estimated saving of AUD \$579,202.13 was achieved. IBD nurse contacts also led to four direct ward admissions, 30 ED visits advised, 86 OPC visits expedited and 374 GP visits advised. They facilitated faster access to investigations (29%), improved patient knowledge (28%), supervision of biologics (25%), medication changes (19%), preventive care recommendations (17%), flare or symptom management (13%) and faster access to allied clinicians (2%). Of the 318 patients who had a preventive care assessment, IBD nurses recommended pneumococcal vaccinations in 72%, skin cancer screening in 66%, bone density testing in 53% and flu vaccinations in 47%.

Conclusion: An IBD nurse service provides significant value in improving patient outcomes, quality of care, and reducing healthcare costs. This study supports the expanding role of IBD nurses in the modern biologic era and the need for greater funding and integration of IBD nurses into specialised IBD clinical services.

Disclosure: Nothing to disclose.

P0461

EFFECT OF MIRIKIZUMAB ON BOWEL URGENCY CLINICALLY MEANINGFUL IMPROVEMENT AND REMISSION: RESULTS FROM THE PHASE 3 LUCENT INDUCTION AND MAINTENANCE STUDIES

S. Travis¹, T. Hibi², T. Hisamatsu^{3,3}, D. Fisher⁴, M. Shan⁴, T. Hunter Gible⁴, D.T. Rubin⁵

¹University of Oxford, Gastroenterology Department, Oxford, United Kingdom, ²Kitasato Institute Hospital IBD Research and Treatment, Keio University, Tokyo, Japan, ³Kyorin University School of Medicine, Department of Gastroenterology and Hepatology, Tokyo, Japan, ⁴Eli Lilly and Company, Indianapolis, United States, ⁵University of Chicago Medicine, Chicago, United States

Contact E-Mail Address: Simon.Travis@ndm.ox.ac.uk

Introduction: Bowel urgency (BU; sudden or immediate need to have a bowel movement) is a common and burdensome symptom for patients with ulcerative colitis (UC)^{1,2}.

BU was assessed in mirikizumab (miri; an IL-23p19inhibitor) Phase 3 LUCENT studies in moderately to severely active UC (NCT03518086, NCT03524092) using the validated Urgency Numeric Rating Scale (UNRS). UNRS measures BU severity in the past 24 hours from 0 (no urgency) to 10 (worst possible urgency)².

Psychometric evaluation of the UNRS showed Clinically Meaningful Improvement (CMI) is ≥ 3 point change; Remission is a score of 0 or 1³. This analysis evaluated the proportions of patients in LUCENT studies achieving BU CMI and BU Remission.

Aims & Methods: The modified intent-to-treat (mITT) population (patients receiving ≥ 1 dose of miri or placebo (PBO); N= 1281) was randomized at induction study baseline in a 3:1 ratio to IV doses of 300mg miri or PBO every 4 weeks (Q4W) during induction (W0, 4, and 8).

Patients achieving Clinical Response, measured by Modified Mayo Score (MMS), to miri during induction were re-randomized at W0 of the maintenance study in a 2:1 ratio to subcutaneous (SC) 200mg miri or PBO Q4W through W40 (52 weeks of treatment). Patients recorded their UNRS score daily in an e-diary. Mean weekly UNRS scores were calculated from diary

data if ≥ 4 days of data were available. Rates of BU CMI and BU remission in the miri v PBO groups were compared at W12 (induction) in the mITT population with a baseline UNRS score ≥ 3 , and W52 (maintenance) among miri clinical responders at W12 with a baseline UNRS score ≥ 3 . Cochran-Mantel-Haenszel tests with non-responder imputation for missing values were used for all treatment comparisons.

Results: Patient population: mean age 43 years, 60% male, disease duration 7 years; 63.0% left-sided colitis; 36.3% pancolitis; 46.7% moderate disease (MMS 4-6); 53.2% severe disease (MMS 7-9). Significantly higher proportions of miri versus PBO patients achieved BU CMI (48.7% v 32.2%) and BU remission (22.1% v 12.3%) at W12 (both $p < 0.001$; Table) in the induction study. Similarly, at W40 of maintenance, significantly greater proportion of miri patients achieved BU CMI (65.2% v 41.9%) and BU remission (43.3% v 25.7%) compared to PBO among miri induction responders (both $p < 0.001$; Table).

	Induction (W12 Analysis)			Maintenance (W40 Analysis)		
	300mg miri IV N= 868	PBO IV N= 294	P-value	200mg miri SC N= 365	PBO SC N= 179	P-value
Baseline bowel urgency W0 UNRS Score (Mean $\pm$ SD)	6.1 $\pm$ 2.2	6.2 $\pm$ 2.2	-	6.0 $\pm$ 2.2	6.2 $\pm$ 1.9	-
UNRS change from baseline (LSM $\pm$ SE)	-2.6 $\pm$ 0.083 ^a	-1.63 $\pm$ 0.141 ^a	$p < 0.00001^a$	-3.8 $\pm$ 0.139	-2.7 $\pm$ 0.202	$p < 0.001^b$
Bowel urgency clinically meaningful improvement ^c (N [%])	395 [48.7%] ^e	89 [32.2%] ^e	$p < 0.001^a$	219 [65.2%] ^f	72 [41.9%] ^f	$p < 0.001^a$
Bowel Urgency Remission ^d (N [%])	179 [22.1%] ^e	34 [12.3%] ^e	$p < 0.001^a$	158 [43.3%] ^f	46 [25.7%] ^f	$p < 0.001^a$

^aResults previously disclosed at ECCO 2022; D'Haens et al. J Crohn's Colitis. 2022;16(Supplement 1): i028-i029.

^bTreatment comparison is from a mixed model for repeated measures model that contains treatment, baseline value, visit, interaction of baseline value by visit, interaction of treatment by visit, and stratification factors.

^cBowel urgency clinically meaningful improvement is defined as a reduction in the UNRS of ≥ 3 points.

^dBowel urgency remission is an UNRS score of '0' or '1'.

^eComparisons between miri and PBO at W12 are shown for patients with a baseline UNRS score ≥ 3 ; N=811 for 300mg miri and N= 276 for PBO.

^fComparisons between miri and PBO at W40 are shown for miri induction responders with a UNRS score ≥ 3 at baseline; N= 336 for 200mg miri and N=172 for PBO.

^gCochran-Mantel-Haenszel tests with non-responder imputation were used for treatment comparisons.

Abbreviations: miri=mirikizumab IV = intravenous; LSM = least squares mean; PBO = placebo; SC = subcutaneous; SD = standard deviation; UNRS = Urgency Numeric Rating Scale.

Table. Assessment Bowel Urgency Clinically Meaningful Improvement and Remission in Patients Treated with Mirikizumab v Placebo at Weeks 12 and 40.

Conclusion: Miri had a highly significant and clinically meaningful benefit on reducing bowel urgency, one of the most disruptive UC symptoms. The Urgency Numeric Rating Scale usefully quantified the baseline level and change in bowel urgency after treatment across a spectrum of severity.

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PERI-PARTUM INFECTIONS AMONG WOMEN WITH INFLAMMATORY BOWEL DISEASE

B. Narkis¹, E. Hadar¹, S. Barbash-Hazan¹, O. Houry¹, V. Shay², J. Ollech², H. Yanai², I. Dotan², I. Avni-Biron²

¹Rabin Medical Center, Helen Schneider Hospital for Women, Petah Tikva, Israel, ²Rabin Medical Center, IBD Center, Division of Gastroenterology, Petah Tikva, Israel

Contact E-Mail Address: irit.biron@gmail.com

Introduction: Pregnant patients with inflammatory bowel diseases (IBD) are frequently treated with immunomodulatory agents and may be at increased risk of adverse outcomes, including peripartum infections.

Aims & Methods: Our aim was to examine the risk for peripartum infections in patients with IBD compared to controls and identify potential risk factors associated with peripartum infections in these patients.

This retrospective cohort study compared peripartum infection rates and associated risk factors between pregnant women with and without IBD. Study population included women attending a dedicated joint maternal-fetal medicine and gastroenterology clinic for pregnant women with IBD between 2012 - 2019 at the Rabin Medical Center in Israel, a major referral center for patients with IBD. For each patient, 5 women without IBD were matched according to the newborn's birth date (± 2 years), age, parity, and body mass index.

Peripartum infection was defined as any one of the following: chorioamnionitis, maternal fever ($>38^{\circ}\text{C}$) detected during labor or post-partum hospitalization, and positive culture taken during the hospitalization.

Results: Overall, 195 pregnant women with IBD (ulcerative colitis - 72 [37%], Crohn's disease - 123 [63%]) were matched with 888 controls. Mean disease duration - 8.4 ± 7.02 years. IBD therapy, used by 81%, included most frequently 5-aminosalicylic acid (44%) and tumor necrosis factor inhibitors (27%).

Peripartum infections were observed in 15 (7.7%) patients, and 49 (5.5%) controls ($p=1.00$).

No medication significantly increased the likelihood of peripartum infection. Cesarean delivery was more likely among women with IBD but was not associated with an increased risk of peripartum infection.

Maternal characteristics	IBD n=195	No IBD n= 888	p-Value
Maternal age, years	32.1 $\pm$ 4.72	32.1 $\pm$ 4.50	0.89
Body Mass Index, Kg/m ²	22.5 $\pm$ 5.08	22.8 $\pm$ 5.3	0.46
Gestational Weight Gain, kg	7.1 $\pm$ 5.68	11.3 $\pm$ 5.50	<0.05
Smoking	12 (6.2%)	37 (4.2%)	0.23
Mode of Conception:			
Controlled Ovarian Hyperstimulation	10 (5.1%)	22 (2.5%)	0.14
Assisted Reproduction	11 (5.6%)	54 (6.1%)	
Nulliparity	72 (36.9%)	338 (38.1%)	0.77
T1DM/T2DM	2 (1%)	79 (8.9%)	<0.05

Data presented as mean $\pm$ standard deviation for continuous variable and as n (%) for categorical variables
 IBD - Inflammatory Bowel Disease
 T1DM/T2DM - Type 1 or Type 2 Diabetes Mellitus

Table 1: Baseline Characteristics.

Conclusion: Peripartum infections were comparable in patients with IBD and controls. This reassuring data augments existing knowledge of obstetrical outcomes in IBD patients and contributes to the discussion between caregivers and patients.

Disclosure: Nothing to disclose.

P0463

IMPACT OF MIRIKIZUMAB TREATMENT ON HEALTH-RELATED QUALITY OF LIFE IN PATIENTS WITH CROHN'S DISEASE: A PHASE 2 STUDY ANALYSIS USING THE SF-36

V. Jairath¹, T. Hibi², L. Shan Chan³, T. Hunter Gible³, H. Carlier³, X. Zhou⁴, M. Protic³, D.T. Rubin⁵

¹Western University & London Health Sciences Centre, Division of Gastroenterology, Ontario, Canada, ²Kitasato Institute Hospital IBD Research and Treatment, Keio University, Tokyo, Japan, ³Eli Lilly and Company, Indianapolis, United States, ⁴Syneos Health, Strategic Resourcing, Clinical Solutions, Morrisville, United States, ⁵University of Chicago Medicine, Chicago, United States

Contact E-Mail Address: vjairath@uwo.ca

Introduction: Mirikizumab (miri), a p19-directed IL-23 inhibitor, showed efficacy in studies of moderately to severely active ulcerative colitis (UC; Phase [Ph]2¹ and 3²) and Crohn's disease (CD; Ph2³). In the Ph2 UC study, miri improved health-related quality of life (HRQoL) assessed by the 36-Item Short Form Health Survey (SF-36)⁴, a patient-completed questionnaire measuring 8 domains (physical/social functioning, mental/general health, role-physical and -emotional, bodily pain, and vitality) and summary physical and mental component scores (PCS and MCS, respectively).

This analysis evaluated miri effects on SF-36 in the Ph2 randomised, double-blind, parallel, placebo (PBO)-controlled study in patients with moderately-to-severely active CD (NCT02891226).

Aims & Methods: *12-Week(W) Induction:* 191 patients were randomized 2:1:1:2 to 4 treatment arms: intravenous (IV) PBO, 200, 600, or 1000mg miri every 4 weeks (Q4W; W0, 4, and 8). *40-W Maintenance:* For miri induction dose, patients achieving ≥1-point improvement in Simple Endoscopic Score for CD (SES-CD) at W12 were re-randomized 1:1 to double-blind maintenance treatment from W12 to W48: continuation of induction IV treatment assignment (IV-IV; N=41) or subcutaneous (SC) 300mg miri Q4W (IV-SC; N=46).

Due to small sample sizes, maintenance IV arms and SC arms were pooled. W12 SES-CD non-improvers (N=30) and patients receiving PBO during induction (N=59) received IV 1000mg miri Q4W from W12 to W48. No statistical comparisons were made between miri treatment groups in the maintenance period. SF-36 was assessed at baseline and at W4,12,16, 24, 32, 44, and 52.

Results: Statistically significant improvement in MCS was observed at W4 (600mg dose level) and at W12 (all dose levels), whereas statistically significant improvements in PCS were observed only at W12 (600 and 1000mg dose levels) compared to PBO (Table).

Though statistical comparisons were not made between treatment groups during maintenance, comparison of mean changes in MCS and PCS suggest that improvements during induction were sustained or further numerically increased with miri maintenance treatment, even in induction SES-CD non-improvers (Table).

Conclusion: These data show that miri treatment improves HRQoL in patients with moderately to severely active CD and suggest an earlier impact on mental compared to physical well being. Maintenance treatment effects were numerically consistent or increased compared to induction effects, even among more refractory patients.

These findings will be validated in the ongoing miri Ph3 CD study (NCT03926130). Proinflammatory signals can induce anxiety and depressive symptoms; better understanding of how the effects of anti-inflammatory treatment on the gut-brain axis may improve mental and physical subjective wellbeing requires additional mechanistic studies⁴.

Induction Period	Mental Component Score (MCS)				Physical Component Score (PCS)			
	PBO (N=64)	200 mg IV miri (N=31)	600 mg IV miri (N=32)	1000 mg IV miri (N=64)	PBO (N=64)	200 mg IV miri (N=31)	600 mg IV miri (N=32)	1000 mg IV miri (N=64)
W0 Baseline (Mean ± SD)	37.0 ± 13.2	35.2 ± 10.2	41.1 ± 10.4	40.4 ± 11.6	38.9 ± 8.3	38.4 ± 6.4	42.9 ± 7.8	39.5 ± 8.6
W4 CFBL (LSM ± SE)	1.9 ± 1.0	2.6 ± 1.4	5.2 ± 1.4*	3.1 ± 1.0	2.4 ± 0.7	3.3 ± 1.0	3.4 ± 1.0	4.2 ± 0.7
W12 CFBL (LSM ± SE)	2.3 ± 1.1	7.5 ± 1.6*	6.5 ± 1.6*	6.1 ± 1.2*	3.1 ± 0.8	4.7 ± 1.1	8.0 ± 1.1**	6.7 ± 0.8**
Maintenance Period	PBO-1000mg IV miri (N=59)	NI-1000mg IV miri (N=30)	All IV-IV miri (N=41)	All IV-SC miri (N=46)	PBO-1000mg IV miri (N=59)	NI-1000mg IV miri (N=30)	All IV-IV miri (N=41)	All IV-SC miri (N=46)
W0 Baseline (Mean ± SD)	37.2 ± 13.0	38.0 ± 11.2	42.0 ± 10.1	38.7 ± 10.7	39.5 ± 8.1	40.8 ± 8.3	41.1 ± 8.5	38.1 ± 7.1
W24 CFBL (Mean ± SD)	7.4 ± 8.7	7.7 ± 11.7	7.0 ± 10.6	5.9 ± 13.1	6.8 ± 7.3	7.1 ± 7.8	9.6 ± 5.6	7.1 ± 8.3
W52 CFBL (Mean ± SD)	7.1 ± 10.6	7.3 ± 9.8	8.5 ± 11.3	11.5 ± 11.4	9.9 ± 7.2	7.1 ± 8.2	10.2 ± 8.7	10.7 ± 9.9

Abbreviations: CFBL = change from baseline; IV = intravenous; IV-IV = pooled maintenance IV treatment arms for patients at each miri induction dose level who achieved ≥1-point improvement in SES-CD at W12 who were re-randomized to continued induction IV treatment assignment during maintenance; IV-SC = pooled maintenance SC treatment arms for patients at each miri induction dose level who achieved ≥1-point improvement in SES-CD at W12 who were re-randomized to SC 300mg miri Q4W during maintenance; LSM = least squares mean; NI = SES-CD non-improver (a patient who received miri during induction who did not achieve a ≥1-point improvement in SES-CD at W12); PBO = placebo; SC = subcutaneous; SD = standard deviation; SE = standard error; W = week. For statistical comparisons across induction treatment groups, a mixed model for repeated measures was used. The model includes treatment, region, prior biologic CD therapy used, baseline, visit and baseline by visit, and treatment by visit.

p-values versus PBO: *p<0.05; **p<0.001. Bolded values are statistically different versus PBO.

Table. Effect of mirikizumab on SF-36 MCS and PCS Change from Baseline

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ASSOCIATION OF HISTOLOGIC MEASUREMENT WITH ENDOSCOPIC OUTCOMES AFTER ONE YEAR OF TREATMENT WITH MIRIKIZUMAB IN PATIENTS WITH MODERATE TO SEVERE CROHN'S DISEASE

F. Magro¹, G. De Hertogh², M. Protic³, L.S. Chan³, P. Pollack³, B. Feagan⁴, N. Harpaz⁵, R. Pai⁶, W. Reinisch⁷

¹University Hospital São João, Porto, Portugal, ²University Hospital Leuven, Leuven, Belgium, ³Eli Lilly and Company, Indianapolis, United States, ⁴Robarts Clinical Trials Inc., London, Canada, ⁵Icahn School of Medicine at Mount Sinai, New York City, United States, ⁶Mayo Clinic, Scottsdale, United States, ⁷Medical University of Vienna, Wien, Austria

Contact E-Mail Address: fm@med.up.pt

Introduction: There is a scarcity of data regarding the role of histopathology evaluation in Crohn's disease (CD) and how it relates to endoscopy. Mirikizumab (miri) has shown efficacy in Ph2 studies in CD and ulcerative colitis (UC).

Aims & Methods: We explore the agreement of histologic response and remission with endoscopic outcomes after 12 and 52 weeks of treatment with miri in a phase 2 randomized clinical trial (SERENTIY; NCT02891226) in patients with moderate-to-severe CD. Patients were randomized 2:1:1:2 across 4 treatment arms (PBO, 200, 600, 1000mg miri) administered intravenously (IV) every four weeks (Q4W) at Weeks 0, 4, and 8. Those who received miri and achieved ≥ 1 point improvement from baseline (BL) at W12 in Simple Endoscopic Score for Crohn's Disease (SES-CD) were re-randomized 1:1 into double-blind maintenance to continue their IV dose assignment Q4W (IV/IV) or to 300mg miri SC Q4W (IV/SC); due to small numbers, maintenance IV arms were pooled for analysis. W12 non-improvers and all induction PBO patients received 1000mg miri Q4W from W12 through W52. Biopsies were obtained during endoscopy at W0, 12 and 52 from the edge of the ulcers and the most inflamed mucosa in terminal ileum and 4 colonic segments (ascending, transverse, descending, rectum; N=10/patient, 2 per location with the more severe score used), and scored by central readers blind to study treatment, timepoint, and response status. Histologic endpoints were defined post-hoc but prior to performing the analyses (see Table footnotes for definitions). Cohen's Kappa Coefficient was used to evaluate the degree of agreement of two measures.

Results: At Week 12, there was an overall 69.6% agreement in histologic and endoscopic response, and 84.2% agreement between histologic remission and endoscopic remission (Table). After 52 weeks of miri treatment, the agreement between histologic and endoscopic response was 61.9%, while the agreement between histologic and endoscopic remission was 70.6% (Table).

Interestingly, in every comparison, the percentage of patients achieving the histologic outcome but not the endoscopic outcome was greater than that of patients achieving the endoscopic outcome but not the histologic outcome.

	Histologic Response					Histologic Remission			
	Week 12 N=158		Week 52 N=126			Week 12 N=158		Week 52 N=126	
	Values n (%)		Values n (%)			Values n (%)		Values n (%)	
Endoscopic Response	No	Yes	No	Yes	Endoscopic Remission	No	Yes	No	Yes
No	72 (45.6)	36 (22.8)	29 (23.0)	24 (19.1)	No	122 (77.2)	19 (12.0)	72 (57.1)	20 (15.9)
Yes	12 (7.6)	38 (24.1)	23 (18.3)	50 (39.7)	Yes	6 (3.8)	11 (7.0)	17 (13.5)	17 (13.5)
Endpoint agreement*	110 (69.6)		79 (62.7)		Endpoint agreement*	133 (84.2)		89 (70.6)	
K coefficient (95% CI)	0.38 (0.24, 0.52)		0.23 (0.06, 0.40)		K coefficient (95% CI)	0.38 (0.19, 0.57)		0.28 (0.09, 0.46)	

*Endpoint agreement = where endoscopic and histologic response or endoscopic and histologic remission have the same value (NO or Yes for both). Assessed by Cohen's Kappa coefficient. Histologic response: absence of neutrophils in lamina epithelia, absence of epithelial damage, erosions and ulceration or decrease of either RHI or active GHAS (sum Q1, 4, 5, 6 >0) of $\geq 50\%$. Histologic remission: absence of mucosal neutrophils (epithelium and lamina propria), epithelial damage, erosions, and ulceration (GHAS Q1=Normal, GHAS Q4=Normal, GHAS Q5=Absent, and GHAS Q6=No or sum of RHI Q2-4 = 0 when total RHI ≤ 3 .)

Table: Association of histologic and endoscopic endpoints at Week 12 and Week 52

Conclusion: Histologic and endoscopic outcomes demonstrated fair association after both 12 and 52 weeks of miri treatment. Histologic endpoints, despite the stringent criteria, appear to be more sensitive to change than endoscopic endpoints. However, variability of biopsy sampling may be an additional factor contributing to these differences.

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ABDOMINALLY TARGETED, YOGA-BASED PHYSICAL EXERCISES AS A THERAPEUTIC INTERVENTION FOR INFLAMMATORY BOWEL DISEASE

L. Werner^{1,2}, M. Fibelman^{1,2}, I. Shapiro³, A. Siderskyi⁴, Y. Ostrinski^{5,6}, A. Hirsch^{1,2}, Y. Ron^{1,2}, N. Fliss-Isakov^{1,2}, N. Maharshak^{1,2}

¹Tel Aviv University, Sackler School of Medicine, Tel Aviv, Israel,

²Tel Aviv Medical Center. Dept. of Gastroenterology, Tel Aviv, Israel,

³Ostmed, Israel, Tel Aviv, Israel, ⁴Yoga Workout Self-Adjustment System, Kiev, Ukraine, ⁵Ariel University, Ariel, Israel, ⁶Zabludowicz Center for Autoimmune Diseases, Sheba Medical Center, Ramat Gan, Israel

Contact E-Mail Address: wernerlael@gmail.com

Introduction: Inflammatory bowel diseases (IBD), comprised of Crohn's disease (CD) and ulcerative colitis (UC), are chronic inflammatory disorders of the gastrointestinal tract. Patients with IBD commonly suffer from symptoms that impact quality of life (QoL) parameters such as pain, fatigue, and stress.

Physical activity has positive effects on general well-being and stress; and may modify perceived pain, stress, sleep quality, and bowel circadian rhythm. In particular, physical activity that target the abdomen may assist in intestinal blood flow and therefore is thought by some to positively affect patient-reported outcomes. However, the effect of routine physical activity on disease measures and patient's QoL is currently unknown.

Aims & Methods: The aim of this pilot study was to examine the effect of routine, abdominally targeted, physical exercise sets, designed exclusively for IBD patients, on patients' QoL and clinical response.

Methods: This is a randomized, controlled, double-blinded pilot study that assessed the effect of a set of specific abdominally targeted physical exercises, in comparison to a control exercise regimen, on patient's clinical disease activity and QoL. A set of three repeating videos of exercises, sequenced and performed by a trained and experienced yoga instructor, were available online for patients to follow daily from their home. Each exercise regimen included explicit drills inspired by yoga poses, postulated to increase blood flow to the abdomen. Before and after a 1 month intervention, patients were assessed for disease activity using the Harvey Bradshaw Index (HBI) or simple clinical colitis activity index (SCCAI), and for QoL by the PROMIS questionnaire.

Results: The study included 19 mild-moderate patients with IBD (9 CD, 10 UC), mean age 21.7±4.2 years, randomized to perform either intervention (n=12) or control (n=7) set of exercises. No differences were observed

between groups at baseline in clinical or demographic parameters. Upon completion, patients training with the interventional videos, but not with the control videos, reported significant improvements in clinical scores. Among patients with CD in the interventional arm, the HBI score decreased from 6.3±0.8 to 2.8±0.4 (p<0.05), while in the control group, the average HBI score remained unchanged (5.3 ±0.2 and 5.3 ±0.4). Similarly, in patients with UC in the interventional group, SCCAI score decreased significantly from 4.7±0.7 to 2.5±0.7 (p<0.05), while in the control group SCCAI decreased from 5.7±0.9 to 4.0±0.8 (p=NS).

Correspondingly, among patients in the interventional group, significant improvements in several QoL parameters were detected after 1 month of training. Thus, the number of daily liquid stools (2.8±0.6 vs. 1.2±0.5, p<0.01), self-perceived pain intensity (3.8±1.0 vs. 1.3±0.6, p<0.001) and fatigue score (13.0±1.1 vs. 9.1±1.6, p<0.05) were all improved after 4 weeks of participation in the study. This is in contrast to the control group where no significant change occurred in these symptoms after 4 weeks of daily exercises: number of daily liquid stools (2.6±0.7 vs. 2±0.6, p=NS), self-perceived pain intensity (3.7±0.8 vs. 3.1±0.6, p=NS), or fatigue score (13.6±0.7 vs. 11.8±0.6, p=NS). No differences were observed in sleep disturbances between the two groups.

Conclusion: Routine, abdominally targeted, physical activity can significantly improve IBD clinical scores and symptoms. Despite our small cohort and short duration of study, these preliminary results suggest a positive effect of physical exercise in IBD and prompt further study.

Disclosure: Nothing to disclose.

P0466

USE OF TUMOR NECROSIS FACTOR-A ANTAGONISTS IS ASSOCIATED WITH ATTENUATED IGG ANTIBODY RESPONSE AGAINST SARS-COV-2 IN VACCINATED PATIENTS WITH INFLAMMATORY BOWEL DISEASE

A.T. Otten¹, A.R. Bourgonje¹, P. Horinga¹, H. van der Meulen¹, E.A.M. (. Festen¹, H. van Dullemen¹, R.K. Weersma¹, C. van Leer-Buter², G. Dijkstra¹, M.C. Visschedijk¹

¹University Medical Center Groningen, Gastroenterology and Hepatology, Groningen, Netherlands, ²University Medical Center Groningen, Department of Medical Microbiology, Groningen, Netherlands

Contact E-Mail Address: a.t.otten@umcg.nl

Introduction: Patients with Inflammatory Bowel Disease (IBD) frequently receive immunomodulating treatment, which may render them at increased risk of an attenuated immune response upon vaccination. In this study, we assessed the effects of different types of commonly prescribed immunosuppressive medications on the serological response after vaccination against SARS-CoV-2 in patients with IBD.

Aims & Methods: In this prospective observational cohort study, IgG antibody titers against SARS-CoV-2 were measured 2-10 weeks after completion of standard vaccination regimens in patients with IBD. Clinical characteristics, previous history of SARS-CoV-2 infection, type of vaccine (mRNA- or vector-based) and medication use were recorded at the time of sampling. Subsequently, a chemiluminescent microparticle immunoassay was used for the quantitative determination of IgG antibodies against the receptor-binding domain (RBD) of the S1 subunit of the spike protein of SARS-CoV-2.

Results: Three hundred and twelve (312) patients with IBD were included (172 Crohn's disease [CD] and 140 ulcerative colitis [UC]). Seroconversion (defined as titer of >50 AU/ml) was achieved in 98.3% of patients. Antibody concentrations were significantly lower in patients treated with TNF-α-antagonists vs. non-users of TNF-α-antagonists (geometric mean [95% confidence interval]: 2204 [1655-2935] vs. 5002 [4089-6116] AU/ml,

$P < 0.001$). In multivariable models, use of TNF- α -antagonists ($P < 0.001$), vector vaccines ($P < 0.001$), age (> 50 years) ($P < 0.01$) and CD ($P < 0.05$) were independently associated with lower anti-SARS-CoV-2 antibody titers. In patients who received mRNA vaccines, users of thiopurines (either prescribed as monotherapy or in combination with biologicals) demonstrated significantly lower antibody titers compared to those who were thiopurine non-users ($P < 0.05$).

Conclusion: Despite reassuring findings that most patients with IBD have detectable antibodies after anti-SARS-CoV-2 vaccination, TNF- α -antagonists were found to be strongly associated with an attenuated IgG antibody response after vaccination against SARS-CoV-2, independent of vaccine type, the time elapsed after vaccination and blood sampling, prior SARS-CoV-2 infection and patient age. Patients treated with thiopurines and receiving mRNA-based vaccines demonstrated lower anti-SARS-CoV-2 antibody titers compared with non-users. This specific subgroup of patients treated with TNF- α -antagonists may benefit from active booster vaccine prioritization, preferably with mRNA-based vaccines.

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P0467

ESTIMATING LOCAL TNF MRNA LEVELS PRIOR TO ANTI-TNFA TREATMENT MAY HELP THERAPEUTIC OPTIMIZATION IN CHILDREN WITH IBD

J. P. James¹, B.S. Nielsen², E. Langholz^{3,4}, M. Malham^{5,6}, E.H. Hoegdall^{1,4}, L.B. Riis^{1,4}

¹Copenhagen University Hospital - Herlev and Gentofte, Department of Pathology, Herlev, Denmark, ²Bioneer A/S, Hørsholm, Denmark, ³Copenhagen University Hospital - Herlev and Gentofte, Department of Gastroenterology, Herlev, Denmark, ⁴University of Copenhagen, Department of Clinical Medicine, Copenhagen, Denmark, ⁵Copenhagen University Hospital - Amager and Hvidovre, Copenhagen Center for Inflammatory Bowel Disease in Children, Adolescents and Adults, Hvidovre, Denmark, ⁶Copenhagen University Hospital, Hvidovre, Paediatric Department, Hvidovre, Denmark

Contact E-Mail Address: jaslin.pallikkunnath.james@regionh.dk

Introduction: Inflammatory bowel disease (IBD) is characterized by the activation of proinflammatory cytokines such as tumor necrosis factor- α (TNF). TNF antagonists have shown a radical transformation in the management of IBD. However, there is a substantial number of patients who do not respond to anti-TNF agents, and many patients experience a loss of response over time. It is vital to differentiate these responders and non-responders from the initiation of treatment as the reason for failure and their treatment strategies differ.

Aims & Methods: Methods: Formalin-fixed, paraffin-embedded (FFPE) mucosal biopsies of IBD patients with the luminal disease, collected at the time of initiation of biologics were used in this study. Samples were stratified into three groups according to treatment response: Responders

(treated with anti-TNF for a minimum of 3 years with no relapse of disease), Primary non-responders (PNR, relapse within the first year of treatment), and Secondary non-responders (SNR, minimum 3 years of treatment with no relapse, then subsequent loss of response). Discontinuation of the treatment for the sample cohort was not due to the formation of anti-drug antibodies or any other side effects.

TNF mRNA was analyzed in tissue sections by RNAscope in situ hybridization (ISH). The ISH signal dots were seen in both lamina propria and in lymphoid follicles (LF) and were measured by image analysis. TNF mRNA expression estimates were obtained as area fractions with and without LF.

Results: Significant differences in the TNF mRNA levels were observed between adults and children in analysis with and without LF ((Median values for adults and children with LF are 0.17 and 0.09 ($P = 6.82 \times 10^{-3}$) and without LF are 0.13 and 0.09 ($P = 0.03$)). In children, we found a significant difference in TNF levels between responders and SNRs in areas without LF, (Median values for Responders and SNRs are 0.07 and 0.17 ($P = 0.05$)), and between PNRs and SNRs (Median values for PNRs and SNRs are 0.07 and 0.17 ($P = 0.05$)).

Conclusion: It is concluded that TNF mRNA levels are higher in adult's than children's IBD tissue, that the contribution to the expression is not linked to LF in children, and that SNR among children has higher TNF mRNA levels than responders and PNR.

Estimating the level of local TNF mRNA prior to anti-TNF treatment may help stratification of the IBD patients into dosage-regulated groups. It is suggested that TNF antagonist dose intensification is considered for children with high TNF mRNA expression estimates from the start of treatment.

Disclosure: Nothing to disclose.

P0468

IMPROVEMENT IN FATIGUE WITH MIRIKIZUMAB THERAPY IS ASSOCIATED WITH CLINICAL REMISSION AND PAIN IMPROVEMENTS BUT NOT WITH ENDOSCOPIC RESPONSE IN PATIENTS WITH MODERATELY TO SEVERELY ACTIVE CROHN'S DISEASE

M. Reguiero¹, M. Fischer², D.T. Rubin³, T. Hibi⁴, P. Bossuyt⁵, P. Juillerat⁶, P. Pollack⁷, X. Zhou⁸, M. Protic⁹, T. Hunter Gibble¹⁰, L.S. Chan¹¹, H. Carlier¹², P. Hindryckx¹³

¹Cleveland Clinic, Cleveland, United States, ²IUPUI, Gastroenterology, Indianapolis, United States, ³University of Chicago Medicine, Chicago, United States, ⁴Kitasato Institute Hospital IBD Research and Treatment, Keio University, Tokyo, Japan, ⁵Imelda General Hospital, Dr., Bonheiden, Belgium, ⁶Inselspital Bern University Clinic for Visceral Surgery and Medicine, Abt. Gastroenterology, Bern, Switzerland, ⁷Consultant, Bexley, OH, United States, ⁸Syneos Health, Morrisville, United States, ⁹Eli Lilly & Company, IBU, Vernier, Genève, Switzerland, ¹⁰Eli Lilly and Company, Global Patient Outcomes and Real World Evidence, Indianapolis, United States, ¹¹Eli Lilly and Company, Indianapolis, United States, ¹²Eli Lilly and Company, Brussels, Belgium, ¹³Ghent University Hospital Dept. of Gastroenterology, Dept. of Gastroenterology, Ghent, Belgium

Contact E-Mail Address: peter.bossuyt@imelda.be

Introduction: Mirikizumab (miri) is a humanized immunoglobulin G4 (IgG4) monoclonal antibody directed against the p19 subunit of IL-23 which was efficacious and well tolerated in a phase 2 randomized clinical trial (AMAG; NCT02891226) in patients with Crohn's disease (CD).¹ Fatigue is common in patients with CD and negatively impacts quality of life.² We

previously reported that fatigue improved in patients with CD receiving miri in the AMAG study in all treatment arms.³ The association between changes in clinical and inflammatory markers and changes in fatigue might reveal the mechanism of fatigue relief.

Aims & Methods: Patients (N=191) with moderately to severely active CD were randomized 2:1:1:2 into 4 treatment arms (placebo, 200 mg, 600 mg, and 1000 mg miri), administered intravenously every four weeks at Weeks (W) 0, 4, and 8. At W12 patients were switched from placebo to miri and re-randomized between miri doses based on response.

Fatigue was assessed using the Functional Assessment of Chronic Illness Therapy-Fatigue (FACIT-F) questionnaire, which has been validated for use in patients with inflammatory bowel disease.

Endoscopic response was defined as $\geq 50\%$ reduction from baseline in total Simplified Endoscopic Activity Score for Crohn's Disease. For continuous variables, Pearson's correlation coefficients, 95% confidence intervals, and p-values were calculated. Cohen's conventions were used to assess strength of correlations (>0.5 is strong, 0.3 to ≤ 0.5 is moderate, 0.1 to <0.3 is weak, and <0.1 is insubstantial).⁴

Analysis of covariance was used to assess the relationship between change in FACIT-F and endoscopic response at the same timepoint adjusting for baseline FACIT-F values. Data were pooled for all treatment arms including placebo.

Results: Overall, mean change in FACIT-F scores for patients with and without endoscopic response at W12 were 8.1 and 7.2, respectively ($p=0.33$) and at W52 were 13.9 and 13.7, respectively ($p=0.54$). At W12, change in FACIT-F showed a moderate but statistically significant correlation with change at the same timepoint in Crohn's Disease Activity Index (CDAI) total score ($r=-0.404$), abdominal pain ($r=-0.380$), and stool frequency ($r=-0.354$). Weak but statistically significant correlations were observed with calprotectin ($r=-0.269$), and C-reactive protein ($r=-0.165$) (Table).

At W52, change in FACIT-F was moderately but significantly correlated with change in CDAI total score, abdominal pain, and stool frequency (Table).

Clinical Measure	Week 12 (N=191)			Week 52 (N=176)		
	Pearson corr.	95% CI	p-value	Pearson corr.	95% CI	p-value
Total Score						
CDAI	-0.404	(-0.530, -0.259)	<0.0001	-0.492	(-0.614, -0.346)	<0.0001
SES-CD	-0.146	(-0.290, 0.004)	0.0572	-0.076	(-0.238, 0.090)	0.3702
Hematocrit (%)	-0.039	(-0.194, 0.119)	0.6319	0.152	(-0.016, 0.312)	0.0756
Hemoglobin	-0.011	(-0.167, 0.145)	0.8916	0.120	(-0.049, 0.282)	0.1638
Fecal calprotectin (log)	-0.269	(-0.419, -0.105)	0.0015	-0.175	(-0.342, 0.003)	0.0544
C-reactive protein (log)	-0.165	(-0.310, -0.013)	0.0331	-0.151	(-0.310, 0.016)	0.0756
Abdominal pain average score	-0.380	(-0.504, -0.240)	<0.0001	-0.438	(-0.565, -0.292)	<0.0001
Stool frequency average score	-0.354	(-0.481, -0.212)	<0.0001	-0.290	(-0.437, -0.128)	0.0006

Table. Correlation of change in FACIT-F with change in clinical measures

Abbreviations: CDAI=Crohn's Disease Activity Index; corr=correlation; N=number of patients in the analysis (including patients with non-missing change scores); FACIT-F=Functional Assessment of Chronic Illness Therapy-Fatigue; SES-CD=Simplified Endoscopic Activity Score for Crohn's Disease.

Table.

Conclusion: Considering the limitation of the posthoc analysis and design of this Phase 2 trial, improvements in fatigue were significantly associated with improvement in CDAI score, abdominal pain, and stool frequency

in patients with CD. Although fatigue has been hypothesized to be mediated in part by inflammatory cytokines,⁵ our data showed no consistent relationship of improvement in fatigue with changes in objective markers of disease activity, suggesting the possibility of alternative or additional mechanistic processes for fatigue in CD.

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P0469

VEDOLIZUMAB IS ASSOCIATED WITH STEROID-FREE CLINICAL REMISSION AND DISCONTINUATION-FREE SURVIVAL IN PATIENTS WITH MODERATE-TO-SEVERE ULCERATIVE PROCTITIS

P. Lemmens¹, J. Sabino^{1,2}, E. Louis³, W. Van Moerkercke⁴, L. Pouillon⁵, M. Somers⁶, H. Peeters⁷, S. Dr. Vanden Branden⁸, J. Busschaert⁹, F. Baert¹⁰, A. Cremer¹¹, P. Potvin¹², S. Dewit¹³, A. Colard¹⁴, J. Swinnen¹⁵, G. Lambrecht¹⁶, C. Claessens¹⁷, B. Willandt¹⁸, P. Dewint^{6,19}, E. Van Dyck²⁰, S. Vermeire^{1,2}, M. Ferrante^{1,2}

¹University Hospital Leuven, Department of Gastroenterology, Leuven, Belgium, ²Catholic University Leuven, Translational Research Center for Gastrointestinal Disorders (TARGID), Leuven, Belgium, ³CHU Liège and Liège University, Department of Gastroenterology, Liège, Belgium, ⁴AZ Groeninge, Department of Hepatology and Gastroenterology, Kortrijk, Belgium, ⁵Imelda Hospital, Department of Gastroenterology, Bonheiden, Belgium, ⁶University Hospital Antwerp, Department of Gastroenterology, Antwerp, Belgium, ⁷University Hospital Gent, Department of Gastroenterology, Gent, Belgium, ⁸Onze Lieve Vrouw Hospital, Department of Gastroenterology, Aalst, Belgium, ⁹AZ Sint Lucas, Department of Gastroenterology, Brugge, Belgium, ¹⁰AZ Delta, Department of Gastroenterology, Roeselare, Belgium, ¹¹Erasmus University Hospital, Department of Gastroenterology, Brussels, Belgium, ¹²AZ Rivierenland, Department of Gastroenterology, Bornem, Belgium, ¹³Noorderhart Maria Hospital, Department of Gastroenterology, Pelt, Belgium, ¹⁴Centre Hospitalier Chrétien - Clinique St Joseph, Department of Gastroenterology, Liège, Belgium, ¹⁵Sint Franciscus Hospital, Department of Gastroenterology, Heusden-Zolder, Belgium, ¹⁶AZ Damiaan, Department of Gastroenterology, Oostende, Belgium, ¹⁷AZ Turnhout, Department of Gastroenterology, Turnhout, Belgium, ¹⁸AZ Sint Jan, Department of Gastroenterology, Brugge, Belgium, ¹⁹AZ Maria Middelaers, Department of Gastroenterology, Gent, Belgium, ²⁰AZ Klina, Department of Gastroenterology, Brasschaat, Belgium

Contact E-Mail Address: marc.ferrante@uzleuven.be

Introduction: Although adalimumab (ADM), golimumab (GOL), infliximab (IFX), tofacitinib (TFC), ustekinumab (UST) and vedolizumab (VDZ) have been shown efficacious for the treatment of moderate-to-severe ulcerative colitis (UC), data for ulcerative proctitis (UP, inflammation up to 15cm from the anal verge) are scarce.

Aims & Methods: We conducted a multicentric retrospective study in patients with active UP (Mayo endoscopy sub-score of ≥ 2) in order to evaluate the outcome of biological therapy (ADM, GOL, IFX, UST, and VDZ) and small molecules (TFC). The total Mayo score was available both at baseline and at week 20. The primary endpoint was steroid-free clinical remission at week 20 without prior need for dose optimization. Clinical remission was defined as a total Mayo score ≤ 2 with no individual sub-score >1 . Next, we evaluated discontinuation-free survival. We collected demographic, clinical, biochemical, endoscopic and treatment-related data, and evaluated their relationship with both short- and long-term outcome. Both binary logistic and Cox regression analysis were performed for the overall cohort as well as for the bio-naïve patients.

Results: In total 168 consecutive patients (48% male, median age 41 (IQR 32-53) years) undergoing 225 courses of therapy for UP (38 ADM, 15 GOL, 54 IFX, 10 UST, 99 VDZ, 9 TFC) in 19 centres between February 2005 and October 2021 were included. Forty percent of the patients (68/168) had a more extensive disease in the past, and 137/168 (81.6%) patients were bio-naïve.

At baseline, the median (IQR) total Mayo score was 8 (7-9) and 44.9% had an endoscopic Mayo sub-score of 3. At week 20, 34.7% patients (78/225) achieved the primary endpoint of steroid-free clinical remission without prior need for dose optimization.

In multivariate analysis, treatment with vedolizumab, a normal baseline CRP and a Mayo endoscopic sub-score of 2 (vs. 3) were associated with the primary endpoint (Table 1).

In the subpopulation of bio-naïve patients, vedolizumab and a Mayo endoscopic sub-score of 2 (vs. 3) were the only independent factors associated with the primary endpoint. After a median (IQR) follow-up of 15.8 (5.0-37.9) months, 112/225 (49.8%) had discontinued the advanced therapy. In multivariate analysis, discontinuation-free survival was significantly higher in patients treated with vedolizumab, both in the overall cohort as in bio-naïve patients.

In the overall cohort, patients who never had a more extensive disease also had a better discontinuation-free survival. Only three patients developed a serious adverse event related to the advanced therapy, namely one tuberculosis infection, one pneumonia and one infusion reaction.

	Overall cohort (n=225)		Bio-naïve (n=137)	
	Primary endpoint Odds ratio (95% CI), p-value	Discontinuation-free survival Odds ratio (95% CI), p-value	Primary endpoint Odds ratio (95% CI), p-value	Discontinuation-free survival Odds ratio (95% CI), p-value
Vedolizumab	3.20 (1.75-5.85), p<0.001	2.03 (1.36-3.05), p<0.001	4.86 (2.29-10.34), p<0.001	2.02 (1.15-3.57), p=0.015
Normal baseline CRP	2.12 (1.00-4.48), p=0.049	-	-	-
Baseline Mayo endoscopic sub-score 2 (vs. 3)	1.88 (1.02-3.48), p=0.044	-	2.40 (1.11-5.18), p=0.026	-
Never more extensive disease	-	1.63 (1.12-2.36), p=0.010	-	1.49 (0.91-2.43), p=0.114

Table 1: Independent predictors of steroid-free clinical remission at week 20 (primary endpoint) and discontinuation-free survival in the overall population and patients who were bio-naïve

Conclusion: Biological therapies and small molecules are a safe treatment for patients with UP. At week 20, one third of patients achieved steroid-free clinical remission rate without prior need of dose optimization. Half of the patients continued the drug after a median follow-up of 16 months. Vedolizumab was the only independent predictor of both short- and long-term outcome.

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P0470

POSTOPERATIVE IMMUNOSUPPRESSIVE THERAPY DOES NOT INFLUENCE ENDOSCOPIC RECURRENCE RATES AFTER BOWEL RESECTIONS DUE TO CROHN'S DISEASE – A RETROSPECTIVE MULTICENTRE ANALYSIS

N. Pfisterer^{1,2}, T. Dengler³, V. Fink³, L. Schmalz³, D. Bauer⁴, L. Schlager³, M. Bergmann³, K. Kozbial⁵, W. Reinisch⁶, M. Schneider⁷, T. Feichtenschlager², K. Sonneck², M. Pramhas⁷, C. Madl⁸, A. Stift³, L.W. Unger³

¹Medical University of Vienna, Vienna, Austria, ²Klinik Landstrasse, 4. Medizinische Abteilung für Gastroenterologie und Hepatologie, Wien, Austria, ³Medical University of Vienna, Division of Visceral Surgery, Department of General Surgery, Vienna, Austria, ⁴Klinik Ottakring, 4. Medizinische Abteilung für Gastroenterologie und Hepatologie, Vienna, Austria, ⁵Medical University of Vienna, Division of Gastroenterology and Hepatology, Department of Medicine III, Vienna, Austria, ⁶Medical University of Vienna, Dep. of Internal Medicine IV, Division of Gastroenterology and Hepatology, Wien, Austria, ⁷Klinik Landstrasse, Chirurgische Abteilung, Wien, Austria, ⁸Klinik Landstrasse, Head of Division of Gastroenterology and Hepatology, 4. Medizinische Abteilung für Gastroenterologie und Hepatologie, Wien, Austria

Contact E-Mail Address: nikolauspfisterer@hotmail.com

Introduction: Crohn's disease (CD), an inflammatory bowel disease, is usually treated pharmacologically, but lifetime risk for surgical interventions due to complications such as fibrostenotic lesions or perforations remains high. The rate of postoperative recurrence (POR) in patients with Crohn's disease (CD) is reported in up to 75% within the first year after surgery and remains of significant importance despite novel therapies.(1) According to current guidelines, thiopurines and anti-tumor necrosis factor (anti-TNF) therapy should be administered depending on risk factors, including histological findings as well as other patient characteristics, to prevent POR.(2) However, the benefit of such preventive immunosuppressive therapy has been questioned lately.(3,4)

Thus, we set out to evaluate the effect of novel immunosuppressants on postoperative endoscopic recurrence rates in two high-volume referral centers.

Aims & Methods: In this real life multicenter study, we assessed the effectiveness of currently available immunosuppressive therapy to prevent endoscopic POR after surgery due to CD complications. We collected data from 328 patients after surgery between 01/2010 and 12/2021 at two referral centers (Medical University of Vienna and Klinik Landstrasse, Vienna) of which 151 (46%) patients had available endoscopy results. Endoscopic-POR (E-POR) was defined as occurrence of endoscopically detected disease activity according to the Rutgeerts' score (i2-i4).(3)

Results: In total, 87 (57.6%) patients had received at least one conventional immunosuppressant and/or biological, including azathioprine or anti-TNF agents (table 1) starting directly after surgery. Additional intermittent systemic corticosteroids were necessary in a total of 28 (8.5%) patients. In total, E-POR was found in 69 (45.7%) patients.

In terms of immunosuppressive therapy, the lowest rate of E-POR was observed in 19/44 (43.2%) patients who received anti-TNF therapy, followed by n=4/9 (44.4%) patients with combined long-term immunosuppressants, n=7/15 (46.7%) ustekinumab, n=1/2 (50%) with other medications (6-Mercaptopurine, Mycophenolate mofetil), n=3/5 (60%) vedolizumab, and n=8/12 (66.7%) azathioprine monotherapy.

In multivariate analysis, neither relatively novel treatments with ustekinumab (adjusted odds ratio, OR 0.83, confidence interval 95% CI: 0.27-2.58, p=0.753) or vedolizumab (OR 0.49, 95% CI 0.08-3.12, p=0.447), nor conventional treatment with anti-TNF therapy (OR 0.96, 95% CI 0.44-2.09),

p=0.918), azathioprine (OR 0.37, 95%CI 0.10-1.34, p=0.128) or other medications (OR 0.73, 95%CI 0.44-12.19, p=0.826) showed a significantly lower or higher risk for E-POR compared to no treatment.

Immunosuppressants	Multivariate odds ratio (95% CI)	p-value
Azathioprine(n=12)	0.37 (0.10-1.34)	0.128
Anti-TNF therapy (n=44)	0.96 (0.44-2.099)	0.918
Ustekinumab (n=15)	0.83 (0.27-2.58)	0.753
Vedolizumab (n=5)	0.49 (0.08-3.12)	0.447
Other medications (n=2)	0.73 (0.44-12.19)	0.826
Combined treatment (n=9)	0.91 (0.22-3.72)	0.898

Conclusion: The rate of E-POR in this retrospective real-life study is comparable to other studies, however, initiating long-term immunosuppression and biological therapies has not been associated with lower risk for endoscopic recurrence. Novel studies are warranted to identify eligible subgroups for specific treatment options.

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P0471

PREDICTORS OF RESPONSE TO WASHED MICROBIOTA TRANSPLANTATION IN PATIENTS WITH ULCERATIVE COLITIS: DATA ENVELOPMENT ANALYSIS APPROACH

F. Tabak¹, S. Assani², W. Gao¹, X. Lu¹, F. Zhang^{3,1}

¹Sir Run Run Hospital, Nanjing Medical University, Nanjing, China,

²Nanjing University of Aeronautics & Astronautics, Department of Mathematics, Nanjing, China, ³the Second Affiliated Hospital of Nanjing Medical University, Medical Center for Digestive Disease, Nanjing, China

Contact E-Mail Address: fatema-t@hotmail.com

Introduction: Fecal microbiota transplantation (FMT) has been shown as a highly effective and safe treatment for recurrent clostridium difficile infections (CDI) with reliable and potential role in induction of remission in patients with ulcerative colitis (UC). Washed microbiota transplantation (WMT) is a promising methodology have been applied in China since 2016,

using an automatic purification system (GenFMter), aiming to decrease the processing time for preservation of living bacteria, deliver a precise enriched dose of fecal microbiota and reduce adverse events [1]. Clinical factors that contribute to FMT response in UC need to be widely investigated especially with the limited data about the FMT efficacy in IBD.

Aims & Methods: A protocol of multiple transfusions of WMT through either mid-gut or colonic transendoscopic enteral tubing (TET) was applied to patients with ulcerative colitis in our tertiary referral center. We utilized a promising approach based on a solid data-driven method, data envelopment analysis (DEA) which is a mathematical approach for efficiency evaluation of decision system [2,3].

Recently, DEA has been applied to evaluate the performance of medical procedures and treatment plans [4,5]. In this work, the WMT was evaluated at the patients level by taking into account a combination of WMT's inputs and outputs. The set of inputs in DEA-based analysis were related to patient characteristics, UC disease characteristics including severity, extension, and medications.

Considering patients' response and WMT- related adverse events (AEs) together as outputs, we generated an overall efficiency index to classify the patients based on their relative efficiency performance across the input variables. The supper efficiency DEA model was then applied to rank the patients and thereby to select the best 15% of the patients in order to study their characteristics.

Within the proposed WMT-decision system that retrospectively analyzed the evolution of UC patients treated with WMT, we aimed to identify the specific variables that potentially contribute to the best performance of WMT.

Results: A total of 200 patients received WMT, 85 (42.5%) achieved clinical remission, 80 (40%) had a clinical improvement and 35 (17.5%) failed to achieve response, with related AEs were observed in 31 (15.5%).

Using DEA method, we identified the most efficient patients who achieved clinical remission with minimum adverse events, these patients' and UC characteristics (severity, behavior, extension) are presented in table (1).

We found that 96.6%, 83.3% of patients with the best response to WMT had mild or moderate stage of UC, at the time of WMT, according to clinical and endoscopic Mayo score respectively, with 83.3% of them classified as E1, E2 for UC extension. Mild AEs occurred in 10% (3/30), including mild abdominal pain and fever, all of them were self-limiting, with no serious adverse events.

Characteristics	Results
Age, years, mean ± SD	41.83 ± 17.3
Male Gender, n (%)	18 (60%)
BMI, mean ± SD	20.29 ± 3.23
Mayo clinical score before WMT, mean ± SD	5.20 ± 2.89
Mild	13 (43.3%)
Moderate	16 (53.3%)
Severe	1 (3.4%)
Mayo endoscopic score before FMT, mean ± SD	1.77 ± 0.88
Mild	16 (53.3%)
Moderate	9 (30%)
Severe	5 (16.7%)
Extension of UC, n (%)	
E1, proctitis	12 (40%)
E2, left-sided colitis	13 (43.3%)
E3, pancolitis	5 (16.7%)
Treatment history, n (%)	
5-ASA	26 (86.7%)
Corticosteroid	9 (30%)
Immunosuppressants	1 (3.3%)
Anti-TNF antibody	2 (6.7%)

Table 1.

Conclusion: WMT appears to be a safe and promising therapy for UC patients, taken into consideration the location, clinical and endoscopic severity of UC. Using DEA method to evaluate the impact of clinical factors on FMT could help to identify UC patients who are more likely to response to this therapy.

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P0472 WITHDRAWN

P0473

INTERLEUKIN-23 AND INTERLEUKIN-12/23 INHIBITORS FOR THE TREATMENT OF CROHN'S DISEASE: SYSTEMATIC REVIEW AND META-ANALYSIS

S.K. Vuyyuru^{1,2}, V. Solitano³, M. Hogan¹, J.K. MacDonald¹, A. Zayadi¹, C.E. Parker¹, N. Narula⁴, S. Singh⁵, B.G. Feagan^{1,2,6}, C. Ma⁷, V. Jairath^{1,2,6}

¹Alimentiv Inc., London, Canada, ²Western University, Department of Medicine, Division of Gastroenterology, London, Canada, ³Humanitas University, Department of Biomedical Sciences, Emanuele, Italy, ⁴McMaster University, Department of Medicine (Division of Gastroenterology) and Farncombe Family Digestive Health Research Institute, Hamilton, Canada, ⁵University of California, San Diego, Division of Gastroenterology, Department of Medicine, La Jolla, United States, ⁶Western University, Department of Epidemiology and Biostatistics, London, Canada, ⁷University of Calgary, Division of Gastroenterology and Hepatology, Departments of Medicine & Community Health Sciences, Cumming School of Medicine, Calgary, Canada

Contact E-Mail Address: sudheer.kumar@alimentiv.com

Introduction: Interleukin-23 (IL-23) is a key inflammatory mediator implicated in the pathogenesis of Crohn's disease (CD). We assessed the efficacy of selective IL-23 and IL-12/23 inhibitors in patients with moderate-to-severe CD.

Aims & Methods: MEDLINE, Embase, and the Cochrane library (CENTRAL) were searched from inception to October 2021 for randomized, placebo- or active comparator-controlled induction and/or maintenance trials of selective IL-23 and IL-12/23 inhibitors in pediatric and adult patients with CD. The primary outcome was the proportion of patients achieving clinical remission. Secondary outcomes were clinical response, endoscopic remission, and endoscopic response. Data were pooled using a random effects model and pooled risk ratios (RRs) and 95% confidence intervals (CIs) were calculated for each outcome.

Results: Eighteen studies (10 induction, 2 maintenance, 6 induction/maintenance) were included. Ten studies assessed IL-12/23 inhibitors (ustekinumab [UST], briakinumab [BRI], and apilimod mesylate [AM]) and eight studies assessed IL-23 inhibitors (brazikumab [BRA], risankizumab [RIS], guselkumab [GUS], and mirikizumab [MIR]).

All studies except two were placebo-controlled; in these studies, two active agents (UST vs. adalimumab) and two doses of the same agent (UST) were evaluated, respectively. Only one study included paediatric patients. Compared to placebo, UST (RR 1.89, 95% CI 1.51-2.35), RIS (RR 1.90, 95% CI 1.55-2.33), GUS (RR 3.40, 95% CI 1.77-6.54), and MIR (RR 2.94, 95% CI 1.30-6.62) were statistically superior for inducing clinical remission (Crohn's Disease Activity Index Score [CDAI] <150). BRI (RR 1.88, 95% CI 1.16-3.30), UST (RR 1.73, 95% CI 1.49-2.01), RIS (RR 1.83, 95% CI 1.56-2.16), GUS (RR 1.69, 95% CI 1.69-4.66), and MIR (RR 2.16, 95% CI 1.31-3.55) were statistically superior to placebo for induction of clinical response (100-point CDAI reduction).

Among the agents assessed for induction of endoscopic remission (UST, RIS, GUS, and MIR), RIS (RR 3.43, 95% CI 2.04-5.77) and MIR (RR 10.0, 95% CI 1.38-73.4) were statistically superior to placebo. Endoscopic response data were available for UST, RIS, GUS, and MIR. A statistically significant difference was observed between RIS (RR 2.86, 95% CI 2.16-3.79), GUS (RR 3.17, 95% CI 1.46-6.92), and MIR (RR 3.46, 95% CI 1.66-7.20) relative to placebo. Maintenance of clinical remission was assessed in five agents (BRI, UST, BRA, RIS, and AM). UST (RR 1.73, 95% CI 1.34-2.23) and RIS (RR: 1.32, 95% CI 1.07-1.63) were statistically superior to placebo for this outcome.

With respect to clinical response (100-point CDAI reduction), UST reached the level of statistical significance (RR 1.46, 95% CI 1.22-1.74) compared to placebo while single studies of AM and BRA failed to show this effect. Maintenance of endoscopic remission was assessed for three agents (BRA, UST, and RIS). RIS demonstrated statistical significance over placebo for this outcome (RR 2.67, 95% CI 1.74-4.11). Endoscopic response data were available from single maintenance studies of BRA (RR 2.02, 95% CI 0.13-30.53), UST (RR 4.17, 95% CI 0.55-31.45), and RIS (RR 2.14, 95% CI 1.57-2.93); only RIS was found to be statistically superior to placebo.

Conclusion: Drugs targeting IL-23 are effective for inducing and maintaining clinical remission in patients with moderate-to-severe CD.

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VS: has no relevant conflicts of interest to declare.

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P0474

SZN-1326, A TETRAVALENT, BISPECIFIC ANTIBODY DEVELOPED FOR THE TREATMENT OF ULCERATIVE COLITIS, HAS A FAVORABLE PROFILE IN 13-WEEK GLP TOXICITY STUDIES

A. Diep¹, J. Tibbitts¹, S. Roberts², P. Stathis¹, W. Nowatzke¹, M. Newman^{1,3}, T. Vanhove¹

¹Surrozen, Inc., Development, South San Francisco, United States,

²SAR Safety Assessment, Northbrook, United States, ³Nautilus Biotechnology (current affiliation), San Carlos, United States

Contact E-Mail Address: anh@surrozen.com

Introduction: WNT/b-catenin signaling promotes intestinal stem cell renewal which is essential for intestinal epithelial homeostasis and regeneration. There is a clear unmet need for agents that directly repair and regenerate the intestinal epithelium for the treatment of ulcerative colitis as mucosal healing has been associated with lower steroid use, reduced hospitalizations and longer-term remission. SZN-1326 is a tetravalent, bispecific antibody that binds specifically to low-density lipoprotein receptor-related protein 6 (LRP6) and Frizzled 5 (FZD5) and/or Frizzled 8 (FZD8). LRP6, FZD5 and FZD8 are expressed across many tissues, but FZD5 receptors are highly enriched on the intestinal epithelium including stem and progenitor cells.

Aims & Methods: The aims of these Good Laboratory Practice (GLP) toxicity studies conducted in Sprague-Dawley rats and cynomolgus monkeys were to evaluate the nonclinical safety and toxicokinetic profile. In both species, SZN-1326 was intravenously (IV) administered once per week for 13 consecutive weeks with a 4-week recovery period at doses of 0-, 3-, 10-, 30- and 75 mg/kg.

An additional group received 30 mg/kg SZN-1326 subcutaneously (SC) once weekly for 13 weeks. Assessments included clinical observations, clinical pathology, histopathology, toxicokinetics (TK), and immunogenicity.

Results: SZN-1326 was well-tolerated with no drug-related adverse effects observed when administered IV or SC. The No Observed Adverse Effect Level (NOAEL) was the highest dosage of 75 mg/kg/week (IV) with no SZN-1326 related adversity observed at 30 mg/kg/week (SC) in both species. Minimal, non-adverse, and reversible decreases in reticulocytes, hemoglobin, hematocrit, red blood cells and platelets and minimal increases in blood urea nitrogen (BUN) were observed in Sprague-Dawley rats. No SZN-1326-related effects in hematology, coagulation, clinical chemistry, or urinalysis were identified in the cynomolgus monkeys. The TK of SZN-1326 was consistent with monoclonal antibodies with serum exposure proportional to dose.

The estimated SC bioavailability in the rat was poor (11%) but good (55%) in the monkey. In both species, the incidence of anti-drug antibodies (ADA's) ranged from ~10 to 50% and had minimal impact on drug exposure except for rats dosed SC.

Conclusion: SZN-1326 has a favorable safety profile in 13-week rat and cynomolgus monkey GLP toxicology studies. The minimal, non-adverse, clinical pathology findings in rats were not correlated with any macro- or microscopic histopathological changes. Thus, the NOAEL is the highest IV administered dosage of 75mg/kg/dose with no SZN-1326 related adversity observed at 30 mg/kg dosed SC.

Disclosure: Current employees of Surrozen, Inc.

P0475

LONG-TERM TREATMENT PERSISTENCE OF ADALIMUMAB AND USTEKINUMAB IN BIO-NAÏVE PATIENTS WITH CROHN'S DISEASE: A RETROSPECTIVE DATABASE STUDY

A. Biščanin¹, V. Tomasic¹, F. Babić¹, P. Čačić¹, Z. Dorosulic¹, D. Kralj¹, D. Ogresta¹, D. Hrabar¹

¹Sestre milosrdnice University Hospital Center, Department of Gastroenterology and Hepatology, Zagreb, Croatia

Contact E-Mail Address: alen.biscanin@gmail.com

Introduction: Recent head-to-head studies have shown that both adalimumab (ADA) and ustekinumab (UST) are highly effective in treatment of bio-naïve Crohn's disease (CD) patients with similar rates of clinical and endoscopic remission at week 52.

On the other hand, time to treatment discontinuation was longer with UST vs ADA in post hoc analysis. Aim of this study was to provide real-world evidence on long-term comparative persistence among bio-naïve CD patients treated with ADA vs UST for a minimum period of six months.

Aims & Methods: A single-center, non interventional, retrospective cohort review study (January 2015-January 2022) was performed on real-life data of adult bio-naïve CD patients who were treated with adalimumab (160/80 mg SC at BL/W2, then 40 mg SC every 2 Ws) or ustekinumab (6 mg/kg IV at BL then 90mg SC every 12 Ws) for a minimum of 6 months. Patient characteristics were assessed using descriptive statistics.

Continuous variables were analysed using Mann-Whitney test and categorical variables using Chi-square test. Treatment persistence was assessed using Kaplan-Meier analysis and Log-rank test, while Cox proportional hazards regression model was used to identify potential independent predictors of persistence.

Results: A total of 70 bio-naïve participants with CD (47.1% male, median of age 36 (IQR 27.5)) were included in the analysis. The median of disease duration prior to biologic induction was 61 (IQR 112.5) months. Among the studied cohort, ADA was administered in 68.6% of patients. Corticosteroid usage at the start of biologic was observed in 28.6% of participants (without difference between ADA and UST group ($\chi^2(1, N=70)=0.17$, $P=0.68$)). Dose escalation was observed in 39.1% and 27.3% of ADA and UST group of patients respectively (without difference between ADA and UST group ($\chi^2(1, N=68)=0.592$, $P=0.34$)).

There was no significant difference in persistence between ADA and UST ($\chi^2(1, N=70)=0.317$, $P=0.57$). After 36 months, persistence rates for ADA and UST were 61.9% and 76.3% respectively. Statistically significant predictor (BMI, age, gender, disease duration, corticosteroid treatment during the biologic induction period, smoking status) for biologic's discontinuation wasn't found.

Conclusion: In a Croatian real-world setting, after 36 months of treatment, although persistence was numerically higher for UST versus ADA, comparable overall long-term persistence rates were observed in bio-naïve CD patients treated with ADA or UST.

Disclosure: Nothing to disclose.

P0476

MIRIKIZUMAB IMPROVES QUALITY OF LIFE IN MODERATELY TO SEVERELY ACTIVE ULCERATIVE COLITIS: IMPROVEMENT IN INFLAMMATORY BOWEL DISEASE SCORES IN PARTICIPANTS OF THE LUCENT-1 AND LUCENT-2 RANDOMIZED, DOUBLE-BLIND, PLACEBO-CONTROLLED PHASE 3 INDUCTION AND MAINTENANCE TRIALS

B.E. Sands¹, B. Feagan², T. Hunter Gible³, K.A. Traxler³,

N. Morris³, X. Li³, S. Schreiber⁴, V. Jairath⁵, A. Armuzzi⁶

¹Icahn School of Medicine at Mount Sinai, Division Of Gastroenterology, New York, United States, ²Western University, Alimentiv Inc., London, Canada, ³Eli Lilly and Company, Indianapolis, United States, ⁴University Hospital Schleswig-Holstein, Department of Internal Medicine I, Kiel, Germany, ⁵Western University, London, Canada, ⁶Humanitas University, IBD Center, IRCCS Humanitas Research Hospital, Milan, Italy

Contact E-Mail Address: bruce.sands@mssm.edu

Introduction: The inflammatory bowel disease questionnaire (IBDQ) is a measure of health-related quality of life (QoL), with higher scores indicating greater QoL. In a prior phase 2 study (NCT02589665), mirikizumab, an anti-IL23p19 antibody, demonstrated efficacy and improvement in IBDQ scores in participants with moderately to severely active ulcerative colitis (UC).¹

Aims & Methods: This analysis evaluated the effect of mirikizumab vs placebo on IBDQ scores in participants with moderately to severely active UC who had failed prior conventional or biologic therapy in a Phase 3, double-blind, 12-week induction study (LUCENT-1/NCT03518086) followed by a 40-week maintenance study (LUCENT-2/NCT03524092) for a total of 52 weeks of continuous therapy.

Participants (N=1162) in LUCENT-1 were randomized 3:1 to receive 300mg mirikizumab or placebo intravenously once every four weeks (Q4W). Participants (N=544) who achieved Modified Mayo Score Clinical Response to mirikizumab by Week 12 of induction were re-randomized 2:1 in LUCENT-2 to subcutaneous mirikizumab 200mg or placebo Q4W during the maintenance period.

Randomization was stratified by previous biologic therapy failure, baseline corticosteroid use, and region. Additionally, LUCENT-1 stratification included baseline disease activity, and LUCENT-2 included LUCENT-1 clinical remission status. The least squares mean change from baseline in IBDQ scores at Week 12 of induction and Week 40 of maintenance was determined using analysis of covariance models. Baseline was Week 0 of therapy and stratification factors and baseline scores were used as covariates. The Minimal Clinically Important Difference (MCID) was defined as an improvement of ≥16 points in the total IBDQ score (IBDQ response) and IBDQ remission as a total score ≥170 points.²

IBDQ response and remission were calculated using non-responder imputations. Treatments were compared using the common risk difference (risk diff).

Results: Mirikizumab treatment resulted in a significantly greater improvement from baseline in the IBDQ total and domain scores vs placebo at both Week 12 of induction and Week 40 of maintenance (52 weeks of treatment) (Table).

The proportions of participants who achieved an IBDQ response was significantly greater for those treated with mirikizumab vs placebo at Week 12 (risk diff = 17.1 [95% confidence interval: 10.7, 23.5]) and Week 40 (29.5 [21.0, 37.9]). Significantly greater proportions of participants receiving mirikizumab achieved IBDQ remission at Week 12 (18.1 [11.8, 24.4]) and Week 40 (28.5 [20.1, 37.0]) vs placebo (all evaluations and timepoints: p<0.001).

	IBDQ Total Score ¹		IBDQ Response ² Score Improvement ≥16		IBDQ Remission ² IBDQ Total Score ≥170	
	LSM Change from BL (SE)	LSM Diff (SE)	n (%)	Risk Diff (95% CI)	n (%)	Risk Diff (95% CI)
LUCENT-1 Week 12 of Induction						
PBO IV Q4W (N=294)	25.21 (1.80)		164 (55.8)		117 (39.8)	
Miri 300 mg IV Q4W (N=868)	38.42 (1.11)	13.21 (2.01)*	631 (72.7)	17.1 (10.7, 23.5)*	499 (57.5)	18.1 (11.8, 24.4)*
LUCENT-2 Week 40 of Maintenance (52 Weeks of Continuous Therapy) of Miri Induction Responders						
PBO SC (N=179)	24.51 (2.77)		88 (49.2)		77 (43.0)	
Miri 200 mg SC (N=365)	49.75 (2.10)	25.24 (3.09)*	289 (79.2)	29.5 (21.0, 37.9)*	264 (72.3)	28.5 (20.1, 37.0)*

Abbreviations: BL=baseline; CI=confidence interval; Diff=difference; IBDQ=Inflammatory Bowel Disease Questionnaire; IV=intravenous; LSM=least squares mean; Miri=mirikizumab; n=number of patients in the specified category; N=number of patients in the analysis population; PBO=placebo; Q4W=every 4 weeks; Risk Diff=common risk difference; SC=subcutaneous; SE=standard error

¹Inflammatory Bowel Disease Questionnaire domains and total scores were evaluated by analysis of covariance with modified baseline observation carried forward and adjustment for covariates.

²Inflammatory Bowel Disease Questionnaire-based measurements for clinical response and remission were analyzed using non-responder imputation. The common risk difference was the stratification-adjusted difference in the proportion of participants receiving mirikizumab minus the proportion of participants receiving placebo.

*p<0.001

Table. LUCENT-1 and LUCENT-2 Trials Change from Baseline in the Inflammatory Bowel Disease Questionnaire.

Conclusion: Participants with moderately to severely active UC reported significantly greater improvements in IBDQ scores at induction and maintenance with mirikizumab compared to placebo. Over 75% of participants achieved a clinically meaningful improvement in QoL, as measured by IBDQ response, at the end of the 52 weeks of mirikizumab treatment.

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P0477

LONG TERM SAFETY AND EFFICACY OF THIOPURINES WITHDRAWAL IN IBD PATIENTS

D. Shbita¹, E. Koiffman², D. Ben-Hur², M. Waterman², R. Weisshof²
¹Rappaport Faculty of Medicine, Israel Institute of Technology, Haifa, Israel, ²Rambam Medical Center, Department of Gastroenterology, Haifa, Israel

Contact E-Mail Address: dima.301@hotmail.com

Introduction: The optimal duration of thiopurine treatment for patients with inflammatory bowel disease (IBD) is unknown. Prolonged thiopurine treatment is correlated with risk of lymphoma, skin cancer and infection¹. Conversely, discontinuation of thiopurine treatment may lead to a recurrence of active inflammation².

Aims & Methods: We aimed to assess the safety of discontinuation of thiopurine treatment and discover factors that can predict the outcome of treatment cessation.

This is a retrospective study conducted in a tertiary hospital that included patients with inflammatory bowel disease who discontinued thiopurine treatment during complete clinical remission. All patients included had follow up for at least 2 years. The patients were followed until the last clinic visit or until documented disease relapse defined as requiring introduction of new therapy, dose escalation, rescue therapy with corticosteroids, hospitalization, or surgery.

A Kaplan Meier curve was used for survival analysis. In addition, a uni-variant analysis was performed to determine factors that predict recurrence. P value <0.05 was defined as statistically significant

Results: 46 patients were included in the cohort. 50% males, 80% Crohn's disease. The median age at diagnosis was 25 and at thiopurine cessation 34 (table 1). Eighty percent the patients had concomitant therapy during thiopurines termination and 10.86% had drug related adverse events. After thiopurine withdrawal, 37% of patients experienced a relapse. The median time to relapse among relapses was 15.8 months. Relapse free probability was 95.65% 6 months after treatment withdrawal, 84.7% after one year and 67.3% after 36 months.

One patient was hospitalized after thiopurines termination and two patients required surgery. Current or past smoking, IBD subtype, concomitant anti-TNF therapy, or male gender were not associated with disease relapse after univariate analysis (Hazard ratio [HR] 0.42, 95% confidence interval [CI] [0.12 -1.49], 0.21[0.02-1.62], 1.45[0.46 - 4.49], 1.02 [0.33 - 3.13], and 1.01[0.38-2.64] respectively. All not statistically significant).

Male gender, n (%)	23 (50)
IBD type	Crohn's - 37 (80.4) Ulcerative colitis - 9 (19.6)
Age at diagnosis (median), yr	25
Age at TP end (median), yr	34
Current smoker, n (%)	12 (26)
Disease behaviour Crohn's patients, (%)	inflammatory 12 (32.4) stricture 12 (32.4) penetrating 13 (35.2)
TP treatment duration (median), months	5
Drug related adverse events, n (%)	5 (10.86)
CRP, mg/dL, median (IQR)	0.5 (0.225-1.4)
Calprotectin, median (IQR)	71.9 (44-141)

Table 1: Clinical and Demographic Characteristics of the Population

Conclusion: Thiopurine discontinuation appears safe with most of the patients remaining in remission at 36 months

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P0478

A PH-SENSITIVE OPIOID PROVIDES SUSTAINED AND SAFE PAIN RELIEF BY TARGETING THE ACIDIFIED LAYERS OF THE INFLAMED COLON

C.E. Degro^{1,2}, N.N. Jiménez-Vargas¹, Q. Tsang¹, Y. Yu¹, A.E. Lomax¹, D.E. Reed¹, C. Stein³, N. Bunnett⁴, S. Vanner¹

¹Queen's University, Department of Medicine, Gastrointestinal Diseases Research Unit, Kingston, Canada, ²Charité Universitätsmedizin Campus Benjamin Franklin, Department of General and Visceral Surgery, Berlin, Germany, ³Charité Universitätsmedizin Campus Benjamin Franklin, Department of Experimental Anesthesiology, Berlin, Germany, ⁴NYU College of Dentistry, Department of Molecular Pathobiology, New York, United States

Contact E-Mail Address: claudius-erwin.degro@charite.de

Introduction: Adequate pain control during flares of inflammatory bowel disease relies mainly on opioids whose prevalent and long-term use are limited by serious side effects. Acute administration of a novel pH-sensitive opioid agonist, called NFEPP², was shown to provide analgesic effects in the inflamed acidified colon without immediate opioid typical on-target side effects³.

However, the effects of repeated application of NFEPP during the evolution of acute colitis when tissue-pH can vary remain elusive.

Aims & Methods: Acute colitis in male C57BL/6 mice was induced via 2.5% dextran sulphate sodium (DSS) dissolved in drinking water for 5 days. Mice were then randomly assigned to either vehicle, NFEPP or fentanyl treatment. NFEPP, fentanyl (each opioid at 0.4 mg/kg) and vehicle (0.5% DMSO) were administered s.c. twice daily over 5 days followed by a final injection at day 6. Visceral nociception was assessed by visceromotor responses (VMRs) to colorectal distension at different time points during acute colitis. Gastrointestinal side effects were evaluated using:

1. Oral contrast-enhanced abdominal CT-scans (before/after treatment) and defecation assessments to analyze gastrointestinal transit and functional colon motility in-vivo and;
2. Isometric tension recordings of colonic longitudinal muscle contractile activity in-vitro.

Side effects within the cardiorespiratory system were additionally analyzed based on pulse oximeter measurements.

Finally, inflammation of the colon was examined by combining histological analysis, myeloperoxidase activity assays and whole tissue pH measurements. Selective visualization of acidified microenvironments within the inflamed colon was achieved by using pH low insertion peptides (pHLIP) combined with confocal imaging.

Results: NFEPP decreased VMRs to colorectal distension over the entire course of acute DSS colitis (day 6: 40.5% reduction, $p < 0.001$, $N = 5$, compared to baseline). However, strongest VMR inhibition was observed at day 3 (66.7% reduction, $p < 0.05$, $N = 5$, compared to baseline), consistent with the peak of inflammation (MPO: 4.6 U/mg tissue, $p < 0.001$, $N = 9$; Histo-Damage-Score: 2.7, $p < 0.001$, $N = 9$; colon pH: 6.3, $p < 0.01$, $N = 5$, all compared to healthy control). Treatment with NFEPP had no effect on gastrointestinal transit (GIT: $p = 0.60$, $N = 5$, compared to baseline) and fecal output ($p > 0.99$, $N = 6$, compared to vehicle) whereas fentanyl blocked gastrointestinal motility (GIT: $p < 0.05$, $N = 6$, compared to baseline; fecal output: $p < 0.05$, $N = 6$, compared to vehicle). In-vitro colonic contractile responses induced by electrical field stimulation were reduced in fentanyl treated mice ($N = 9$) compared to NFEPP (10 Hz: $p < 0.05$, $N = 6$).

Visualization of acidified areas within the inflamed colon using pHLIP indicated a decreased pH in the mucosa/submucosa, but less signal in the muscle layer (mucosa/submucosa vs. muscle layer: $p < 0.01$, $N = 8$). These findings were in keeping with little or no effect of NFEPP on the muscle layer and thus no significant effect on colon motility.

Fentanyl reduced blood oxygen saturation (15 min: 85%, $p < 0.01$, $N = 6$, compared to baseline) and caused a sustained reduction in heart rate (60 min: Δ BPM -91.8 from baseline, $p < 0.01$, $N = 6$) at day 2 whereas NFEPP had no effect on oxygen saturation ($p > 0.99$, $N = 6$, compared to baseline) and revealed less effect on heart rate (15 min: Δ BPM -75.6 from baseline, $p < 0.01$, $N = 6$) with a recovery after 60 min ($p = 0.23$).

Conclusion: NFEPP provides in a preclinical mouse model effective and targeted analgesia throughout the course of acute colitis without altering gastrointestinal transit, colon motility and blood oxygen saturation.

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P0479

PROBIOTIC TREATMENT OF ULCERATIVE COLITIS WITH *TRICHURIS SUIS* OVA: A RANDOMIZED, DOUBLE-BLINDED, PLACEBO-CONTROLLED CLINICAL TRIAL

M.V. Prosberg¹, S.I. Halkjaer¹, B.Z.S. Lo¹, C.B. Koeser¹, J.F.K.F. Ilvemark², J.B. Seidelin², M.F. Kristiansen³, A. Kort³, T. Kallemose⁴, P.M. Bager⁵, F. Bendtsen¹, I. Nordgaard-lassen¹, H. Kapel⁶, H. Kringel⁶, C.M.O. Kapel^{7,6}, A. Petersen^{1,8}
¹Copenhagen University Hospital Amager and Hvidovre, Gastro Unit, Medical Division, Hvidovre, Denmark, ²Copenhagen University Hospital - Gentofte and Herlev, Department of Gastroenterology and Hepatology, Herlev, Denmark, ³Bispebjerg Hospital, University of Copenhagen, Digestive Disease Center, Copenhagen, Denmark, ⁴Copenhagen University Hospital Amager and Hvidovre, Clinical Research Center, Hvidovre, Denmark, ⁵Statens Serum Institut, Division of Infectious Disease Preparedness, Copenhagen, Denmark, ⁶ParaTech A/S, Horsholm, Denmark, ⁷University of Copenhagen, Department of Plant and Environmental Sciences, Frederiksberg, Denmark, ⁸Copenhagen University Hospital Amager and Hvidovre, Department of Clinical Microbiology, Hvidovre, Denmark

Contact E-Mail Address: michelle.vernstroem.prosberg@regionh.dk

Introduction: In the search for new treatment options for ulcerative colitis (UC), exposure to the porcine whipworm *Trichuris suis* ova (TSO) has previously shown a favorable immune response that may improve UC with few side effects. Large phase-2 studies on UC patients treated with TSO are needed.

Aims & Methods: A single-center, randomized, double-blinded, placebo-controlled, phase-2b clinical trial of 7500 TSO compared to placebo, initiated in 2018 and completed in 2022 at Hvidovre Hospital, Copenhagen, Denmark. Moderately active UC patients with Mayo score (MS) 6-10 and fulfilling all in- and exclusions were included from hospitals, through advertisements and referrals.

Primary aim: To demonstrate if oral administration of 7500 TSO every two weeks for 24 weeks compared to placebo could induce clinical remission ($MS \leq 2$).

Secondary aims: Clinical response defined at 24 weeks as:

- i. A reduction in MS (≥ 4 points),

- ii. Complete steroid-free clinical remission ($MS \leq 2$),
- iii. Endoscopic remission (endoscopy sub-score ≤ 1), and;
- iv. Symptomatic remission (stool frequency sub-score ≤ 1 and rectal bleeding sub-score = 0) at 12 and 24 weeks and (v) partial MS over time (week 0-24).

Main outcome measures are presented as risk ratios (RR) with corresponding confidence intervals (CI) and p-values (p).

Results: Out of 207 screened UC patients, we included 119 moderately active UC patients and randomly allocated 1:1 to receive TSO (n=60) or placebo (n=59). Here, intention-to-treat (ITT) analysis (n=119) and complete steroid-free (CSF) subgroup analysis (n=60) are presented.

Primary outcome: At week 24, clinical remission was achieved in 30% of TSO-treated patients compared to 34% of placebo-treated patients (RR=0.89; CI:0.52–1.50; p=0.80, ITT).

Secondary outcomes: At week 24, clinical response showed no differences between TSO and placebo treatment in

- i. Reduction of MS (RR=0.98; CI:0.64–1.52; p=1.00, ITT), (RR=1.19; CI:0.67–2.11; p=0.74, CSF),
- ii. Complete steroid-free clinical remission (RR=1.18; CI:0.60–2.33; p=0.83, CSF),
- iii. Endoscopic remission (RR=1.02; CI:0.68–1.54; p=1.00, ITT), (RR=1.41; CI:0.82–2.43; p=0.30, CSF), or;
- iv. Symptomatic remission (RR=1.31 at week 12; CI:0.95–1.81; p=0.15, ITT), (RR=1.21 at week 24; CI:0.78–1.86; p=0.50, ITT).

However, in the CSF analysis of symptomatic remission, patients treated with TSO were able to induce remission at week 12 (RR=2.09; CI:1.17–3.73; p=0.01) but not at week 24 (RR=1.41; CI:0.82–2.43; p=0.30) and in (v) the analysis of partial MS over time (week 0-24) the TSO group differed from the placebo group (p=0.04, ITT), (p=0.21, CSF).

Surprisingly, in the placebo group, 43% (ITT) and 41% (CSF) achieved endoscopic remission in comparison to 34% (ITT) and 33% (CSF) who achieved clinical remission at week 24.

Harms: The majority of Adverse Events (AEs), AEs=475 (210 related and 265 not related), were symptoms of UC. Of 23 Serious Adverse Events (SAEs), 12 SAEs were seen in the TSO group, all were considered not related to TSO and primarily due to aggravation of UC. Both SAEs and AEs do not raise any safety concerns.

Conclusion: Compared to placebo, TSO treatment was not superior in achieving clinical remission at week 24 in moderate UC patients or in achieving:

- i. Clinical MS reduction,
- ii. Complete steroid-free clinical remission or endoscopic remission at week 24 compared to placebo.

However, TSO treatment induced symptomatic remission at week 12 but not at week 24 and improved partial MS over time. Of notice, the study may be compromised by a high placebo effect and exposure to corticosteroids. *ClinicalTrials.gov ID: NCT03565939*.

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P0480

NEED FOR USTEKINUMAB INTENSIFICATION IN REAL LIFE CLINICAL PRACTICE

T. Argirakis¹, C. Thanos², T. Alexopoulos³, S. Vrakas¹, G. Michalopoulos², P. Karatzas³, V. Ntelis², G. Papatheodoridis³, V. Xourgias¹

¹General Hospital of Piraeus "Tzaneion", Gastroenterology Department, Piraeus, Greece, ²General Hospital of Athens "G. Gennimatas", Gastroenterology Department, Athens, Greece, ³Medical School of National and Kapodistrian University of Athens School of Health Sciences, General Hospital of Athens "Laiko", Gastroenterology Department, Athens, Greece

Contact E-Mail Address: sbrakas@yahoo.gr

Introduction: Loss of response in Ustekinumab has not been extensively studied. In the majority of cases empirical dose intensification every 4 weeks rather than therapeutic drug monitoring is used as a measure to regain response. According to several studies almost 58% of patients can regain response with this approach.

Aim of this study was the recording of the percentage of patients receiving intensified regimen of ustekinumab as well as the basic characteristics of these patients.

Aims & Methods: This is a retrospective study with recording of patients currently in Ustekinumab treatment from 3 tertiary centers. Data regarding disease extension, location, behavior, reason of intensification, duration of treatment before intensification were recorded

Results: A total of 74 patients with Crohn's disease (CD) were enrolled. 19 patients were classified as L1, 3 as L2 and 52 as L3 according to Montreal classification for disease location. Only 1 patient received Ustekinumab every 12 weeks (1.3%).

Of the 74 patients, 9 (12.1%) were on intensified dose every 4 weeks. Of the patients in need of intensification, 3 had Montreal B3, 2 B2 and 4 B1, while in terms of localization, 7 had L3 and 2 L1. The reason for intensification was partial response in 3 patients and disease exacerbation in 6 patients. The average time of need for intensification from the start of treatment was 17 months. Intensification was accompanied with corticosteroids in 8/9 patients

Conclusion: 12.1% of CD patients on Ustekinumab treatment need intensified treatment to maintain response, while only 1.2% of patients are on the 12-week dosing regimen. The majority of patients also received steroids during intensification.

Disclosure: Nothing to disclose.

P0481

IDENTIFICATION OF TARGET USTEKINUMAB LEVELS IN MAINTENANCE THERAPY IN INFLAMMATORY BOWEL DISEASE

C. McDonald¹, H. Kerr¹, E. Gibbons², A. O'Toole¹, S. Patchett¹, T. Lukose¹, G. Harewood¹, D. Cheriyan¹, O. Kelly², K. Boland¹
¹Beaumont Hospital, Gastroenterology, Dublin, Ireland, ²James Connolly Hospital, Gastroenterology, Dublin, Ireland

Contact E-Mail Address: ciaranmac53@hotmail.com

Introduction: Ustekinumab (UST), a human monoclonal antibody that binds the p40 subunit of IL-12 and IL-23, is licensed for induction and maintenance therapy of moderate to severe inflammatory bowel disease (IBD). To date, little data have been published on a potential association between ustekinumab trough concentrations and mucosal healing in order to guide treatment strategies and appropriate dosing for clinicians.

Aims & Methods: **Aim:** To identify maintenance target ustekinumab trough concentrations associated with mucosal healing and response in IBD.

Methods: This is a multicentre retrospective observational study of patients on UST for management of Crohn's Disease (CD) or Ulcerative Colitis (UC) between 2016 and 2021. Trough ustekinumab levels and antibody titres were analysed in patients on maintenance drug using a drug-tolerant assay. Mucosal response was determined using a combination of faecal calprotectin (FC), endoscopic and radiological assessments.

Mucosal response (MR) was defined as > 50% reduction in faecal calprotectin, reduction in segmental Mayo score by at least 1 Mayo point or > 50% reduction in segmental simple endoscopic score for Crohn's disease (SES-CD) score. Mucosal healing (MH) was defined as faecal calprotectin <200 µg/ml, global SES-CD score < 5 or segmental Mayo score 0-1. Median trough levels were analysed using Kruskal-Wallis test and logistic regression was used to determine sensitivity and specificity of levels predicting mucosal response.

Results: Fifty-three patients on maintenance ustekinumab were included in this study. The majority were female (64.2%) with a median age of 40 years (range 21 – 78 years). The vast majority of patients had previously been treated with a biologic (90.5%). Crohn's disease represented 88.7% (n=47) of the cohort. Disease distribution was predominantly ileocolonic (L3) (60.4%, n= 32) and 24.5% (n=13) had a history of perianal disease. Over one-third of patients (n=34, 64.2%) were on higher than standard dosing of 90 mg every 8 weeks with a highest dose of 180 mg every 8 weeks (n=1, 2%). Mean trough levels were 6.4 mcg/ml and no antidrug antibodies were detected in all 53 patients.

Patients with mucosal healing (n=32) had significantly higher mean UST levels (7.3 µg/ml, SD 6.0) compared to those with no response (1.1 µg/ml, SD 0.67; n=11, p<0.0001. The median time from induction to assessment of UST trough levels was 14 months (SD 9.95). An UST serum trough level > 2.5 µg/ml was associated with MH with a sensitivity of 100% and specificity 91% (likelihood ratio 10.7).

Similarly, MR compared with non-response identified that serum trough levels >2.5 µg/ml was associated with endoscopic improvement or > 50% reduction in faecal calprotectin (sensitivity 100%, specificity 90.5%, likelihood ratio 10.5)

Conclusion: This multi centre study demonstrates that higher ustekinumab trough levels are associated with higher levels of mucosal healing and response in a predominantly non biologic naïve population across all groups. While 15% (n=10) patients were treated with concurrent immunomodulator therapy, this had no significant impact on likelihood of achieving mucosal healing (p=0.4). The median time to UST levels from induction was 14 months. No anti- drug antibodies were detected in all 53 samples with this immunogenicity data comparing favourably with current data on anti- tumour necrosis factor (TNF) biologics.

Further prospective studies are required to correlate target maintenance trough levels and the optimal time to dose-escalate in order to improve patient outcomes, as well as the potential impact of dual biologic therapy or concurrent immunomodulator use in patients with IBD.

Disclosure: Nothing to disclose.

P0482

REAL WORLD EXPERIENCE OF USTEKINUMAB IN A WEST OF IRELAND COHORT

O. Fagan¹, V. Madhu¹, C. McGrath¹, A. Keogh¹, E. Slattery¹, M. Hussey¹

¹University Hospital Galway, Gastroenterology, Galway, Ireland

Contact E-Mail Address: olgafagan@gmail.com

Introduction: A subset of patients with IBD do not respond to USTE at standard dose of 90mg every 8-weeks. Data is lacking on the efficacy of shortening the interval between dosing and overall long term efficacy.

Aims & Methods: The aim was to evaluate the outcome of patients with inflammatory bowel disease (IBD) receiving Ustekinumab (USTE) treatment. We performed a retrospective study examining all IBD patients treated with USTE from February-2017 to February-2022. Data were obtained from electronic health records.

Results: 72 IBD patients were assessed: 74% (n=53) Crohn's disease (CD), 25% (n=18) Ulcerative colitis (UC), 1% (n=1) Indeterminate. 43% male, with a median age of 43-years (range: 17-97-years). Of those with CD, 26% (n=14) had small bowel disease, 25% (n=13) had colonic disease, 47% (n=25) ileocolonic disease and 3% (n=2) had isolated perianal disease. Amongst the CD patients, 23 patients (32%) had previous surgery. Regarding UC, 17% (n=3) had proctitis, 33% (n=6) had left sided colitis and 50% (n=9) had pancolitis. The median treatment duration was 4-months (2-36) and 21-months (2-62) for UC and CD patients respectively.

Overall, 59 patients (82%) had received at least 1 previous biologic agent and 39% (n=28) had failed 2 or more biologic agents. All patients received IV induction dosing with a median cumulative induction dose of 390mg (range 240-520mg). In all, 26% (n=19) were on immunomodulators and 35% (n=25) concomitant steroids at induction.

Clinical response at 12-weeks was seen in 85% (n=54) [19% (n=10) UC, 81% (n=44) CD]. Average Partial-Mayo-score and Harvey-Bradshaw-Index-score prior to the introduction of USTE (6.8 and 8.8) improved to 1.7 and 3.6 respectively following commencement of USTE.

Of those with a minimum of 6-months treatment duration (n=55), 85% (n=45) had sustained response. Of those with a minimum of 12-months treatment duration (n=45), 78% (n=35) have also had a sustained treatment response.

In all, 16% (n=12) of the total cohort stopped USTE therapy of which the majority (67%, n=8) had a primary non-response, 16% (n=2) had a secondary loss of response and 16% (n=2) were lost to follow-up.

Furthermore, 54% (n=7) went on to have surgery, 15% (n=2) were placed on an alternative biologic and 23% (n=3) were lost to follow-up. Of those that remained on USTE at 12-months (n=35), numerically more, 54% (n=19) underwent dose escalation compared to 42% (n=5) who failed treatment (p=0.4).

Prior biologic exposure (p=0.6), concomitant immunomodulator (p=0.3) and steroid use at the time of induction (p=0.2) were not associated with sustained response at 12 months. Interestingly, small bowel disease involvement appeared to be associated with lower response rates at 12-months amongst non-responders compared with responders (83% vs. 20%, p=0.05, 95% CI -0.064-0.01)

Amongst UC patients, 61% (n=11) have completed a minimum of 12-weeks of treatment to date, 82% (n=9) of which have had a clinical response and remain on therapy at 6-months.

Conclusion: Ustekinumab is an efficacious therapy for IBD and in particular a promising therapy for UC. Dose-escalation is a common but effective strategy in the use of USTE.

Disclosure: Nothing to disclose.

P0483

EFFICACY AND SAFETY OF ADVANCED ORAL THERAPIES FOR THE TREATMENT OF INFLAMMATORY BOWEL DISEASE: A SYSTEMATIC REVIEW AND META-ANALYSIS

V. Solitano^{1,2}, S.K. Vuyyuru^{3,1}, J.K. MacDonald¹, A. Zayadi¹, C.E. Parker¹, N. Narula⁴, L. Peyrin-Biroulet⁵, S. Danese⁶, B.G. Feagan^{1,3,7}, S. Singh⁸, C. Ma^{9,1}, V. Jairath^{1,3,7}

¹Alimentiv Inc., London, Canada, ²Humanitas University, Department of Biomedical Sciences, Emanuele, Italy, ³Western University, Department of Medicine, Division of Gastroenterology, London, Canada, ⁴McMaster University, Department of Medicine (Division of Gastroenterology) and Farncombe Family Digestive Health Research Institute, Hamilton, Canada, ⁵University Hospital of Nancy, Department of Gastroenterology and Inserm NGERE U1256, Vandoeuvre-les-Nancy, France, ⁶IRCCS Ospedale San Raffaele and University Vita-Salute San Raffaele, Gastroenterology and Endoscopy, Milan, Italy, ⁷Western University, Department of Epidemiology and Biostatistics, London, Canada, ⁸University of California, San Diego, Division of Gastroenterology, Department of Medicine, La Jolla, United States, ⁹University of Calgary, Division of Gastroenterology and Hepatology, Calgary, Canada

Contact E-Mail Address: virginiasolitano@gmail.com

Introduction: Advanced oral small molecule therapies, including Janus kinase (JAK) inhibitors and sphingosine-1-phosphate (S1P) receptor modulators, are expanding the therapeutic armamentarium for inflammatory bowel disease (IBD).

Aims & Methods: MEDLINE, Embase, the Cochrane CENTRAL Register of Controlled Trials, conference proceedings, and trial registries were searched to October 15, 2021. Randomised, placebo-controlled trials (RCTs) of JAK inhibitors and S1P receptor modulators in adult patients with Crohn's disease (CD) or ulcerative colitis (UC) were eligible. Clinical, endoscopic, histologic, and safety outcomes were extracted and pooled using a random-effects model. Statistical heterogeneity was quantified using the I^2 statistic, with values below 50% representing low heterogeneity.

Results: A total of 25 RCTs (6 CD, 19 UC) were included. Patients were randomised to placebo (n=1685), a JAK inhibitor (tofacitinib, n=1879; peficitinib n=176; upadacitinib, n=732; TD-1473, n=31; SHR0320, n=123; filgotinib, n=1199; ritilecitinib, n=150; brepocitinib, n=152) or an S1P receptor modulator (ozanimod, n=928; etrasimod, n=214; amiselimod, n=40; and KRP203, n=17). In UC, there was a statistically significant difference in clinical (risk ratio [RR] 3.33, 95% confidence interval [CI] 2.12-5.23, $I^2=57\%$) and endoscopic remission (RR 4.05, 95% CI 2.15-7.60, $I^2=51\%$) rates at 8-10 weeks when JAK inhibitor treatment was compared to placebo. JAK inhibitor therapy was also statistically superior to placebo for induction of clinical (RR 1.91 95% CI 1.49-2.44, $I^2=66\%$) and endoscopic (RR 2.73 95% CI 1.68-4.42, $I^2=72\%$) response. For histologic remission and response, a statistically significant difference was observed when filgotinib (remission: RR 1.86 [95% CI 1.34-2.60] $I^2=0\%$) and upadacitinib (response: RR 6.76 [95% CI 2.24-20.42]) were compared to placebo. Pooled data (52-58 weeks) demonstrated that tofacitinib and filgotinib were statistically superior to placebo for maintaining clinical (RR 2.92, 95% CI 2.18-3.92, $I^2=0\%$) and endoscopic remission (RR 2.75, 95% CI 1.50-5.04, $I^2=53\%$). S1P modulator therapy was statistically superior to placebo for induction of clinical (RR 2.96, 95% CI 1.91-4.59, $I^2=0\%$), endoscopic (RR 2.39 95% CI 1.07, 5.33] $P<0.03$, $I^2=0\%$), and histologic remission (RR 2.21, 95% CI 1.48-3.32, $I^2=0\%$). In CD, pooled analyses demonstrated that there was a statistically significant difference between JAK inhibitor therapy and placebo for induction of clinical (RR 1.38, 95% CI 1.04, 1.84, $I^2=14\%$), but not endoscopic (RR 2.83, 95% CI 0.76, 10.56, $I^2=15\%$), remission. Patients with IBD were not at a statistically significantly higher risk of experiencing an adverse event when

treated with a JAK inhibitor (UC: RR 1.05, 95% CI 0.91-1.20, $I^2=63\%$; CD: RR 1.05, 95% CI 0.94-1.17, $I^2=0\%$) or an S1P receptors modulator (UC: RR 1.04, 95% CI 0.91-1.20, $I^2=0\%$; CD: RR 1.22, 95% CI 0.85-1.75), relative to placebo.

Conclusion: JAK inhibitors and S1P receptor modulators are effective for inducing clinical and endoscopic remission in UC. Filgotinib, upadacitinib, ozanimod, and etrasimod are also associated with improved histological outcomes in UC. JAK inhibitors are effective for inducing clinical remission in CD but may not provide a benefit for maintenance of remission. S1P receptor modulators do not appear to provide a benefit for induction of remission in CD. S1P receptor modulators have not been assessed for maintenance in CD. Both classes of advanced small molecules have an acceptable safety profile in IBD.

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JKM: is an employee of Alimentiv Inc.

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P0484

TOLERANCE TO ADALIMUMAB CITRATE-FREE AND CITRATE FORMULATIONS IN PATIENTS WITH INFLAMMATORY BOWEL DISEASE

B. Gros¹, P. Rodríguez Fernández², S. Marin¹, P. Soto¹, R. Medina Medina¹, J.M. Benítez Cantero¹, E. Iglesias-Flores¹
¹Reina Sofía University Hospital, Gastroenterology, Cordoba, Spain, ²University of Córdoba, Córdoba, Spain

Contact E-Mail Address: begrosal@gmail.com

Introduction: The original formulation of Adalimumab contained citrate, an inactive ingredient associated with injection-related pain. This formulation was changed onto citrate free in 2016. Adalimumab biosimilar started its commercialization in 2018, after having proved its efficacy and safety profile compared to the originator drug. Some of these new biosimilars contained citrate.

The present study aimed to analyse the tolerance compared to originator, citrate-free (ADA-CF) drug in patients with inflammatory bowel disease (IBD) in clinical remission who switched to a biosimilar containing citrate (ADA-C).

Aims & Methods: Prospective, observational and single-center study. All patients with IBD in clinical remission on ADA-CF (Humira®) for more than 3 months and switching to biosimilar ADA-C (Hyrimoz®) were included and followed-up during at least 3 months.

Primary outcome: To evaluate tolerance to ADA-C formulation after switch. Secondary outcomes: To describe the rates of drug cessation due to intolerance and associated anticipatory anxiety prior to self injecting, and to identify predictive factors of poor tolerance to the drug. Demographic data collected from hospital intranet. Visual Analogue Scale (VAS) score was used to measure pain. Telephonic interviews were performed to assess side effects after injection and anticipatory anxiety.

Results: A total of 37 patients were included, 54% women, mean age 40.3 (17-61). Baseline characteristics are shown in Table 1.

Regarding tolerance comparing ADA-CF to ADA-C formulation, pain presence was more frequent in ADA-C formulation (38% vs 73%, p<0.002). In terms of pain severity as per VAS score, ADA-CF formulation pain was mild 30% (11) or moderate 16% (6), whereas citrate formulation pain was mild 3% (1), moderate 46% (17) and severe 24% (9), p<0.001.

After having switched, 22% (8) patients expressed suffering from anticipatory anxiety prior to self-injecting compared to 3% (1) when they were on ADA-CF, p=0.016.

All the patients continued on treatment at the end of follow-up (37.3 weeks IQR (36-38.9). No differences were found in flushing after injection (16% vs 19%, p>0.05). No statistical association was found between pain and baseline characteristics of the patients.

Age at switch, years, median (IQR)	40.3 (17-61)
IBD, n (%)	
Crohn's disease (CD)	33 (89)
Ulcerative colitis (UC)	4 (11)
Extra intestinal manifestations, n (%)	7 (18.9)
Current treatment, n (%)	
Aminosalicylates	6 (16.2)
Immunosuppressant	11 (29.7)
Previous biologic treatment, n (%)	
Infliximab	15 (40.5)
Adalimumab dose at switch, n (%)	
40 mg/ every other week	36 (97.3)1 (2.7)
40 mg/weekly	

Table 1.

Conclusion: Citrate formulation of Adalimumab is associated with higher pain at the site of injection and increased anticipatory anxiety prior to self-injecting compared to citrate-free formulation. However, poorer tolerance was not related with drug cessation in the short term. Long-term follow-up would be needed to confirm these results.

Disclosure: Nothing to disclose.

P0485

POTENTIAL OF HIGH-ACETATE PRODUCING SACCHAROMYCES BOULARDII TO ATTENUATE INFLAMMATION IN DSS-INDUCED COLITIS

S. Deleu¹, B. Trindade de Carvalho², I. Jacobs³, K. Arnauts^{1,4}, L. Deprez¹, E. Vissers¹, G.R.B. Huys^{5,6}, J. Thevelein^{2,6,7}, J. Raes^{5,6}, S. Vermeire^{1,8}
¹KU Leuven, Department of Chronic Diseases, Metabolism & Ageing (CHROMETA), Leuven, Belgium, ²Erasmus High School, Novelyeast bv, Open Bio-Incubator, Brussels, Belgium, ³KU Leuven, Department of Microbiology, Immunology and Transplantation, Allergy and Clinical Immunology Research Group, Leuven, Belgium, ⁴KU Leuven, Department of Development and Regeneration, Stem Cell Institute Leuven, Leuven, Belgium, ⁵Rega Instituut, Department of Microbiology and Immunology, Leuven, Belgium, ⁶VIB, Center for Microbiology, Leuven, Belgium, ⁷KU Leuven, Laboratory of Molecular Cell Biology, Institute of Botany and Microbiology, Leuven, Belgium, ⁸University Hospital Leuven, Dept. of Gastroenterology, Leuven, Belgium

Contact E-Mail Address: sara.deleu@kuleuven.be

Introduction: Short-chain fatty acids, including acetate and butyrate, have gained interest as potential therapeutic targets in inflammatory bowel diseases. Of these, butyrate has been most extensively studied primarily due to its anti-inflammatory properties. Acetate might be of additional interest due to its lower toxicity and cross-feeding potential with butyrate-producing bacteria. In fact, the beneficial effects of acetic acid production by *Saccharomyces cerevisiae* var. *boulardii* (*Sb*) for its antimicrobial potency have been shown by Offei et al. (2019).

To evaluate the importance of its acetic acid production for attenuation of inflammation in colitis, several *Sb* strains with different acetate production levels have been constructed. Hence, the aim of this pre-clinical study was to evaluate the effect of genetically modified *Sb* strains with different levels of acetate production in a DSS-induced mice model of colitis.

Aims & Methods: Nine week old female C57/BL6 mice (N=120) were allocated to 12 treatment groups receiving either regular drinking water or 2.75% DSS in combination with PBS, Baker's yeast (non-probiotic control), SDH1, a non-acetate producing *Sb* strain, ENT, the *Sb* Enterol strain with transient acetate production (probiotic control), SbP, a high acetate producing *Sb* strain (5 g/L) and ENT3, a super high acetate producing *Sb* strain (8.5 g/L). Disease activity including weight loss, diarrhoea and the presence of occult blood was scored daily.

On day 7, the DSS groups were transferred to regular drinking water and on day 14 mice were sacrificed and blood was collected for cytokine and chemokine analysis with Mesoscale's pro-inflammatory panel 1. Statistics were performed using GraphPad Prism 9 (One-way ANOVA for parametric data and Kruskal-Wallis tests for non-parametric data).

Results: Disease activity, determined by the area under the curve, was significantly lower for strain SbP compared to PBS and Baker's yeast (p=0.015 and p=0.011 respectively). Remarkably, *Sb* strain SDH1 showed significantly higher disease activity compared to the *Sb* strains ENT (p=0.0009), SbP (p<0.0001) and ENT3 (p=0.0001). At sacrifice, the colon weight/length-ratio was borderline significantly decreased with for ENT and SbP compared to the *Sb*SDH1 strain (p=0.06 and p=0.08 respectively).

Moreover, macroscopical damage scores were significantly lower for SbP ($p=0.002$) and ENT3 ($p=0.02$) compared to Sb SDH1. Additionally, these damage scores for SbP were significantly lower than PBS ($p=0.048$) and Baker's yeast ($p=0.033$). Significantly lower IL1 β , IL2 and IL4 concentrations for SbP and ENT3 compared to Sb SDH1 and ENT were observed (all $p<0.05$). In contrast, IL10, TNF α and KC/GRO were significantly lower for the DSS subgroups on Sb SDH1 and ENT compared to DSS subgroups on SbP and ENT3, and even to DSS+PBS for IL2 and 4 (all $p<0.05$).

Finally, compared to PBS no differences (all $p>0.05$) were observed between groups of healthy mice for disease activity, colon weight/length ratio and macroscopical damage score.

Conclusion: Engineered high acetate producing *Sb* strains showed a trend towards improved attenuation of DSS-induced colitis compared to the parent *Sb* strain on disease activity. Unexpectedly, the engineered *Sb* strain, that did not produce acetate at all, increased inflammation.

Moreover, a mixed pro-inflammatory serum profile was observed potentially pointing in the direction of another mechanism based on acetate accumulation. Furthermore, healthy mice did not show side effects indicating the strains to be safe. Thus, our data indicate a role for *Sb*-produced acetate in attenuating inflammation.

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Carvalho Bruna: Inventor on a patent application (EP 22153700.4.) that has been submitted by VIB on the commercial exploitation of the results.

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P0486

VEDOLIZUMAB SUBCUTANEOUSLY: REAL-WORLD DATA BEFORE AND AFTER SWITCH IN IBD PATIENTS - A HESSIAN COHORT

A. Kubesch¹, N. Kruse¹, Ü. Balaban², K. Stratmann¹, K. Sprinzl¹, A. Dienethal¹, M. Knabe¹, T. Krause³, S. Zeuzem¹, I. Blumenstein¹

¹University-Hospital Frankfurt, Department of Internal Medicine 1, Frankfurt am Main, Germany, ²University Hospital, Goethe University, Institute of Biostatistics and Mathematical Modeling, Frankfurt am Main, Germany, ³Gastroenterologie Opernstraße, Private Banking, Kassel, Germany

Contact E-Mail Address: alica.kubesch@kgu.de

Introduction: Vedolizumab (VDZ) for subcutaneous injection have been approved for use in Europe in 2020. Good efficacy and tolerability have been proven in the pivotal trials. However, real-world data on the subcutaneous of VDZ are scarce.

Aims & Methods: We therefore aimed to determine treatment adherence and efficacy of IBD patients in remission and with residual disease activity at the time of the switch. Patients treated for IBD in a tertiary care centre and an outpatient clinic from 07/2020 to 12/2021 were retrospectively analysed.

Laboratory parameters and data on treatment adherence were collected via the electronic patient file. Vedolizumab trough levels concentrations as well as disease activity after switch from intravenous to subcutaneous injections was monitored. Patients were followed up until week 20.

Results: One hundred and three patients were included. Forty-five patients were female (44.6%), 60 patients (58.3%) were diagnosed with ulcerative colitis. Most patients with CD were previously exposed to another biologic agent and had received more Vedolizumab (VDZ) infusions prior to the switch.

Forty patients had residual disease activity at the time of the switch. We observed an increase of VDZ trough levels from baseline to week 8 and week 20 for patients in remission and with residual activity at switch.

Furthermore, we observed a significant reduction in fecal Calprotectin levels in patients with residual disease activity at switch at week 20. Vedolizumab trough level of 13.25, 17.8 and 35.15 ug/ml at baseline, week 8 and week 20 were identified to discriminate between remission and disease activity in our cohort.

Conclusion: The subcutaneous application of VDZ proved to be safe and efficient in achieving adequate trough levels and reduce disease activity even in patients with residual disease activity.

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P0487

CROHN'S DISEASE PATIENTS WITH USTEKINUMAB-INDUCED REMISSION ARE CHARACTERIZED BY HIGH BASELINE IL23 RECEPTOR EXPRESSION IN THE LAMINA PROPRIA TH1 CELLS

S. Onali¹, A. Di Petrillo¹, A. Favale¹, C. Carpineti¹, M. Cadoni¹, E. Loddo¹, M.C. Fantini¹

¹University of Cagliari, Medical Sciences and Public Health, Monserrato (CA), Italy

Contact E-Mail Address: amalia.dip@unica.it

Introduction: Crohn's disease (CD) is a chronic relapsing disorder of the gastrointestinal tract characterized by excessive inflammation sustained by the induction and expansion of Th1 and Th17 cells. IL12 and IL23 play a pivotal role in the maturation and expansion of Th1 and Th17 cells respectively¹ and Ustekinumab (UST), a fully humanized monoclonal antibody, which neutralizes both IL12 and IL23 by binding the common subunit p40, is currently used for the therapy of CD patients (pts)².

To be effective UST needs, in addition to the expression of target cytokines, the presence of cells responsive to either or both IL12 and IL23 thus implying that the expression of IL12 and IL23 receptors on inflammatory cells is a necessary condition for UST to work.

Aims & Methods: The purpose of this study was to assess the correlation between the expression of IL12 and IL23 receptors in the lamina propria mononuclear cells (LPMC) from CD pts at baseline and the clinical disease activity evaluated after 16 weeks of therapy with UST.

This is an ongoing prospective, observational, single-center open-label study. All CD pts, in regular follow-up at the UOC of Cagliari, with clinical indication to receive UST for active luminal disease were enrolled. All pts had baseline endoscopy to confirm disease activity by Simple Endoscopic Score-CD (SES-CD). LPMCs were isolated from biopsies collected from the most inflamed areas and analyzed by flow cytometry. Th1 cells were defined as: CD45+CD3+CD4+CXCR3+ CCR6-, Th17 as CD45+CD3+CD4+CCR6+ CXCR3-, Th1/Th17 as CD45+CD3+CD4+CXCR3+ CCR6+³. Innate lymphoid cells (ILCs) subsets were also analyzed. iLC1 were defined as CD45+Lin-CD127+CD161- and iLC2/3 as CD45+Lin-CD127+CD161+⁴. IL12 receptor-beta-2 (IL12Rb2) and IL23 receptor (IL23R) expression was analyzed in all the described cell populations. Results were associated with clinical response (defined as a decrease in Harvey-Bradshaw Index (HBI) by at least 3 points from baseline) and clinical remission (HBI<5) at week 16. Differences between groups were analyzed by Mann-Whitney test and statistical significance was considered for p<0.05.

Results: From April 2019 to April 2022, 12 CD pts were enrolled. One patient was not considered for analysis due to inability to obtain LPMC. 11 CD pts (M 6; mean age 51,3 yrs) were analyzed. Montreal Classification was: L1 (n=6) L2 (n=3) L3 (n=2); B1 (n=4) B2 (n=3) B3 (n=4) p(n=4). All pts were previously treated with anti-Tumor Necrosis Factor α . Median baseline SES-CD was 10 (range 5-14).

Baseline HBI and C-reactive protein (CRP; nv 0,5mg/dL) diminished at week 16 from 10.5 ($\pm$ 3.7) to 5.8 ($\pm$ 4.2) and from 13.2 ($\pm$ 26.1) to 2.9 ($\pm$ 3.5) respectively. Baseline expression of IL12Rb2 and IL23 was compared between pts who achieved remission at week 16 (i.e. remitters) and those who did not (non-remitters).

There was no difference in Th subgroups frequency between remitters and non-remitters. Similarly, IL12Rb2 and IL23R were equally expressed by Th17 and Th1/Th17 cells from remitters and non-remitters pts. In Th1 cells, IL23R expression was higher in the remitters group (18.0%) as compared to non-remitters (5.8%; p=0.009). IL12Rb2 expression in Th1 cells was similar between the groups.

Neither iLC1 and iLC2/3 frequency nor IL12Rb2 and IL23R expression in iLC1 and iLC2/3 differed between remitters and non-remitters groups of pts.

Conclusion: In CD pts treated with UST, baseline expression of IL23R in the lamina propria Th1 cells was more expressed in pts who were in remission at week 16 as compared to those who still had active disease at this time point.

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P0488

ASSESSMENT OF HISTOLOGICAL REMISSION IN PATIENTS TREATED WITH FILGOTINIB BY DIFFERENT SCORES AND CONCORDANCE WITH ENDOSCOPIC AND HEALTH-RELATED QUALITY OF LIFE OUTCOMES: POST HOC ANALYSIS FROM THE SELECTION STUDY

F. Magro^{1,2}, L. Peyrin-Biroulet³, G. Rogler⁴, A. Oortwijn⁵, H. Patel⁶, A. de Haas⁵, E. Santermans⁶, H. Ruan⁷, L. Dron⁸, B. Feagan^{9,10}
¹University of Porto, Porto, Department of Biomedicine, Unit of Pharmacology and Therapeutics, Porto, Portugal, ²São João University Hospital, Department of Gastroenterology, Porto, Portugal, ³University Hospital of Nancy, University of Lorraine, Department of Gastroenterology, Vandoeuvre-lès-Nancy, France, ⁴University of Zurich, University Hospital of Zurich, Zurich, Switzerland, ⁵Galapagos NV, Leiden, Netherlands, ⁶Galapagos NV, Mechelen, Belgium, ⁷Cytel, Toronto, Canada, ⁸Cytel, Vancouver, Canada, ⁹Alimentiv, London, Canada, ¹⁰Western University, Division of Gastroenterology, London Health Sciences Centre, London, Canada

Contact E-Mail Address: fm@med.up.pt

Introduction: Although histological remission is not a formal therapeutic target for ulcerative colitis (UC), it is acknowledged to be highly associated with improved long-term outcomes. Several histological indices, validated to different extents, are available, including Nancy Index (NI), Robarts Histopathology Index (RHI) and Geboes score (GS). In these *post hoc* analyses of patients treated with filgotinib (FIL; an oral, once-daily preferential JAK1 inhibitor) or placebo (PBO) in SELECTION, we evaluated histological remission by derived NI, RHI and continuous GS, as well as measured categorical GS histological remission, and assessed the concordance between endoscopic/Inflammatory Bowel Disease Questionnaire (IBDQ) outcomes and categorical GS remission. In addition, we evaluated the correlation between endoscopic/IBDQ scores and continuous GS.

Aims & Methods: SELECTION (NCT02914522) was a phase 2b/3 double-blind, randomized, PBO-controlled trial assessing the efficacy and safety of FIL in patients with moderately to severely active UC.¹ Patients were randomized at baseline to receive FIL 200 mg (FIL200), FIL 100 mg (FIL100) or

PBO through to week 10 (induction). Induction responders were re-randomized to their assigned FIL dose ('FIL200-FIL200' or 'FIL100-FIL100') or PBO ('FIL200-PBO' or 'FIL100-PBO') through to week 58 (maintenance). SELECTION reported outcomes of categorical GS remission, endoscopic remission (Mayo endoscopic subscore [MES]=0), endoscopic response (MES=0 or 1) and IBDQ remission (IBDQ total score >170) at weeks 10 and 58.

In these *post hoc* analyses categorical GS² was converted to continuous GS, RHI and NI.³ Rates of histological remission (defined as: NI=0; RHI ≤3; categorical GS=2a ≤1.1, and 0 for grades 2b, 3.0, 4.0 and 5.0; continuous GS ≤6) in each treatment arm were reported at weeks 10 and 58. Concordance between endoscopic/IBDQ outcomes and categorical GS remission was assessed using baseline, week 10 and week 58 data from all treatment arms combined. Spearman's rank correlation coefficient (R_s) was used to quantify the correlation of MES (0–3) and IBDQ total score (32–224) with continuous GS (0–22). No imputation of missing data was used.

Results: Rates of histological remission, endoscopic response and remission, and IBDQ remission at weeks 10 and 58 for each treatment arm are shown in Table 1.

Endoscopic response and IBDQ remission showed higher negative predictive values (NPVs) than positive predictive values (PPVs) for categorical GS remission. The correlation between MES and continuous GS was $R_s=0.55$, and between IBDQ total score and continuous GS was $R_s=-0.34$.

Outcome measure	Induction (week 10)			Maintenance (week 58)			
	FIL200 (n=469)	FIL100 (n=518)	PBO (n=249)	FIL200– FIL200 (n=143)	FIL200– PBO (n=41)	FIL100– FIL100 (n=101)	FIL100– PBO (n=40)
Proportion of patients achieving histological remission, %							
Categorical GS ^a (measured)	29.4	20.3	14.5	53.1	31.7	47.5	40.0
NI=0 (derived measure)	29.4	20.3	14.5	53.1	31.7	47.5	40.0
RHI ≤3 (derived measure)	35.4	26.8	20.4	59.2	36.6	54.0	45.0
Continuous GS ≤6 (derived measure)	21.5	14.5	8.0	42.7	26.8	40.6	30.0
Proportion of patients achieving endoscopic and IBDQ outcomes, %							
MES=0	8.3	4.3	3.2	20.3	14.6	22.8	17.9
MES=0–1	26.9	21.1	16.1	53.8	36.6	45.5	43.6
IBDQ total score >170	50.6	38.9	26.7	76.9	63.4	74.3	77.5
Concordance between outcomes of interest and categorical GS remission^a							
Outcome measure	Sensitivity ^b , % (95% CI)	Specificity ^c , % (95% CI)	Positive predictive value ^d , % (95% CI)	Negative predictive value ^e , % (95% CI)	Accuracy ^f , % (95% CI)		
Endoscopic remission	21.7 (18.2–25.5)	99.0 (98.5–99.4)	82.1 (74.5–88.2)	85.6 (84.2–86.9)	85.4 (84.1–86.7)		
Endoscopic response	56.6 (52.2–61.0)	94.0 (93.0–94.9)	66.7 (62.1–71.2)	91.1 (89.9–92.2)	87.4 (86.2–88.6)		
IBDQ remission	59.8 (55.4–64.1)	78.2 (76.5–79.8)	37.1 (33.7–40.5)	90.1 (88.7–91.3)	74.9 (73.3–76.5)		

95% CIs were calculated using the Clopper–Pearson method.

^aDefined as GS=2a ≤1.1, and scores of 0 for grades 2b, 3.0, 4.0 and 5.0.

^bSensitivity=TP/(TP+FN).

^cSpecificity=TN/(TN+FP).

^dPositive predictive value=TP/(TP+FP).

^eNegative predictive value=TN/(TN+FN).

^fAccuracy=(TP+TN)/(TP+TN+FP+FN).

TP defined as outcome measure giving remission when categorical GS status is remission.

TN defined as outcome measure not giving remission when categorical GS status is not remission.

FP defined as outcome measure giving remission when categorical GS status is not remission.

FN defined as outcome measure not giving remission when categorical GS status is remission.

CI, confidence interval; IBDQ, inflammatory bowel disease questionnaire; FIL100, filgotinib 100 mg; FIL200, filgotinib 200 mg; FN, false negative; FP, false positive; GS, Geboes score; MES, Mayo endoscopic subscore; NI, Nancy Index; PBO, placebo; RHI, Roberts Histopathology Index; TN, true negative; TP, true positive.

Table 1. Outcome measures at week 10 and 58, and concordance between outcomes of interest and categorical GS remission.

Conclusion: FIL200 was efficacious in inducing and maintaining histological remission. Absence of IBDQ remission and endoscopic remission were associated with absence of histological remission, with high NPVs.

Nevertheless, the lower PPVs than NPVs suggest the need for histological assessment even when endoscopic and health-related quality of life improvements are achieved, as disease activity may still be present.

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P0489

EFFECTIVENESS OF POLYMERIC EXCLUSIVE ENTERAL NUTRITION AS AN ADJUNCT TO STANDARD OF CARE IN PATIENTS WITH ACUTE SEVERE ULCERATIVE COLITIS

L. Willmann¹, K. Tognolini¹, D. Subhakaran¹, H. Kuo¹, J. Edwards¹, A. Dorrington¹, D. Shukla¹, N. Ishaq¹, H. Moattar¹, M. Bhullar¹, P. Kakkadasam Ramaswamy¹, W. Mohsen¹

¹Gold Coast University Hospital, Department of Digestive Health, Southport, Australia

Contact E-Mail Address: lawillmann@gmail.com

Introduction: Intravenous corticosteroids (IVCS) are the mainstay of treatment in acute severe ulcerative colitis (ASUC) patients. Exclusive enteral nutrition (EEN) with a semi-elemental formula has been shown to enhance corticosteroid responsiveness in ASUC patients.¹The effectiveness of polymeric EEN in ASUC has not been studied.

Aims & Methods: Aim: To assess the effectiveness and tolerability of polymeric EEN as an adjunctive therapy to current standard of care (SOC) in ASUC patients.

Methods: Between September 2021 - March 2022, 21 consecutive adults hospitalized with ASUC (meeting Truelove and Witts' criteria) received 7 days of polymeric EEN (Ensure Plus) in addition to current SOC. Outcomes were compared to a historical SOC cohort of 38 patients (admitted 2016 - 2020) matched for sex, disease extent, smoking status, biologic and steroid use prior to admission, and number of additional Truelove and Witts' criteria present.

The primary outcome was corticosteroid failure defined as requiring medical rescue therapy or colectomy. The decision to initiate rescue therapy was made at the treating physician's discretion as per international guidelines.

Results: A total of 59 patients were included (EEN n = 21, SOC n = 38). Female gender [EEN: 11 (52.4%), SOC: 21 (55.3%), $P = 1$], median age [EEN: 35 years (IQR 26-41), SOC: 29 years (IQR 24-43), $P = 0.59$] and median disease duration [EEN: 0.9 years (IQR 0-3.1), SOC: 0.9 years (IQR 0.1-5), $P = 0.76$] were similar in both groups. In the EEN group, 15/21 (71.4%) failed to respond to IVCS and required rescue therapy in comparison to 16/38 (42.1%) patients who required rescue therapy in the historical SOC group, $P = 0.029$ [crude RR 1.69 (95%CI 1.07-2.68), crude OR 3.43 (95%CI 1.11-10.51), NNT(harm) 3.41 (95%CI 1.82- 26.43)].

However, after adjusting for sex, disease duration, disease extent, smoking status and current biologic use, the adjusted OR 3.49 (95%CI 0.52-23.37, $P = 0.17$) and the adjusted RR 2.13 (95%CI 0.71-6.43, $P = 0.536$) were not statistically significant. In the EEN group, patients received medical rescue therapy with infliximab (n = 12, 80%), ciclosporin (n = 1, 6.6%), and tofacitinib (n = 2, 13.3%).

None of the patients underwent direct colectomy. In the SOC group, mode of rescue therapy was infliximab (n = 14, 87.5%), ciclosporin (n = 1, 6.25%), and colectomy (n = 1, 6.25%). The total 7 day course of EEN was completed by 19/21 (90%) patients, and 2 patients discontinued EEN treatment (1 due to abdominal discomfort, 1 due to palatability). Stool frequency, CRP and albumin levels on days 3 and 7, and length of hospital stay, did not significantly differ between the groups.

	Total Admissions N=59	EEN N=21	SOC N=38	p value
Median duration of hospital stay (IQR), days	8 (6-10)	8 (7-10)	8 (6-10)	0.63
Disease Extent, n (%)				
Left sided colitis	5 (8.5%)	2 (9.5)	3 (7.9)	1
Pancolitis	54 (91.5%)	19 (90.5)	35 (92.1)	
Oral steroids prior to admission, n (%)	16 (27.1)	6 (28.6)	10 (26.3)	1
Current biologic use, n (%)	16 (27.1)	7 (33.3)	9 (23.7)	0.54
Median stool frequency at admission, n (IQR)	10 (8-15)	10 (8-12)	10 (8-15)	0.34
Median CRP at admission (IQR), mg/L	53 (30-117)	53 (35-152)	56 (28-106)	0.89
Median serum albumin at admission (IQR), g/L	32 (28-36)	30 (27-34)	33 (29-37)	0.20
Median admission Calprotectin (IQR), mcg/g	2500 (1600-3800)	2300 (1600-3500)	2600 (1600-5900)	0.54
Median UCEIS score at admission	5 (4-6)	5.5 (5-6)	5 (4-6)	0.41

Table: Clinical, biochemical and endoscopic parameters between the two groups (on admission and during hospital stay).

Conclusion: Polymeric EEN is well tolerated in patients with ASUC. More patients in the EEN group failed to respond to IVCS and required medical rescue therapy as compared to the SOC group. Further randomized controlled studies are required to determine the benefit of polymeric EEN as an adjunctive therapy to standard of care in ASUC.

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P0490

OPIOID EXPOSURE IN IBD AND ASSOCIATED FACTORS:

A UK PROSPECTIVE MULTICENTRE AUDIT OF 1362 PATIENTS

S. Baillie¹, R. Pollok², C.A. Lamb³, A. Fraser⁴, N. Kennedy⁵, J.K. Limdi⁶, N. Fumis⁷, G. Parkes⁸, G. Scott⁹, M. Smith¹⁰, T. Raine¹¹, A. Nicolaou¹², K. Barrett¹³, A. Bassi¹⁴, C. Selinger¹⁵

¹National Health Service, Gastroenterology, London, United Kingdom, ²St Georges Hospital, Gastroenterology, London, United Kingdom, ³Newcastle University, Newcastle, United Kingdom, ⁴University Hospitals Bristol Gastroenterology, Gastroenterology, Bristol, United Kingdom, ⁵Royal Devon & Exeter Hospital, Exeter, United Kingdom, ⁶The Pennine Acute Hospitals NHS Trust, Gastroenterology, Bury, Greater Manchester, United Kingdom, ⁷Cardiff and Vale UHB, Cardiff, United Kingdom, ⁸The Royal London Hospital, London, United Kingdom, ⁹Kent & Canterbury Hospital, Canterbury, United Kingdom, ¹⁰University Hospital of Sussex, Brighton, United Kingdom, ¹¹Cambridge University Hospital NHS Foundation Trust, Gastroenterology, Cambridge, United Kingdom, ¹²St Georges Hospital, London, United Kingdom, ¹³Central London Community NHS Trust, London, United Kingdom, ¹⁴St Helens and Knowsley NHS Trust, St Helens, United Kingdom, ¹⁵Leeds Teaching Hospitals NHS Trust, The Leeds Gastroenterology Institute, Leeds, United Kingdom

Contact E-Mail Address: s.baillie1@nhs.net

Introduction: Opioid exposure in inflammatory bowel disease (IBD) is associated with premature mortality, yet exposure in IBD increasing. International guidelines have been introduced to rationalise opioid use. While opioids may improve acute pain, long term exposure is rarely beneficial and is associated with side effects. We conducted a multicentre audit aiming to evaluate opioid use and associated factors in patients with IBD.

Aims & Methods: Data were collected from consecutive patients (Oct 21-Mar 22) attending IBD clinics at 12 hospitals across most regions of the UK. Opioid exposure (>2 weeks in the past 12 months), associated factors and concurrent medical management were assessed and analysed.

Results: Of 1362 individuals, 53.0% were female, the median age range was 41-45 yrs and 47.8% had Crohn's disease (CD). Opioid exposure occurred in 11.7% of individuals with 5.0% of the overall cohort reporting IBD as the indication. In the whole cohort 7.8% received codeine and 3.5% strong opioids. Within the opioid exposed group the total number of opioid medications that an individual received was ≥ 3 in 3.3%, 2 in 11.2% and 1 in 85.5%. Antidepressants, gabapentinoids and/or NSAIDs were co-prescribed in 39.7% of those exposed to opioids.

In the opioid exposed group 43% of patients believed they were taking opioids primarily for IBD. Of these 30.8% did not have an objective disease assessment with imaging or colonoscopy in preceding year. Those with objective assessment had evidence of active inflammation in 72.3%, evidence of scarring/adhesions in 17.0% and no evidence of either in

10.6%. Among opioid-exposed patients, 65.8% had comorbidities and ≥ 2 in 15.5% patients. Musculoskeletal (MSK) disease was the most common co-morbidity (62.5%), of which 31.2% had inflammatory arthritis.

Factors associated with opioid exposure on multivariable regression analysis were previous surgery (RR 2.56 [95% CI 1.75-3.74]), while UC (versus CD RR 0.45 [95%CI 0.30-0.67]) and male sex (versus female RR 0.45 [95% CI 0.32-0.65]) were associated with less opioid exposure. Age and disease duration were not associated with opioid exposure.

Pain services reviewed 25% of opioid-exposed patients. We observed significant variations by site with referral rates to pain services ranging from none to 100%. Opioid weaning was attempted in 43% of cases only.

Conclusion: In an analysis of unselected IBD patients attending clinic, just over one tenth had been exposed to opioids in the past year. Co-existent MSK co-morbidities were common, other factors associated with opioid exposure included a diagnosis of CD, female sex, previous surgery. Referral to pain services varied between sites and opioid weaning was attempted in less than half of cases. IBD services should aim to identify patients at risk of opioid exposure, reducing exposure when possible and help to access alternative and more effective pain management solutions.

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P0491

ORAL IRON THERAPY WITH IRON MALTOL VERSUS FERROUS SULPHATE IN INFLAMMATORY BOWEL DISEASE: INTRA-INDIVIDUAL COMPARISON INDICATES LEVEL PEGGING ON INCREASE IN PLASMA HEPcidIN LEVELS

M.C. Wittker¹, K. Farrag^{2,3}, O. Schröder^{2,3}, A. Aksan^{2,4}, J. Stein^{2,3,5}

¹Philipps University, Marburg, Germany, ²Interdisciplinary Crohn-Colitis Centre Rhein-Main, Frankfurt am Main, Germany, ³DGD Clinics Sachsenhausen, Department of Gastroenterology and Clinical Nutrition, Frankfurt am Main, Germany, ⁴Justus-Liebig University, Institute of Nutritional Science, Giessen, Germany, ⁵Institute of Pharmaceutical Chemistry, Goethe University, Frankfurt am Main, Germany

Contact E-Mail Address: farrag@gmx.de

Introduction: Current anaemia guidelines for patients with inflammatory bowel disease (IBD) recommend oral rather than intravenous iron therapy unless patients have severe anaemia, active inflammation or intolerance to oral iron (OI). In IBD, however, OI causes gastrointestinal side-effects and iron absorption is often poor.

Moreover, OI supplements induce an increase in plasma hepcidin that persists for 24h, which impairs iron absorption from supplements given later the same or the next day.

Aims & Methods: We aimed to measure and compare changes in hepcidin levels for 4h following ingestion of oral ferrous vs. ferric iron and to consider implications for the optimisation of OI dosing to maximise intestinal absorption. A comparative, single-centred, open clinical trial with cross-over design was conducted. Diagnosis of anaemia was based on WHO definitions: Hb<13g/dL for men and <12g/dL for women. Iron deficiency was defined as ferritin <100 mg/L, CRP ≥ 5 mg/L and Hb > WHO cut-offs. Plasma CRP level ≥ 5 mg/dL was taken as evidence of inflammation.

To evaluate iron absorption capacity, patients took two oral absorption tests two weeks apart: at the first study visit, with iron(II)-glycine-sulphate complex (Ferro sanol®) and at the second visit, with iron(III)-maltol (Feracru®), or vice-versa. The oral absorption tests took place in the morning after overnight fasting and baseline testing of plasma iron and hepcidin levels. Patients took a 30mg iron tablet, and blood was drawn after 60 and 120 min. After a very low-iron lunch (potato soup, bread) the same protocol was repeated. The area under the curve [AUC] for iron absorption

was calculated for 60 and 120 min from a.m. and p.m. baselines. Blood samples were analysed at Immundiagnostik AG Diagnostic Laboratory, Bensheim using LC/MS/MS.

Results: Of 23 IBD patients enrolled (12f/11m;11CD/12UC;45.1 $\pm$ 14.7y), 7/23(30.4%) had inflammation. After the 1st administration, a significant increase in plasma iron was detected compared to baseline, even in patients with inflammation, in both ferrous sulphate and iron maltol groups ($p<0.001$). In the afternoon, after the 2nd iron dose, plasma iron increased insignificantly in the iron maltol group ($p=0.538$), while it decreased significantly in the ferrous sulphate group ($p=0.011$). Iron absorption capacity a.m. ($p=0.644$) and p.m. ($p=0.280$) were not statistically different in the two groups. In both the ferrous sulphate and the iron maltol groups, plasma hepcidin values were significantly increased at p.m. baseline prior to the second iron dose ($p<0.001$). Whereas in the morning, plasma hepcidin levels correlated negatively with iron absorption capacity independent of inflammatory status (-0.408 , $p<0.05$), in the afternoon, since both groups showed no increase in plasma iron, there was no significant correlation (-0.253 , $p=0.130$).

Conclusion: Both ferrous sulphate and iron maltol resulted in an increase in plasma hepcidin levels, thus impairing iron absorption after the second daily dose. In IDA, the intake of oral iron supplements leads to an acute hepcidin increase for 24 hours - regardless of whether ferric(III) or ferrous(II) iron is ingested, and even if hepatic hepcidin expression is strongly suppressed by iron deficiency and erythropoietic drive. Alternate day dosing of oral iron supplements in anaemic IBD patients may be preferable.

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P0492

THE BENEFICIAL EFFECTS OF INCREASING DIETARY FIBER CONSUMPTION ON CLINICAL FLARE AND INFLAMMATORY MARKERS AMONG PATIENTS WITH CLINICALLY QUIESCENT INFLAMMATORY BOWEL DISEASE: A PROSPECTIVE LONGITUDINAL STUDY

P. Sathirawich¹, O. Sattayalertyanyong¹, P. Pramyothin², I. Thaisittikul³, N. Pausawasdi¹, R. Sarasak², P. Phaophu¹, N. Subdee¹, S. Manatsathit¹, P. Charatcharoenwittaya¹, J. Limsrivilai¹

¹Siriraj Hospital, Mahidol University, Division of Gastroenterology, Department of Medicine, Bangkok, Thailand, ²Siriraj Hospital, Mahidol University, Division of Nutrition, Department of Medicine, Bangkok, Thailand, ³Siriraj Hospital, Mahidol University, Department of Microbiology, Bangkok, Thailand

Contact E-Mail Address: phalat_s@hotmail.com

Introduction: The effect of dietary fiber on inflammatory bowel disease (IBD) is less well defined. This prospective longitudinal study aimed to determine the effect of dietary fiber intake on clinical relapse rate and changes in fecal calprotectin levels in clinically quiescent IBD patients.

Aims & Methods: Sixty-one IBD patients were included, comprising 23 Crohn's disease patients and 38 ulcerative colitis patients. Clinical manifestations and nutritional habits were evaluated at the beginning of the study and weeks 6th, 18th, 30th, 48th, and 54th. Fecal calprotectin was measured at baseline, and weeks 6th, 30th, and 54th. Fecal microbiota was measured at baseline, weeks 6th and 54th or the time that clinical flare was noticed. A nutritionist counseled all participants to increase their dietary fiber consumption and interviewed with a food questionnaire at each visit.

Furthermore, dietary intake was assessed with food photographs taken three days a week before each appointment. A significant change in dietary fiber consumption was defined as a relative change in fiber intake of >25% from baseline. The patients were divided into three groups based on whether their fiber consumption rose, remained steady, or decreased over the follow-up period relative to their baseline. The time to clinical flare was estimated using the Kaplan-Meier method, and a log-rank test was used to compare the clinical flare rate between groups. A linear mixed model was performed to explore the correlation between fecal calprotectin and dietary fiber intake while adjusting for a follow-up visit and patient set as a random intercept.

Results: At baseline, the average dietary fiber consumption was 7.78 g/day (IQR, 5.68-11.9). During the 54-week follow-up, 20 (32.8%) patients increased their fiber intake by a mean of 3.82±2.57 g/day, 28 (45.9%) patients did not modify their fiber intake, and 13 (21.3%) patients decreased their fiber intake by a mean of 12.2±18.0 g/day. At the 54th week, the overall cumulative rate of the clinical flare was 27.7%. The cumulative clinical flare rate was significantly higher in the decreased fiber intake group than in the increased fiber intake group (60.4% vs. 16.9%, $p=0.01$).

Furthermore, increased fiber intake was associated with decreased fecal calprotectin levels; every 1 g increase in fiber intake per day was associated with a decrease in fecal calprotectin of 12.51 mg/g feces (95%CI, 1.0-24.0, $p=0.03$).

According to subgroup analyses, the effect was more pronounced in ulcerative colitis than in Crohn's disease. No significant difference in microbiota diversity change was observed across different groups of fiber intake at the end of study.

Age – mean(SD)	43.39(13.71)
Male gender	39(63.93%)
Crohn's disease : Ulcerative colitis	23(37.70%) : 38(62.30%)
Hb (g/dL) – mean(SD)	13.50(1.75)
Fecal calprotectin (mg/kg of feces) – median(IQR)	168(47-804)
Current medications	
5-ASA	49(80.33%)
Corticosteroids (≤ 10 mg of prednisolone)	23(37.70%)
Immunomodulators	45(73.77%)
Biologics	9(14.75%)

Conclusion: Increasing dietary fiber consumption is independently associated with clinical benefits in IBD patients, including a decreased likelihood of clinical flare and improvements in inflammatory markers of the disease.

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Disclosure: Nothing to disclose.

P0493

PERSONALISED AZITHROMYCIN+METRONIDAZOLE (PAZAZ), IN COMBINATION WITH STANDARD INDUCTION THERAPY, TO ACHIEVE A FAECAL MICROBIOME COMMUNITY STRUCTURE AND METAGENOME CHANGES ASSOCIATED WITH SUSTAINED REMISSION IN PAEDIATRIC CROHN'S DISEASE (CD): INITIAL RESULTS OF A PILOT FEASIBILITY STUDY

C.M. Verburgt^{1,2}, K.A. Dunn^{3,4,5}, A.R. Otley⁶, M.B. Heyman⁷, S. Verstraete⁷, W.M. Sunseri⁸, F. Sylvester⁹, T. de Meij¹, A.M. Comeau¹⁰, M. Langille¹⁰, W. de Jonge^{2,11}, M.A. Benninga¹, J. Van Limbergen^{2,1,6}

¹Amsterdam University Medical Centers - Loc. University of Amsterdam, Emma Children's Hospital, Pediatric Gastroenterology and Nutrition, Amsterdam, Netherlands, ²Amsterdam Gastroenterology Endocrinology Metabolism, University of Amsterdam, Tytgat Institute for Liver and Intestinal Research, Amsterdam, Netherlands, ³Dalhousie University, Biology, Halifax, Canada, ⁴IWK Health Centre, Pediatrics, Division of Hematology & Oncology, Halifax, Canada, ⁵Dalhousie University, Institute for Comparative Genomics, Dalhousie, Canada, ⁶Dalhousie University, Pediatrics, Halifax, Canada, ⁷UCSF Benioff Children's Hospital, University of California, Pediatrics, San Francisco, United States, ⁸UPMC Children's Hospital of Pittsburgh, Pediatrics, Pittsburgh, United States, ⁹UNC Children's Hospital, University of North Carolina, Div. of Pediatric Gastroenterology, Chapel Hill, United States, ¹⁰Dalhousie University, Integrated Microbiome Resource (IMR) and Pharmacology, Halifax, Canada, ¹¹University of Bonn, Surgery, Bonn, Germany

Contact E-Mail Address: c.m.verburgt@amsterdamumc.nl

Introduction: Early relapse in paediatric Crohn's disease (CD) is associated with more severe disease course. The microbiome may play a crucial role in disease development. We have previously shown that a Bayesian approach can predict clinical course in children with CD following the first year after diagnosis with high accuracy when ensuring samples were truly treatment-naïve. We hypothesize that directly targeting the microbiome in high-risk individuals will improve clinical response to standard of care (SOC) induction therapy in a subgroup of patients with a relapse-associated microbiome profile.

We report on initial findings on feasibility of a multicentre pilot study on different continents with treatment allocation based on stool sample results at baseline determined in Canada for all participants.

Aims & Methods: This is a 52-week, multicentre, randomised, controlled, open-label, add-on pilot study to test the feasibility of a larger trial evaluating the efficacy of adjuvant antibiotic therapy in 20 paediatric patients with mild-to-moderate-CD (10<PCDAI≤37.5). SOC induction treatment consists of the Crohn's Disease Exclusion Diet+Partial Enteral Nutrition (CDED+PEN). Relapse-associated microbiome signatures at week 0 are evaluated using 16S rRNA gene sequencing and a previously generated Bayesian predictive model from BioMiCo based on baseline stool sample results.

Patients will be allocated to treatment groups (A1,A2,B,C) depending on their disease activity and relapse-associated microbiome at week 4 (table 1). Subjects in group A2 or C will receive a combination of azithromycin 7.5mg/kg for 5 days/week for 4 weeks and 3 days/week for another 4 weeks, along with metronidazole 20 mg/kg/day for 8 weeks.

The purpose of this pilot trial is to assess feasibility of a multicentre trial on different continents with treatment allocation at week 4 based on stool sample results at baseline (16S rRNA sequencing at Dalhousie University, Canada). Primary outcomes will assess feasibility of treatment allocation and possible efficacy of add-on antibiotic treatment in children with high

risk for relapse by assessing sustained remission (PCDAI $\leq$ 10, no need for re-induction) at 52 weeks. Exploratory outcomes will include changes in PCDAI, inflammatory and microbiome markers and patient reported outcomes.

Disease activity at week 4	Relapse-associated microbiome	Treatment group	SOC induction treatment	Study intervention
Remission	Yes	A1	Crohn's Disease Exclusion Diet	n.a.
		A2		Azithromycin + Metronidazole
	No	B		n.a.
No remission	Yes / No	C		Azithromycin + Metronidazole

Table.

Results: As of April 29th 2022, 12 patients have been enrolled in The Netherlands. Baseline stool sample prediction results were available at week 4 in 11/12 patients. The one exception was due to a technical problem with the sequencing run, and final results became available at the end of week 4. Three out of 11 patients were predicted to be non-responders: one has not reached week 4 yet; one stopped CDED after 1 week due to persisting symptoms and declining to continue diet; one was not in remission at week 4 and started additional antibiotics and is now in sustained low-calprotectin remission after 26 weeks (with CDED+PEN phase 3 maintenance only).

Conclusion: Initial results of our pilot study show that allocation at week 4 based on stool sample results obtained at baseline can be feasible. Future results of this pilot study will provide on distribution of relapse-associated microbiome, inform power calculation for a larger trial, and include possible efficacy of add-on antibiotic therapy.

Disclosure: Nothing to disclose.

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EFFECTIVENESS OF USTEKINUMAB AS INDUCTION THERAPY FOR CHRONIC ANTIBIOTIC REFRACTORY POUCHITIS

A. Outtier¹, E. Louis², O. Dewit³, G. Schops¹, J. Sabino¹, B. Verstockt¹, S. Vermeire¹, M. Ferrante¹

¹UZ Leuven, Leuven, Belgium, ²CHU Liège and Liège University, Liège, Belgium, ³UCL Saint Luc, Brussels, Belgium

Contact E-Mail Address: an.outtier@uzleuven.be

Introduction: Up to 10% of patients with ulcerative colitis who undergo a proctocolectomy with ileal pouch-anal anastomosis will develop chronic antibiotic refractory pouchitis (CARP).¹

As there is a large unmet need in the management of these patients, we evaluated the efficacy and safety of induction therapy with ustekinumab (UST) for this indication.

Aims & Methods: We performed a prospective, Belgian, multicentre, open-label study of patients with CARP. Patients received a weight-range-based infusion of UST at baseline (~6mg/kg) and one subcutaneous injection of 90mg UST at week 8. The first 4 weeks, ciprofloxacin 500mg BID was added as bridging therapy, but need of antibiotics thereafter was regarded as treatment failure. Patients underwent pouchoscopy at baseline and week 16, with assessment of the modified pouchitis disease activity index (mPDAI).

The primary endpoint was the proportion of patients achieving clinically relevant steroid-free remission (mPDAI $\leq$ 5 and reduction by $\geq$ 2 points from baseline) at week 16. Secondary endpoints at week 16 were the proportion of patients achieving response (reduction of mPDAI by $\geq$ 2 points from

baseline), change in symptomatic and endoscopic mPDAI subscore, and change in C-reactive protein (CRP) and faecal calprotectin levels compared to baseline. Descriptive statistics and paired nonparametric tests (Wilcoxon signed-rank) of changes from baseline were performed.

Results: We report 22 patients (59% male, median age 42.2 years, median time after surgery 8.2 years) who were enrolled in the study. Twelve (54.5%) patients had previously been treated with biologics (anti-TNF, n=9; vedolizumab, n=7; tofacitinib, n=1) for CARP (table 1). At week 16, clinically relevant steroid-free remission was reached in 27.3% and response in 54.5% of patients.

A significant decrease in total mPDAI (8 (7-9.5) vs. 7 (4-9), $p<0.01$), clinical subscore (3 (2-4) vs. 2 (1-3), $p<0.01$), and endoscopic subscore (5 (4-6) vs. 4 (3-6), $p=0.03$) was observed at week 16. Faecal calprotectin (293 (186.3-572.3) vs. 195 (92.8-863.3) mg/kg, $p=0.63$) and CRP (4.2 (1.8-7.5) vs. 3.7 (1.8-9.5) mg/L, $p=0.82$) levels did however not decrease significantly. Three serious adverse events (hospitalization for subobstruction, worsening pouchitis and choledocholithiasis) were recorded, but were not considered related to UST.

Male, n (%)	13 (59)
Age at treatment initiation, years, median (IQR)	42.2 (32.2-52.3)
Time since colectomy, years, median (IQR)	8.2 (3.1-16.4)
Previous therapies prior to colectomy, n (%)	
Anti-TNF	15 (68.2)
Vedolizumab	5 (22.7)
Tofacitinib	3 (13.6)
Previous therapies for pouchitis, n (%)	
5ASA (topical/systemic)	6 (27.3)
Steroids (topical/systemic)	17 (77.3)
Immunomodulators	8 (36.3)
Anti-TNF	9 (40.9)
Vedolizumab	7 (31.8)
Tofacitinib	1 (4.5)
Concomitant therapy during induction, n (%)	
Steroids (topical/systemic)	3 (13.6)
Immunomodulators	1 (4.5)

Table 1. Baseline disease characteristics.

Conclusion: In this open-label pilot study in patients with CARP, induction therapy with UST showed a clinical and endoscopic effect in half of the patients, but was not associated with changes in inflammatory biomarkers. Placebo-controlled studies are needed for further positioning UST in the treatment algorithm of CARP.

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OUTCOME PREDICTORS FOR VEDOLIZUMAB THERAPY IN CROHN'S DISEASE PATIENTS IN A REAL-WORLD SETTING

S.J. Han¹, J.H. Ji¹, J. Park¹, E.-A. Kang¹, S.J. Park¹, J.H. Cheon¹, T.i. Kim¹, J.J. Park¹

¹Severance Hospital, Yonsei University College of Medicine, Internal Medicine, Seoul, Korea (Republic of)

Contact E-Mail Address: sjhan92@gmail.com

Introduction: Although vedolizumab (VDZ), a humanized monoclonal antibody against α4β7-integrin, has shown efficacy in Crohn's disease (CD), outcome data are limited in the Asian population in a real-life setting. Our study aimed to determine the predictor for clinical outcomes in patients with CD undergoing VDZ therapy in a real-life setting.

Aims & Methods: We performed a retrospective cohort study of CD patients who received VDZ therapy at a tertiary referral center in Seoul, Korea, between April 2017 and July 2021. We defined clinical remission as CD Disease Activity Index (CDAI) under 150 without concomitant corticosteroid use. Patients could keep vedolizumab treatment with or without dose optimization.

Clinical and serologic variables were included in the analysis. Each potential prognostic factor was compared using a log-rank test, and multivariate analysis was performed using cox regression.

Results: Altogether, 50 patients with CD were enrolled. The mean age of patients was 38 years, and most of the patients (98%) showed moderate disease activity. Anti-TNF naive patients were 11 (22%), and 39 (78%) have used anti-TNF in the past. At the initiation of vedolizumab, 15 patients (30%) had concomitant corticosteroids use, and 38 patients (78%) received immunomodulator therapy.

Forty-three (86%) patients achieved steroid-free remission at a median of 119 days (Interquartile range 95-382 days). The patients were treated with vedolizumab for median days of 598 days (IQR 405-1156 days). 30 patients (60%) keep VDZ treatment with median days of 1002 days (IQR 489-1470 days).

In multivariate Cox analysis for accelerated steroid-free remission, baseline CDAI score (hazard ratio [HR] 0.994, 95% CI; 0.988-1.000) and ESR (HR 0.991, 95% CI; 0.982-1.000) are significant factors for rapid remission. Whereas concomitant use of immunomodulator (HR 0.291, 95% CI; 0.116-0.732) and no hypoalbuminemia (≥3.3g/dL) (HR 0.352, 95% CI; 0.137-0.902) were associated with persistent use of vedolizumab. There was no VDZ discontinuation due to adverse drug reactions.

Conclusion: VDZ offers an effective treatment option for CD patients in real-life settings. Low baseline CDAI score and ESR are related to rapid remission. Meanwhile, concomitant use of immunomodulators and no hypoalbuminemia are associated with persistent use of VDZ in CD patients.

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P0496

FISTULOUS SKIN METASTASES IN CROHN'S DISEASE: A CASE REPORT AND REVIEW OF THE LITERATURE

T. Elger¹, H.C. Tews¹, J. Loibl¹, J. Werner², K. Drexler³, S. Haferkamp³, K. Guelow¹, C. Kunst¹, A. Kandulski¹, M. Müller-Schilling¹

¹University Hospital Regensburg, Department of Internal Medicine I, Gastroenterology, Hepatology, Endocrinology, Rheumatology and Infectious Diseases, Regensburg, Germany,

²University Hospital Regensburg, Department for Visceral Surgery, Regensburg, Germany, ³University Hospital Regensburg, Department for Dermatology, Regensburg, Germany

Contact E-Mail Address: tanja.elger@ukr.de

Introduction: Metastatic Crohn's disease is a rare disease characterized by various granulomatous skin lesions without contact to the gastrointestinal tract. Due to a lack of evidence, there is no standard of care. Therapeutic approaches include immunosuppressive agents including corticosteroids and azathioprine as well as monoclonal antibodies directed against inflammatory cytokines like TNF.

Case Report: A 29-year-old woman presented to the dermatology department of our university hospital with marked abdominal, blind-ending, subcutaneous fistulas and abscesses. Fine tissue workup revealed multiple epithelioid cell granulomas. There was no evidence of infection or rheumatologic disease such as sarcoidosis. The suspected diagnosis was metastatic Crohn's disease. The patient responded to Infliximab (monoclonal anti TNF antibody). This had to be discontinued due to an allergic reaction. Treatment with Adalimumab (monoclonal anti TNF antibody) subsequently did not result in clinical remission, and, therefore, therapy was switched to Ustekinumab (monoclonal anti IL12/IL23 antibody). An intestinal manifestation of Crohn's disease could not be detected so far.

Aims & Methods: More than 300 publications were screened for diagnostic and therapeutic approaches according to metastatic Crohn's disease.

Results: Various cases with cutaneous and genital manifestations were found in the literature review. The majority had concomitant luminal bowel involvement.

Conclusion: Metastatic Crohn's disease is a rare disorder, which is presenting with various phenotypes and thus is difficult to diagnose. Involved sites show granulomatous lesions in the histologic examinations. Treatment includes biologicals such as anti-TNF antibodies and surgical options. In our case, we have decided to treat the patient with Ustekinumab.

Disclosure: Nothing to disclose.

P0497

IN HIGHLY REFRACTORY ULCERATIVE COLITIS PATIENTS, USTEKINUMAB IS A GOOD THERAPEUTIC OPTION

A. Mínguez Sabater¹, M. Iborra¹, C. Soutullo Castiñeiras¹, M. Gimeno¹, G. Bastida¹, M. Aguas¹, E. Cerrillo¹, E. Sáez-González¹, A. Garrido¹, J. Bordetas¹, P. Nos¹

¹Hospital Universitario y Politécnico La Fe, Gastroenterology Department, Valencia, Spain

Contact E-Mail Address: alejandrosab11@gmail.com

Introduction: There are limited data in real-life of ustekinumab (USK) used in ulcerative colitis (UC). The aim of this study was to assess the effectiveness and safety in clinical practice of USK in UC in the medium and long-term.

Aims & Methods: Observational study in UC patients who received USK at the recommended dose based on weight ~6 mg/kg IV week 0.90 mg SC week 8 and maintenance 90 mg SC every 8 or 12 weeks and with 1 year of follow-up. The partial Mayo score (PMS) was used to assess clinical remission (PMS ≤ 2). The PMS, C-reactive protein (CRP) and faecal calprotectin (FC) values were recorded at baseline and after 8, 16, 24 and 52 weeks. Dose adjustment was performed by the measure of UST trough levels by ELISA, when patient lost clinical and/or biochemical response and the levels were low (<1.3 µg/ml). Demographic, clinical, biochemical and endoscopic data, previous treatments, adverse events (AEs), surgeries and hospitalizations, were documented.

Results: Twenty-three patients with UC were analysed. (Table 1). All patients had received previous biological treatment: 52% ≥ 2 anti-TNF, 65% vedolizumab and 30% JAK inhibitors. Treatment discontinuation occurred in 3 patients (13%). The persistence was 83% and 79% at 6 and 12 months (Figure 1). During follow-up, 12 patients (52%) maintained standard dose of USK. Dose adjustment was performed in 13 patients (56%): 3 (13%) required intravenous UST reinduction and 10 (43%) required dose escalation (8 by shortening the interval between doses and 2 by switching to intravenous USK administration). Clinical remission was reached in 61%, 58%, 56%, 79% of the patients after 8, 16, 24, 52 weeks, respectively. Normal CRP (<5mg/L) and FC (<150 µg/g) levels were achieved in 76%, 93% and 80% and in 35%, 31% and 40% of patients after 8, 24, 52 weeks, respectively. Five of 6 patients who had endoscopy before and after treatment showed endoscopic Mayo subscore ≤ 1. There were 2 AEs, 1 hospitalization, and 1 colectomy during follow-up.

Characteristic	N = 23
Gender Male/Female	8 (35%)/15 (65%)
Age (years)	44 (33, 51)
Disease duration (years)	7.8 (5.3, 14.4)
Extent of disease E1-E2-E3	1 (4%), 10 (44%), 12 (52%)
Extra-intestinal manifestations	6 (26%)
Immunosuppressant at baseline	7 (30%)
Corticosteroids at baseline	10 (43%)
Partial Mayo score at baseline	5 (3, 7)
CRP at baseline (mg/L) /FC at baseline (µg/g)	8.1 (4.1, 29.7) / 2276 (1641, 3569)

Table 1. Characteristics of study population. Data are expressed as median (interquartile range), or number (%).

Conclusion: This study demonstrates the safety as well as the clinical, biological and endoscopic effectiveness of USK adjusted by levels in real life in a highly refractory UC cohort.

Disclosure: Nothing to disclose.

P0498

REAL-LIFE EXPERIENCE OF ANTI-DRUG ANTIBODIES AGAINST ANTI-TNF AGENTS AT TWO TERTIARY CARE PAEDIATRIC INFLAMMATORY BOWEL DISEASE CENTRES

J. Jagt¹, K.W. Holleman², M.A. Benninga³, J.E. van Limbergen³, N.K.H. de Boer⁴, T.G.J. de Meij^{1,3}

¹Amsterdam University Medical Center, Vrije Universiteit Amsterdam, Department of Pediatric Gastroenterology, Amsterdam, Netherlands, ²Amsterdam UMC, Academic Medical Center, Faculty of Medicine, Amsterdam, Netherlands, ³Emma Children's Hospital, Amsterdam UMC, Department of Paediatric Gastroenterology, AZ Amsterdam, Netherlands, ⁴VU University Medical Center, Gastroenterology and Hepatology, Amsterdam, Netherlands

Contact E-Mail Address: j.jagt1@amsterdamumc.nl

Introduction: Anti-TNF treatment is increasingly used in moderate to severe paediatric inflammatory bowel disease (IBD). However, a subset of children develop anti-drug antibodies (ADA) against anti-TNF agents, which can result in worsening symptoms, decreased mucosal healing, and ultimately even to progression to bowel resection. Data on the optimal management and predictive factors of ADA, are not yet determined in paediatric IBD.

Aims & Methods: In this retrospective cohort study, we aimed to evaluate treatment interventions to overcome ADA in children with IBD. Secondary aim was to investigate predictive factors of ADA development. Children 4-18 years old, diagnosed with IBD and were prescribed anti-TNF agents including infliximab and adalimumab between January 2006 and November 2021, were included in two tertiary centres.

Primary outcome was the suppression of ADA (<12 AU/mL) after treatment intervention, comprising dose optimisation, switch to another anti-TNF agent, adding an immunomodulator (IM) or alternative treatments in ADA positive children.

Secondary outcomes included predictors of ADA development. These predictive factors were tested by using Cox proportional-hazards model.

Results: A total of 298 paediatric IBD patients (215 Crohn's disease; 71 ulcerative colitis; 12 IBD-unclassified) on anti-TNF therapy (288 infliximab; 10 adalimumab) were included. Fifty-seven patients (19.1%) developed ADA after a median time of 16.4 months (IQR 7.0 – 25.2) following initiation of anti-TNF treatment: 51 to infliximab and 6 to adalimumab (after a switch from infliximab for other reasons than ADA).

Total duration of treatment on anti-TNF agents for the 298 patients was 885 person-years. The incidence rate of ADA was 6.44 per 100 person-years. The interventions to overcome ADA and the effect on ADA suppression is depicted in Table 1.

In the group of patients with ADA <50 AU/mL (*n* = 31), 20 patients continued on the initial anti-TNF agent (dose optimisation, IM addition, or both). Of these patients, 90% and 80% had suppressed ADA and sustained treatment response at 6 and 24 months, respectively.

In patients with high ADA levels >50 AU/mL (*n* = 26) who underwent dose optimisation (*n* = 6), IM addition (*n* = 1) or both (*n* = 4), 45% and 36% of subjects had ADA suppression and continued on the initial anti-TNF agent at 6 and 24 months, respectively. The development of ADA against anti-TNF was positively associated with female sex (hazard ratio [HR] 2.22, 95% CI 1.27 – 3.85, *P* = 0.005) and the presence of infusion reactions (HR 2.94, 95% CI 1.59 – 5.44, *P* = 0.001).

Conclusion: In this real-life cohort of children with IBD, around 20% of patients developed ADA against anti-TNF agents. Our data suggest that dose optimisation and/or IM addition for low-level ADA (<50 AU/mL) is an effective intervention to suppress ADA and prevent loss of response, while this was effective in only one-third of patients with high ADA (response at

24 months). Female sex was predictive of ADA development. A more sex-specific approach might therefore be considered to lower the risk of ADA in female patients.

Disclosure: Nothing to disclose.

Type of intervention	ADA level (UE/mL), median (IQR)	Patients with ADA tested after intervention, n	Median days (IQR) from ADA until subsequent ADA test	ADA suppressed	ADA not suppressed
Continued on same anti-TNF agent (n = 33)	31 (24 – 115)	30*	84 (56 – 156)	18	12
Dose optimization (n = 20)	31 (24 – 94)	17*	84 (55 – 116)	9	8
IM added (n = 3)	40	3	156 (56 – 500)	3	0
Both (n = 8)	52 (21 – 170)	8	75 (55 – 160)	5	3
Watchful waiting (n = 2)	26	2	498 (495 – 500)	1	1
Switch to alternative anti-TNF agent (n = 16)	160 (50 – 468)	10**	175 (87 – 313)	7	3
Other					
Surgery (n = 4)					
IM monotherapy (n = 3)	34 (16 – 80)	n.a.	n.a.	n.a.	n.a.
Switch to other biological (n = 1)					

ADA, anti-drug antibodies; IM, immunomodulator

* switched to alternative anti-TNF agent prior to second test (n = 2), second test >2 years after intervention (n = 1)

** surgery (n = 2), second test >2 years after intervention (n = 3), lost to follow-up (n = 1)

P0498 Table 1. Interventions to suppress anti-drug antibodies to anti-TNF agents in paediatric inflammatory bowel disease patients

P0499

BERBERINE SUPPLEMENTATION SIGNIFICANTLY IMPROVED ANTI-TNFA EFFICACY IN MURINE COLITIS MICE HUMANIZED WITH NON-RESPONDER GUT MICROBIOTA

L. Liu¹, L. Liang², Y. Chen²

¹Shenzhen Hospital, Southern Medical University, Gastroenterology, Shenzhen, China, ²Nanfang Hospital, Southern Medical University, Gastroenterology, Guangzhou, China

Contact E-Mail Address: 13246837972@163.com

Introduction: Immunotherapy based on anti-TNFα mAb has emerged as a promising treatment option for a variety of autoimmune illnesses. However, only a small percentage of ulcerative colitis (UC) patients benefit from it. A growing body of evidence supports the gut microbiota's critical involvement in immune system development. Berberine, a natural plant alkaloid derived from a variety of species, has been shown to regulate gut microbiota imbalance.

Aims & Methods: As a result, we set out to investigate the role of berberine in increasing anti-TNFα mAb efficacy as well as the processes that underpin it.

The C57BL/6 mice were given an antibiotic cocktail (ABX) to deplete the endogenous gut microbiota before being humanized with feces from anti-TNFα non-responders and responders. 3.0% dextran sulphate sodium (DSS) was given to these mice to test the pro-healing efficacies of anti-TNFα coupled with or without berberine. The intestinal immune microenvironment and mucosal repair after therapy was studied using flow cytometry, RT-PCR, and immunohistochemistry. 16S rRNA amplicon sequencing

and gas chromatography-mass spectrometry (GC-MS) analyses were used to assess the gut microbiota profiles and levels of short-chain fatty acids (SCFAs). Fecal microbiota transplantation (FMT) was used to further investigate the influence of gut microbiota on anti-TNFα mAb efficacy after berberine supplementation.

Results: In compared to mice humanized with feces from responded UC patients, animals humanized with feces from non-responded UC patients had considerably lower anti-TNFα mAb efficacy.

However, berberine dramatically increased anti-TNFα mAb efficacy in dextran sulfate sodium (DSS)-induced colitis animals humanized with non-responders gut microbiota. And M2-like macrophage infiltration and repolarization were increased in the pro-inflammatory colonic microenvironment in mice treated with anti-TNFα and berberine. When macrophages were deleted in vivo with clodronate liposomes, the pro-healing effect of anti-TNFα mAb combined with berberine was reduced. Berberine increased gut microbial diversity and exerted favorable control over microbial composition, 16S rRNA amplicon sequencing revealed.

Additionally, we identified novel bacterial modules that were much more abundant in the anti-TNFα mAb & berberine group and were composed of butyrate-producing bacteria, indicating a good immunotherapy response. Meanwhile, GC-MS analysis demonstrated that berberine altered the body's SCFA butyrate concentration.

Additionally, butyrate was found to be sufficient to boost M2-like macrophage polarization and thus the potency of anti-TNFα mAb. Also, the FMT assay demonstrated that berberine's effects were flora-dependent. Notably, the therapeutic effects of berberine were established in mice humanized with anti-TNFα mAb-resistant patients' gut microbiota.

Conclusion: Berberine aided anti-TNFα mAb efficacy in UC by influencing the differentiation of M2-like macrophages in the local immunological milieu, which was possibly mediated via the metabolite butyrate.

Disclosure: Nothing to disclose.

P0500

ASSOCIATION OF ULCERATIVE COLITIS BOWEL URGENCY IMPROVEMENT WITH CLINICAL RESPONSE AND REMISSION

D. Clemow¹, C. Sapin¹, T. Hibi², M.C. Dubinsky³, S. Vermeire⁴, S. Schreiber⁵, T. Hunter Gible¹, L. Peyrin-Biroulet⁶, M. Watanabe⁷, R. Panaccione⁸

¹Eli Lilly and Company, Indianapolis, United States, ²Kitasato Institute Hospital IBD Research and Treatment, Keio University, Tokyo, Japan, ³Mount Sinai Hospital, Mount Sinai, New York City, United States, ⁴University Hospital Leuven, Dept. of Gastroenterology, Leuven, Belgium, ⁵University Hospital Schleswig-Holstein, Dept. of Internal Medicine I, Kiel, Germany, ⁶Nancy University Hospital, Inserm U 1256 - Team 2 Inflammation/Cellular Stress and Exposure to Environmental Risks, Vandoeuvre-Nancy, France, ⁷Tokyo Medical and Dental University, Gastroenterology and Hepatology, Tokyo, Japan, ⁸University of Calgary, Medicine, Calgary, Canada

Contact E-Mail Address: davidclemow@lilly.com

Introduction: Ulcerative colitis (UC) can result in a high prevalence of bowel movement urgency (BU), significantly reducing patient quality of life. Whether early BU improvement is associated with later clinical endpoint improvements was examined in patients (pts) treated with mirikizumab (miri).

Aims & Methods: BU in pts with moderately to severely active UC was evaluated in the Phase 3 randomized placebo (PBO)-controlled 12-week induction (LUCENT-1) and 40-week maintenance (LUCENT-2) trials with miri, an IL23-p19 monoclonal antibody. Pts received miri 300mg IV or PBO

during induction. Week 12 (W12) miri responders were rerandomized at LUCENT-2 study baseline (BL) to miri 200mg subcutaneous or PBO. BU was measured using the 11-point Urgency Numeric Rating Scale (UNRS) from 0 (absent) to 10 (worst possible). Pts' UNRS scores were averaged from the 7 consecutive days prior to visit.

Association of pts with BU Clinically Meaningful Improvement (CMI; UNRS $\geq$ 3 decrease) or BU Remission (UNRS=0 or 1) between BL and week 4 with the proportion of pts achieving clinical response, and clinical, endoscopic, or symptomatic remission at end of induction W12, was assessed.

For pts who achieved clinical response at W12, analyses were repeated for the end of maintenance (W52 of continuous treatment [LUCENT-2 W40]) based on W12 (LUCENT-2 BL) BU status. Pts with UNRS<3 at BL were not included. Non-response imputation was used for missing data.

Logistic regression models with treatment, urgency (BU CMI or BU Remission), treatment-by-urgency group interaction, and stratification factors were fitted to examine association between early urgency improvement and later clinical endpoints. Fisher's Exact test assessed within group treatment differences.

Results: Treatment-by-urgency group interactions were not statistically significant across clinical outcomes for induction and maintenance (all $p>0.05$). For induction, both treatment (all $p\leq 0.001$ for CMI) and urgency status (all $p<0.02$) were statistically significant main effects.

This suggests pts experiencing BU CMI or BU Remission at W4 were consistently more likely to achieve clinical response, and clinical, endoscopic, or symptomatic remission at W12 for both PBO and miri groups. For remission, only the treatment main effect was statistically significant across clinical outcomes (all $p<0.001$).

This suggests that among miri induction clinical responders (enriched population), BU CMI or BU Remission at end of induction (W12) was not associated with later maintenance efficacy outcomes (W52). Miri-treated pts achieved higher rates of clinical response, and clinical, endoscopic, or symptomatic remission at W52 compared with PBO regardless of BU CMI or BU Remission at W12 (Table).

Conclusion: Early BU Improvement, CMI or Remission, was associated with better clinical outcomes during induction for both miri and PBO pts, showing BU is a sensitive predictor of early clinical outcomes. Among miri induction responders, miri consistently provided better maintenance of response and remission rates.

Disclosure: [Dubinsky Marla](#) reports consulting fees from: Abbvie, Arena Pharmaceuticals, Boehringer Ingelheim International GmbH, Bristol-Meyar Squibb, Celgene Corporation, Eli Lilly and Company, F. Hoffmann-La Roche Ltd, Genentech Inc, Gilead, Janssen Global Services, Pfizer Inc, Prometheus Biosciences, Takeda Pharmaceuticals, UCB SA; Contracted Research: Abbvie Inc, Janssen Global Services, Pfizer Inc, Prometheus Biosciences; Stock interest: Trellus Health Inc; Licensing fee: Takeda Pharmaceuticals USA [Hibi Toshifumi](#) reports lecture fees from Aspen Japan K.K., Abbvie GK, Ferring, Gilead Sciences, Janssen, JIMRO, Mitsubishi-TanabePharma, Mochida Pharmaceutical, Pfizer, Takeda Pharmaceutical; Advisory/consultancy fees from Apo Puls Station, Abbvie GK, Bristol-Myers Squibb, Celltrion, EA Pharma, Eli Lilly, Gilead Sciences, Janssen, Kyorin, Mitsubishi-TanabePharma., Nichi-IkoPharmaceutical, Pfizer, Takeda Pharmaceutical, Zeria; Pharmaceutical and research grants from Abbvie GK, Activaid, Alfresa Pharma Corporation, JMDC Inc., Gilead Sciences, Inc., Nippon Kayaku Co., Ltd., Eli Lilly Japan K.K., Mochida Pharmaceutical Co., Ltd., Janssen Pharmaceutical K.K., Pfizer Japan Inc., Takeda Pharmaceutical Co., Ltd.,

LUCENT-1 Induction							
Urgency CMI Urgency Remission							
Endpoint	PBO IV(N=276)	Miri 300mg IV(N=811)	p-value ^a	Endpoint	PBO(N=276)	Miri 300mg IV (N=811)	p-value ^a
Urgency CMI W4 = Yes	n=61	n=230		Urgency Remission W4 = Yes	n=13	n=65	NA ^b
Clin.Response W12, (%)	68.9	78.7	0.126	Clin.Response W12, (%)	76.9	81.5	NA ^b
Clin. Remission W12, (%)	27.9	37.4	0.179	Clin.Remission W12, (%)	46.2	47.7	NA ^b
Endo.Remission W12, (%)	36.1	49.1	0.083	Endo.Remission W12, (%)	46.2	52.3	NA ^b
Sympt.Remission W12, (%)	49.2	63.5	0.055	Sympt.Remission W12, (%)	69.2	70.8	NA ^b
Urgency CMI W4 = No	n=215	n=581		Urgency Remission W4 = No	n=263	n=746	<0.001
Clin.Response W12, (%)	34.9	57.5	<0.001	Clin.Response W12, (%)	40.7	61.9	<0.001
Clin. Remission W12, (%)	8.8	18.4	<0.001	Clin.Remission W12, (%)	11.4	21.7	<0.001
Endo.Remission W12, (%)	16.7	29.6	<0.001	Endo.Remission W12, (%)	19.8	33.6	<0.001
Sympt.Remission W12, (%)	21.4	38.7	<0.001	Sympt.Remission W12, (%)	25.5	43.6	<0.001
LUCENT-2 Maintenance							
Urgency CMI Urgency Remission							
Endpoint	PBO SC (N=172)	Miri 200mg SC (N=336)	p-value ^a	Endpoint	PBO SC (N=172)	Miri 200mg SC (N=336)	p-value ^a
Urgency CMI W12 = Yes	n=112	n=212		Urgency Remission W12 = Yes	n=53	n=105	<0.001
Clin.Response W52 (%)	52.7	82.5	<0.001	Clin.Response W52 (%)	47.2	82.9	0.012
Clin.Remission W52 (%)	29.5	53.3	<0.001	Clin.Remission W52 (%)	34.0	55.2	0.004
Endo.Remission W52 (%)	31.3	60.4	<0.001	Endo.Remission W52 (%)	35.8	61.0	<0.001
Sympt.Remission W52 (%)	43.8	74.1	<0.001	Sympt.Remission W52 (%)	45.3	79.0	<0.001
Urgency CMI W12 = No	n=60	n=124		Urgency Remission W12 = No	n=119	n=231	<0.001
Clin.Response W52 (%)	45.0	79.0	<0.001	Clin.Response W52 (%)	51.3	80.5	<0.001
Clin.Remission W52 (%)	18.3	47.6	<0.001	Clin.Remission W52 (%)	21.8	49.4	<0.001
Endo.Remission W52 (%)	26.7	57.3	<0.001	Endo.Remission W52 (%)	26.9	58.4	<0.001
Sympt.Remission W52 (%)	35.0	69.4	<0.001	Sympt.Remission W52 (%)	38.7	69.3	<0.001

^ap-value = within-group treatment comparison from Fisher's exact tests.

^bSubgroup N was too small for p-value generation.

Note: Using the Cochran-Mantel-Haenszel (CMH) test, treatment-by-subgroup interactions were not statistically significant.

Note: W52 refers to W40 of LUCENT-2, representing 52 weeks of continuous treatment; W12 refers to baseline for LUCENT-2.

Abbreviations: CMI=clinically meaningful improvement; PBO=placebo; miri=mirikizumab; IV=intravenous; n=number of patients in the specified category; SC=subcutaneous; W=week.

P0500 Table. Bowel urgency associations with Clinical Response and Clinical Remission for patients with ulcerative colitis

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P0501

IN PATIENTS WITH CROHN'S DISEASE, FECAL CALPROTECTIN DROP-SLOPE DURING INDUCTION WITH USTEKINUMAB CAN AFFECT ITS LEVELS AND DISCRIMINATE THE NEED FOR INTENSIFICATION AT WEEK 52

A. Mínguez Sabater¹, B. Mateos¹, E. Sáez-González¹, M. Iborra¹, I. Moret¹, A. Cañada², L. Tortosa¹, G. Bastida¹, M. Aguas¹, E. Cerrillo¹, P. Nos¹, B. Beltrán¹

¹Hospital Universitario y Politécnico La Fe, Gastroenterology Department, Valencia, Spain, ²Hospital Universitario y Politécnico La Fe, Biostatistics Area, Valencia, Spain

Contact E-Mail Address: alejandromsab11@gmail.com

Introduction: Ustekinumab (UST) intensification during Crohn's Disease (CD) treatment is becoming quite usual in clinical practice. Little is known about early intensification maintenance regimens and their drug levels utility in discriminating CD-response and the need of further intensification.

Aims & Methods: To analyze the evolution of UST levels in an intensified maintenance regimen, their capacity to discriminate response according to inflammatory parameters and to indicate the need of further intensification. This is a retrospective study with 43 moderate/severe active CD patients (Harvey- Bradshaw Index [HBI] ≥ 4 and Fecal Calprotectin [FC] >250 $\mu\text{g/g}$) who received UST induction treatment (induction dose of 6mg/kg IV,

plus dose of 90mg SC at week 8). Patients received maintenance treatment (90mg SC/8 weeks) and were followed during 52 weeks. They were classified according to the response obtained at first year in: responders (R) (HBI <3 and FC $<200\mu\text{g/g}$), non-responders (NR) (HBI ≥ 4 and FC $>250\mu\text{g/g}$), and intensification

group (IG) (partially responders that needed UST intensification to every 4 weeks). HBI, FC, C-Reactive Protein (CRP) and UST levels data were collected at baseline (w0), week 8 (w8), week 16 (w16) and during the first 52 weeks (w52) of maintenance. IG was followed 12-26 weeks after intensification (al).

Results: Half of the patients (48.8%) were male. Most of them (97.7%) had received previous anti-TNF- α treatment (53.49% >2 anti-TNF- α). Median age of patients at the moment of starting UST was 51 (37.5, 58.5) years. Median disease duration was 11 (7.5, 23) years. Location of disease was ileal in 30% of patients and ileocolic in 53%. One third of the patients associated perianal disease and 41% were smokers. The only demographic factor associated to non-response was ileocolic location. Table 1 shows the evolution of inflammatory parameters and UST levels according to response. A Pearson correlation ($r=0.62$) between higher FC drop (baseline-w16) and higher drug levels at w16 was observed. Biological markers decrease is able to discriminate UST NR during induction, however neither biological markers nor UST levels are able to discriminate between deep remission R and those who will need intensification. R shows a higher UST levels at w52 compared to IG. IG showed a significant increase of UST levels (a mean of 5.39 points) and a significant drop of FC and HBI (a mean of 115.62 and 2.27 points respectively) after intensification. Those patients reported clinical improvement, however they could not reach a FC $<250\mu\text{g/g}$, which could need longer period of time to decrease.

	UST LEVELS ($\mu\text{g/ml}$)				FC ($\mu\text{g/g}$) / CRP (mg/l)			
	w8	w16	w52	al	w0	w16	w52	al
R (n=15)	13.36 (10.1)	2.19 (1.2)	4.37 (2.21)	---	923.3 (670.4) / 4.34 (4.3)	180.1* (129.7) / 2.49* (1.6)	159.1* (167.71) / 1.06* (0.64)	--- / ---
NR (n=15)	8.47 (9.48)	3.07 (2.71)	---	---	1708.06 (1095.2) / 10.66 (8.85)	1401.6 (976.3) / 18.95 (17.8)	---	---
IG (n=13)	11.63 (9.75)	2.42 (0.97)	2.23+ (0.84)	7.61^ (3.1)	1013.2 (450.9) / 10.15 (17.4)	493.7* (407.12) / 7.23 (9.48)	554.7 (529.69) / 5.72 (8.15)	366.5^ (421.8) / 4.28 (4.22)

Table 1. Data: mean (SD); * $p < 0.05$ w16 or w52 vs. w0 in the same group and parameter; + $p < 0.05$ R vs. IG w52; ^ $p < 0.05$ IG w52 vs al.

Conclusion: FC drop-slope is associated to higher levels of UST at the end of induction. UST levels at w52 are useful to discriminate those patients who will benefit from UST intensification to every 4 weeks.

Disclosure: Nothing to disclose.

P0502

PATIENTS PERSPECTIVE ON SWITCHING FROM INTRAVENOUS TO SUBCUTANEOUS THERAPY

E. Karamintziou¹, T. Alexopoulos², M. Tooulia³, G. Michalopoulos¹, P. Karatzas², S. Vrakas³, G. Papatheodoridis², V. Xourgias³, V. Ntelis¹

¹General Hospital of Athens "G. Gennimatas", Gastroenterology Department, Athens, Greece, ²Medical School of National and Kapodistrian University of Athens School of Health Sciences, General Hospital of Athens "Laiko", Gastroenterology Department, Athens, Greece, ³General Hospital of Piraeus "Tzaneion", Gastroenterology Department, Piraeus, Greece

Contact E-Mail Address: sbrakas@yahoo.gr

Introduction: A significant percentage of patients with inflammatory bowel disease (IBD) require treatment with intravenous (IV) biological agents and specifically infliximab or vedolizumab. In the near future it will be possible to change the route of administration of these molecules, as their subcutaneous forms (SC) will be available, allowing the infusion units to be decongested and patients to be relieved of repeated admissions to the hospital.

The purpose of this study is to record whether patients under IV treatment desire this change and what factors influence their decision.

Aims & Methods: An anonymous, simplified questionnaire was given to patients under IV biological agents in 3 tertiary Gastroenterology clinics. Epidemiological characteristics (age, sex, disease, years of illness, current treatment, previous treatment) were collected and the questionnaire aimed at the acceptance or not of change of treatment from IV to SC molecule if it was available as well as the main factors influencing this choice.

Results: In total, the questionnaire was answered by 93 patients (52 with Crohn and 41 with ulcerative colitis) of which 71 (76.34%) received IV Infliximab and 22 (23.66%) IV Vedolizumab. Of the total patients, 31 (33.33%) answered that they would not like a change in SC form, while 62 (66.67%) that they would like to change to a SC form.

The main reasons for staying in IV were:

- a. Closer monitoring by the treating physician (39%),
- b. Feeling safe - fewer side effects and complications (33%) and
- c. Higher efficacy (9.09%).

On the contrary, the main factors for accepting the change of treatment in SC form were:

- a. Ease of administration (46%),
- b. Occupational-social flexibility (38.71%).

No correlation was found between patients' desire for a change in route of administration and age or previous subcutaneous exposure.

Conclusion: 2/3 of the patients in IV biological agent would accept the change of the route of administration, from IV to SC form with the same molecule. The key factors for this choice seem to be ease of delivery and professional-social flexibility. Age and previous exposure to a SC biological agent does not appear to be related with the desire to change from intravenous to subcutaneous drug.

Disclosure: Nothing to disclose.

P0503

THE VEDOLIZUMAB CLINICAL DECISION SUPPORT TOOL FOR CROHN'S DISEASE EFFECTIVELY PREDICTS CLINICAL REMISSION AT 54 WEEKS IN A "REAL WORLD" SETTING

K. Chalakatevaki¹, G. Kokkoti¹, E. Papathanasiou², N. Kioulos¹, M. Gizis¹, S.L. Chatzinikolaou¹, I. Koutsounas¹, S. Michopoulos², E. Zampeli², G. Bamias¹

¹3rd Department of Internal Medicine "Sotiria" Hospital, National and Kapodistrian University of Athens, Gastroenterology Unit, Athens, Greece, ²Alexandra Hospital, Dept. of Gastroenterology, Athens, Greece

Contact E-Mail Address: kchalakatevaki@gmail.com

Introduction: A clinical decision support tool (CDST) was designed and validated based on data acquired from the GEMINI and VICTORY study in order to predict the possibility of clinical response in patients with active Crohn's who received Vedolizumab (VDZ). Further evaluation of the tool's credibility in larger cohorts is mandatory before its application in every day clinical practice.

Aims & Methods: The primary aim of the study is to evaluate the effectiveness and application of the clinical decision support tool in every-day clinical practice regarding Greek patients with active Crohn's disease who received VDZ and their response to therapy. Secondary aim is to determine the utility of the CDST in patients with active Crohn's disease who received Ustekinumab (UST).

Methods: We collected retrospective data of patients with active Crohn's disease treated with VDZ or UST from Sotiria and Alexandra Hospitals. The patients were separated based on their CDST score in high (CDST>19), intermediate (13<CDST≤19) and low (CDST≤13) possibility of clinical remission. Their clinical response was assessed on week 54 of treatment.

Results: In total 58 patients with active Crohn's disease who received VDZ were assessed, out of which 14 were excluded due to lack of data. The remaining 44 were divided into the groups mentioned above (high, intermediate and low).

Only one patient was enrolled in the low probability group and therefore was not included for further evaluation. In the high probability group, 29 patients were enrolled, out of which 24 (82%) achieved clinical remission on week 54 while in the intermediate probability group 14 patients were enrolled out of which 6 (43%) achieved clinical remission.

The difference between the high and intermediate group was found to be statistically significant ($P<0.01$). Similarly, 96 patients with active Crohn's disease who received UST were assessed, out of which 27 were excluded due to lack of data, while the remaining 69 were divided into three groups based on their CDST score. In the high probability group 33 patients were enrolled out of which 23 (69%) achieved clinical remission on week 54, while 34 were enrolled in the intermediate probability group out of which 25 (73%) achieved clinical remission.

The difference between the high and intermediate groups was not statistically significant ($P=0.73$). Only two patients were enrolled in the low probability group and were excluded from further evaluation.

Conclusion: Very few patients who show low probability of response based on the CDST receive treatment with VDZ or UST. Our study confirms the credibility of the CDST as a mean to predict the patients' clinical response in receiving VDZ but not UST. The tool may prove to be a useful clinical indicator in the choice of biological treatment in patients with active Crohn's disease.

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P0504

MEDICAL TREATMENT OF VEO-IBD EXPOSES CHILDREN TO CRITICAL EXCIPIENTS – RESULTS FROM A RETROSPECTIVE OBSERVATIONAL SINGLE CENTER ANALYSIS

C. Pallauf¹, E. Klucker², T.G. Le Thi², J. Pachmayr¹, T. Schwerd², M. Pinter-Hitzl¹

¹Paracelsus Medical University (PMU), Institute of Pharmacy, Salzburg, Austria, ²Dr von Hauner Kinderspital, LMU Klinikum, Department of Pediatrics, Munich, Germany

Contact E-Mail Address: monika.pinter-hitzl@gmx.at

Introduction: Excipients as constituents of medicines can potentially impact drug safety and efficacy in pediatric patients due to their immature metabolic system. ¹Children diagnosed with very early onset inflammatory bowel disease (VEO-IBD) before six years of age could be susceptible to excipients' effects due to their young age and the lack of age-specific IBD formulations.

Aims & Methods: The aim of this study was to analyze the exposure to potentially critical excipients in induction and maintenance therapy of VEO-IBD in order to support patient safety and to improve pediatric drug therapy.

A retrospective observational study was conducted at the Dr. von Hauner children's hospital of the LMU Munich. Medical records of all VEO-IBD patients hospitalized between 2015 and 2021 receiving oral, rectal and parenteral medication were included in this study. Daily exposure to potential critical excipients aspartame, lactose, polyethylene glycol, polysorbate 80, propylene glycol, sodium benzoate, sorbitol, sucrose and sulfites was evaluated. Cumulative excipient exposure levels in pediatric patients were documented and compared to threshold levels set by the European Medicines Agency (EMA) or published safe levels.

Results: A total of 16 VEO-IBD patients (median age 3.0 years, range 0.8 – 6.4 years of age; 4 female, 12 male) were included in the study. Treatment of the study population included mesalazine, prednisolone, methylprednisolone, azathioprine, budesonide, methotrexate, vedolizumab, adalimumab, omeprazole, vitamin D and calcium. All patients were exposed to at least two critical excipients during the observed treatment period. Exposure levels of excipients above the thresholds set by the EMA or respective safe levels have been observed for oral and rectal medicines administered in combination or when used as an off-label treatment.

Oral drugs exposed the patient to lactose, propylene glycol and sodium benzoate above the recommended safe levels. Rectal therapies contained preservatives like sodium benzoate, sodium metabisulfite and potassium metabisulfite. In detail, 4/16 patients were exposed to lactose above a threshold of 5.71 mg/kg/per dose, 4/16 patients were exposed to potassium metabisulfite above a respective safe level of 0.12 mg/kg/d, 1/16 patient was exposed to propylene glycol above a threshold of 50 mg/kg/d, 4/16 patients were exposed to sodium metabisulfite above a respective safe level of 0.1 mg/kg/d, 4/16 patients were exposed to sodium benzoate above a respective safe level of 0.5 mg/kg/d and a 13/16 patients were exposed to oral sucrose. Combination of vitamin D and calcium contained high amounts of sucrose or sorbitol.

Conclusion: We found VEO-IBD children exposed to high levels of potentially critical excipients. Levels of potentially irritating preservative potassium metabisulfite were exceeding up to 8-fold the recommended threshold and propylene glycol exceeded the safe level by a factor of 2 in

drug therapy of VEO-IBD patients. In order to improve drug therapy and consequently patient safety in VEO-IBD it is important to raise awareness on excipient levels which might reach proinflammatory activities and contribute to treatment refractoriness or impact on therapy tolerance.

Tailored formulations for pediatric drug therapy in VEO-IBD should be considered, such as replacing Vitamin D/calcium combinations with sugar-free formulations, to improve patient safety. Overall, there is a strong need for pediatric formulations of drug products and support by clinical pharmacist in VEO-IBD therapy and beyond.

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P0505

THE ROLE OF THE GUT MICROBIOTA AND EXPRESSION OF TIGHT JUNCTION PROTEINS IN ALLEVIATION BY INTESTINAL ALKALINE PHOSPHATASE TREATMENT OF EXPERIMENTAL COLITIS EXACERBATED IN HIGH-FAT-DIET FED MICE BY FORCED PHYSICAL ACTIVITY

D. Wójcik¹, Z. Sliwowski¹, A. Targosz¹, M. Strzalka¹, M. Magierowski¹, S. Kwiecien¹, A. Ptak-Belowska¹, A. Wojcik¹, T. Kosciolk², T. Brzozowski¹

¹Jagiellonian University Medical College, Department of Physiology, Cracow, Poland, ²Jagiellonian University, Malopolska Centre of Biotechnology, Cracow, Poland

Contact E-Mail Address: mpbrzozo@cyf-kr.edu.pl

Introduction: Inflammatory bowel diseases (IBD) are a group of chronic inflammatory intestinal diseases with an autoimmune background, cyclic nature altering between active and quiescent state that markedly impair the quality of patient's life. In obese IBD patients an overgrowth of white mesenteric adipose tissue release results in a number of adipokines as biomarkers of an inflammatory response.

Recently, we have reported that the mesenteric adipose tissue overgrowth as a result of obesity induced by a high-fat diet feeding of rodents leads to a deterioration of the course of experimental colitis, but the role of extensive physical activity in experimental colitis in obesity has not been elucidated. Intestinal alkaline phosphatase (IAP) is an important apical brush border enzyme dephosphorylating bacterial lipopolysaccharide (LPS) of pathogenic bacteria during stressful conditions but the potential protective impact of IAP supplementation to exercising obese mice with colitis as well as the changes in gut microbiota and expression of barrier proteins have not been studied before.

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 in 6 weeks, Panlab, Harvard Apparatus, MA, USA) with or without the intragastric treatment with IAP (200 U/day) followed by induction of trinitrobenzene sulfonic acid (TNBS) colitis.

Following 4 days after colitis induction, the animals of both groups were anesthetized and the colonic blood flow (CBF) was examined by Laser Doppler flowmetry, the disease activity index (DAI), histology of intestinal mucosa was examined and the composition of intestinal microbiota was determined in stool samples collected from mice by Next-Generation Sequencing.

The blood and biopsies of colonic mucosa was excised for the determination of pro- and anti-inflammatory cytokines using Luminex microbeads and the expression of intestinal barrier proteins ZO-1, Muc2, Claudin-4 and -8 has been evaluated by RT-PCR.

Results: The forced physical activity significantly increased DAI index and significantly raised the colonic level and leptin, MCP, TNF- α , IL-6 and IL-17a while decreasing the IL-2 levels in obese mice with colitis, these effects being significantly reduced by the treatment with IAP which significantly improved the gross and histologic appearance of colonic mucosa. The predominance of Bacteroidetes and Firmicutes was observed at the phylum level in IAP-treated mice along with the relative proportion of Firmicutes in favor of higher content of Verrucomicrobiota. At genus level, the lower level of pathogenic Clostridia was noticed in IAP-treated HFD-fed mice as compared to SD controls. Both, Campilobacterota and Deferribacterota were more common in HFD group with TNBS colitis but lower level of Odoribacteria with shift to predominance of Bacteroides and Parabacteroides was observed in IAP-treated obese mice. The mRNA expression for ZO-1, Muc2 and Claudin-8 and -4 was downregulated in HFD-fed exercising mice as compared to SD group and these effects were reversed by IAP administration.

Conclusion: IAP treatment ameliorates the exacerbation of murine colitis induced by forced physical activity due to improvement of diversity of intestinal microbiota, the favorable effect on the expression of tight junction proteins and the downregulation of proinflammatory biomarkers in colonic mucosa (Support:UMO-2015/19/B/NZ4/03130 by the National Centre of Science in Poland).

Disclosure: Nothing to disclose.

P0506

CROHN'S DISEASE EXCLUSION DIET (CDED) FOR THE TREATMENT OF CROHN'S DISEASE – AN OBSERVATIONAL STUDY FROM A TERTIARY CENTER

N. Fliss-Isakov¹, N.A. Cohen², A. Brumberg², G. Herbert², R. Anbar³, A. Hirsch², T. Thurm², N. Maharshak²

¹Tel Aviv Medical Center, Gastroenterology, Tel Aviv, Israel, ²Tel Aviv Medical Center, Department of Gastroenterology and Liver Diseases, Tel Aviv, Israel, ³Tel Aviv Medical Center, Nutrition and Dietetic Department, Tel Aviv, Israel

Contact E-Mail Address: ayal.red@gmail.com

Introduction: The Crohn's Disease (CD) exclusion diet (CDED), is a whole-food diet which has been shown to induce remission and decrease objective markers of inflammation in pediatric and adult CD populations.

Aims & Methods: We aimed to describe our real-world experience with the CDED, in a tertiary referral center for IBD patients. This retrospective cohort study, performed at the Inflammatory Bowel Disease (IBD) Unit of the Tel Aviv Medical Center, collected data from all CD patients with clinically active disease, defined by a Harvey Bradshaw Index (HBI) ≥ 5 , who were referred for the CDED by their treating physician. Medical, nutritional and anthropometric data was collected from dietician clinic visits and medical records throughout the three phases of the diet. Clinical and biomarker improvement, response and clinical remission were determined

Results: 220 CD patients were referred for the CDED. 124 patients were excluded due to incomplete documentation (5%), previous CDED experience (13%), unwilling to adhere to diet or loss to follow up (28%). Patients who did not initiate the CDED were significantly older and had higher BMI, but did not differ otherwise from patients who initiated the CDED.

The remaining 96 patients initiated the CDED, 48 (50%) of whom had a clinically active disease and were included in the study. The mean age of the cohort was 35.4 (± 16.35) years with a mean duration of disease

of 9.1 (± 8.8) years. 28 patients (58%) were female and mean body mass index (BMI) at diet initiation was 21.9 (± 3.5) kg/m². Most patients had ileal (62.5%) or ileocolonic (35%) disease location. 12 patients (25%) had a stricturing phenotype and 16 patients (33%) had undergone prior CD surgery. 21 patients (44%) were on CDED alone and 21 (44%) started CDED as an adjunctive therapy or bridge to advanced therapy.

Indications, adaptations for and adherence to the CDED n, (%)	Clinical remission (n=30)	No clinical remission (n=18)	P-value
CDED alone	17, (56.7)	4, (22.2)	0.060
Adjunctive therapy	7, (23.3)	4, (22.2)	
Bridge therapy	4, (13.3)	6, (33.3)	
With steroids / antibiotic	2, (6.7)	4, (22.2)	0.940
Partial enteral nutrition	13, (43.3)	8, (44.3)	
Low fiber – adaptations for post-surgical or stricturing disease	10, (33.3)	4, (22.2)	0.412
High adherence to the CDED	23, (76.7)	9, (50.0)	0.058
High adherence to mandatory foods	22, (78.6)	9, (50.0)	0.049

Table 1: Comparison of indications, adaptations to CDED and adherence to diet of patients following 6 weeks of the CDED based on remission status

Table 1 details the indications for, adaptation of and adherence to the CDED in the patient cohort. At week 6, clinical remission was achieved in 30 patients (62.5%) and 14 (46.6%) patients, maintained remission by week 12. HBI improved by an average of 3.7 $\pm$ 3.5 and Fcal decreased by 668 $\pm$ 1284mg/kg (n=19) by week 12 of the CDED. There were no significant differences in baseline disease phenotype, severity or BMI between remitters and non-remitters. There was a positive association between high adherence to the CDED and clinical remission at week 12, when adjusting for age, gender, disease duration, BMI, and baseline HBI score (OR=7.6, 95%CI 1.07-55.2, P=0.043). Most patients were highly adherent (n=32, 67%) to the diet and only three patients reported intolerance to the diet due to palatability issues.

Conclusion: These encouraging data indicate that the CDED may be an effective adjunct intervention for multiple CD presentations and indications. These findings should be further validated in a larger, prospective studies

Disclosure: Nothing to disclose.

P0507

TOFACITINIB OR USTEKINUMAB FOR THIRD-LINE TREATMENT OF REFRACTORY ULCERATIVE COLITIS: A MULTICENTER RETROSPECTIVE PROPENSITY SCORE-MATCHED ANALYSIS

C. Meunier¹, A.-L. Charlois¹, A. Buisson², X. Roblin³, N. Mathieu⁴, P. Danion¹, C. Gay¹, S. Nancey¹, G. Boschetti¹

¹Lyon-Sud Hospital, Dept. of Gastroenterology, Pierre-Benite, France, ²CHU Estaing Clermont-Ferrand, IBD Unit, Clermont-ferrand, France, ³University of St. Etienne Dept. de Gastroenterologie, Saint Etienne, France, ⁴Hôpital Albert Michallon, La Tronche, France

Contact E-Mail Address: camille.b.meunier@gmail.com

Introduction: Biologic therapies are the standard of care for moderate-to-severe ulcerative colitis (UC). For patients who do not respond to conventional treatment, first-line biologics involve either an anti-TNF or an anti-integrin (vedolizumab).

However, a significant proportion of patients do not respond or secondarily lose response to these drugs. Ustekinumab, an interleukin 12/23 inhibitor, and tofacitinib, a pan-JAK inhibitor, have recently completed the ther-

apeutic arsenal after failure of a previous biologic therapy. However, there are few objective data to guide the therapeutic decision between these two molecules after failure of both anti-TNF and anti-integrin therapy.

Aims & Methods: In this study, our aim was to compare the efficacy of ustekinumab and tofacitinib in achieving clinical remission in real-life conditions, using a propensity score-matched analysis of a retrospective cohort of UC patients who had previously failed both anti-TNF and vedolizumab.

Results: Ninety-three UC patients were enrolled in 4 French tertiary centers: 41 received ustekinumab, 52 received tofacitinib. Both groups were comparable at baseline, particularly in terms of disease severity, with a mean disease duration of 8 years, 60% of pancolitis, and 41% of steroid-dependent patients. The mean treatment persistence was 11.5 months with ustekinumab, and 10.7 months with tofacitinib. Prior to statistical adjustment, neither treatment was found superior in achieving clinical remission. Clinical remission rates at induction (week 12) were 28.2% for ustekinumab and 35.6% for tofacitinib, and of 19% and 30% at week 54, respectively.

Overall, treatment failure occurred for 69.2% of patients treated with ustekinumab, and for 64.7% of patients treated with tofacitinib, with primary non-response for 30.8% and 33.3% of patients, respectively. Colectomy rates were comparable between the two groups, occurring for 12.2% of ustekinumab patients and 3.8% of tofacitinib patients.

In univariate analysis, age over 60 years was significantly associated with ustekinumab treatment, with an odds ratio (OR) of 7.7 (CI95 [1.5 - 39]); and a history of primary non-response to first-line biologics was associated with tofacitinib treatment, with an OR of 3.47 (CI95 [1.37 - 8.78]).

These variables were therefore included in the propensity score. After adjustment, neither treatment was significantly superior for induction and maintenance of clinical remission. In terms of safety, no unexpected side effects were reported in this work.

Conclusion: This multicenter real-life study confirms, in a homogeneous cohort of patients, that ustekinumab and tofacitinib are two valid options for third-line therapy in refractory UC. Despite the use of a propensity score, it was not possible to highlight a difference in terms of clinical remission between these two molecules.

A trend towards superiority of tofacitinib over ustekinumab was observed, especially in terms of colectomy rates, although our study lacked statistical power to reach significance.

However, in these multidrug-resistant patients, reported induction efficacy rates were high and colectomy rates low, suggesting that third-line biologic therapy is an acceptable alternative to surgery in refractory UC.

Disclosure: Nothing to disclose.

P0508

COMPARISON OF TWO ANALYTICAL TECHNIQUES FOR QUANTIFYING INFlixIMAB LEVELS IN PATIENTS WITH INFLAMMATORY BOWEL DISEASE

T. Valdes-Delgado¹, A. Aguado², V. Merino-Bohórquez², M. Díaz³, J. Martínez-Manzanas³, L. Castro Laria¹, B. Maldonado-Pérez¹, F. Argüelles-Arias¹

¹Hospital Universitario Virgen Macarena, Aparato Digestivo, Seville, Spain, ²Hospital Universitario Virgen Macarena, UGC Pharmacy, Seville, Spain, ³Hospital Universitario Virgen Macarena, Nursing, Seville, Spain

Contact E-Mail Address: teresavaldes4@hotmail.com

Introduction: ELISA (Enzyme-Linked Immunosorbent Assay) is the most commonly used technique for the determination of infliximab (IFX) levels in patients with inflammatory bowel disease (IBD). The main limitations of the ELISA are that it requires a specialized laboratory and accumula-

tion of several dozen samples to reduce the cost of each determination to an acceptable level, thereby delaying the results. The development of rapid tests could circumvent these delays and allow earlier determination of IFX levels to guide the patient's biological therapy. Few studies have been conducted to demonstrate the effectiveness of rapid tests against the ELISA.

Aims & Methods: **Aim:** The objective of this study is to compare the reference technique (ELISA) for quantifying IFX levels to a rapid "point-of-care" (POC) test.

Material and methods: The IFX levels of 135 IBD patients on maintenance IFX treatment were analyzed. The samples were obtained prior to infusion of IFX (trough levels) and were analyzed using both methods. For the ELISA, PromonitorIFXv2[®] kits from Progenika Biopharma (Derio, Spain) were used. The POC test, a rapid immunochromatographic analysis: the PromonitorQuick[®] IFX system, was also from Progenika Biopharma. For the POC test, only a capillary sample from the patient's fingertip was needed and the results were obtained within 20 minutes.

The quantitative comparison of the techniques was performed using Bland-Altman plots and Student's t-test. A p-value of <0.05 was considered statistically significant. The 95% concordance limits were calculated using the mean $\pm$ 1.96*SD. The correlation was assessed using the Pearson correlation coefficient (r).

Results: The median IFX concentration was 5.9 μ g/mL (RIC 0.035-14.4 μ g/mL) using the ELISA test and 3.90 μ g/mL (RIC 1-15.9 μ g/mL) using the POC test. The correlation between the results of both tests was high (r=0.84, p<0.001). The mean difference between ELISA test and POC test was 1.46 μ g/mL (p<0.001). The Bland-Altman plot indicates that at concentrations above 8 μ g/mL the POC test underestimates the IFX concentration.

Conclusion: This rapid immunochromatographic POC test showed a high degree of correlation with the ELISA reference test indicating the POC test was reliable. It also has the potential advantage of more rapid results.

Disclosure: Nothing to disclose.

P0509

EFFECT OF STANDARD AND MODIFIED BUDESONIDE THERAPEUTIC PROTOCOL ON MAINTENANCE OF ONE-YEAR REMISSION IN PATIENTS WITH MICROSCOPIC COLITIS-PILOT STUDY FROM A TERTIARY REFERRAL CENTER

K. Grubelic Ravic¹, M. Brinar², R. Prijic³, V. Sesa⁴, M. Jelakovic⁵, I. Huml¹, I. Škrlec³, A. Ladic⁶, M. Kalauz⁷, Z. Krznaric⁸

¹Department of Gastroenterology, University Hospital Center Zagreb, University Hospital Zagreb - Rebro, Zagreb, Croatia, ²University Hospital Centre Zagreb, Department of Gastroenterology, Zagreb, Croatia, ³University Hospital Center Zagreb, Division of Gastroenterology and Hepatology, Zagreb, Croatia, ⁴University hospital Zagreb, Internal medicine - gastroenterology, Zagreb, Croatia, ⁵UHC Zagreb, Gastroenterology and Hepatology, Zagreb, Croatia, ⁶Clinical Hospital Rebro-Zagreb, Division of Gastroenterology and Hepatology, Zagreb, Croatia, ⁷Clinical Hospital Center Zagreb, Gastroenterology, Zagreb, Croatia, ⁸KBC Zagreb/ University Hospital Zagreb, Gastroenterology, Hepatology & Nutrition, Zagreb, Croatia

Contact E-Mail Address: katjagrubelic@gmail.com

Introduction: Microscopic colitis (MC) is a chronic inflammation of the colon that causes chronic, non-bloody watery diarrhoea. Patients with MC can have abdominal pain, faecal incontinence and weight loss, symptoms that heavily impair their quality of life. Forms of MC are collagenous colitis (CC) and lymphocytic colitis (LC).

According to the literature data, 40 to 50 % of patients with MC treated with the standard therapy protocol (budesonide 9 mg through 6-8weeks) have relapsed within one year of therapy discontinuation.

Aims & Methods: Standard ileocolonoscopy with colonic biopsies was performed due to chronic diarrhea on 220 patients and on 74 patients histologically MC was confirmed.

24 patients with histologically confirmed MC (both histologic types included, LC and CC) were treated with the standard protocol (6-8weeks) and 50 patients of the second group were treated according to a modified therapeutic protocol (24 weeks – first 8 weeks 9 mg per day , 8-16 week 6 mg per day , 16-24 week 3 mg per day). Comparison of standard and modified therapy protocol results in achieving MC remission and maintaining it within one year of discontinuation of treatment was performed.

The achievement of clinical remission was monitored according clinical criteria (Hjortswang criteria), followed by its duration within one year in both groups of patients.

Results: During one year in the standard protocol patients group, disease relapse occurred in 45% of cases.

In the group of patients treated according to the modified therapy protocol,disease relapse occurred in 5% of patients during one year.

Conclusion: According to our results, the modified therapeutic protocol showed significantly better results in maintaining clinical remission in patients with MC at follow-up after one year.

Further studies are needed in order to optimize treatment options for MC.

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P0510

EFFECTIVENESS AND SAFETY OF SWITCHING FROM INTRAVENOUS TO SUBCUTANEOUS VEDOLIZUMAB FORMULATION IN INFLAMMATORY BOWEL DISEASE PATIENTS IN CLINICAL REMISSION

L. Parisio¹, C.R. Settanni¹, D. Napolitano¹, S. Varca¹, E. Schiavoni¹, L. Laterza¹, L.R. Lopetuso^{1,2,3}, M. Pizzoferrato¹, S. Bibbò¹, N. Alfieri¹, L. Guidi^{1,4}, A. Papa^{1,4}, A. Gasbarrini^{1,4}, A. Armuzzi⁵, D. Pugliese¹, F. Scaldaferri^{1,4}

¹Fondazione Policlinico Gemelli, IRCCS, Gastroenterology Department, CEMAD, Center for Diagnosis and Treatment of Digestive Diseases, Rome, Italy, ²University of Chieti-Pescara "G. d'Annunzio", Department of Medicine and Ageing Sciences, Chieti, Italy, ³University of Chieti-Pescara "G. d'Annunzio", Center for Advanced Studies and Technology (CAST), Chieti, Italy, ⁴Università Cattolica del S. Cuore, Department of Translational Medicine and Surgery, School of Medicine, Roma, Italy, ⁵Humanitas University, IBD Center, IRCCS Humanitas Research Hospital, Department of Biomedical Sciences, Pieve Emanuele, Milan, Italy

Contact E-Mail Address: laura.parisio@guest.policlinicogemelli.it

Introduction: Recently, subcutaneous vedolizumab (scVDZ) formulation has been approved for the treatment of Inflammatory Bowel Disease (IBD). In the randomized controlled trials for Crohn Disease (CD) and ulcerative colitis (UC), scVDZ formulation was comparable to intravenous (ivVDZ) one in terms of efficacy and safety.

Aims & Methods: The aim of our study was to evaluate the safety and the effectiveness of switching IBD patients (pts) in clinical remission from ivVDZ to scVDZ in a real-life setting. In this prospective cohort study, we collected data on consecutive IBD pts in steroid-free clinical remission who switched from ivVDZ to scVDZ from September 2021 to April 2022 at our IBD-Unit center. Demographic characteristics, baseline and 12-weeks follow-up clinical activity and C-reactive protein (CRP) levels, and adverse events (AEs) were recorded.

Clinical IBD activity was evaluated with Harvey Bradshaw Index (HBI) for CD, and Partial Mayo Score (PMS) for UC. The primary outcome of the study was to evaluate steroid-free clinical remission plus biochemical remission (CRP <5 mg/l) at week 12.

Results: 94 pts (42 CD, 52 UC, median age 52 years [IQR 42-67.2]) switched from ivVDZ to scVDZ-maintenance therapy. Median duration of disease was 11.5 years [IQR 7-18.2] and median duration of ivVDZ treatment was 36.5 months [IQR 16-52.2]; hence, 51/94 pts (54.2%) were anti-Tumor Necrosis Factor-α exposed. Most of pts (94.7%) were on every 8-weeks maintenance therapy. At baseline, 46 (85.2%) UC pts and 36 (85.7%) CD pts had normal CRP levels. 78/94 (82.9%) pts (35 CD, 43 UC) reached the 12-weeks follow up visit. Of 66/78 pts (84.6%) with normal CRP values at baseline, 58/66 (87.9%) pts maintained clinical steroid-free remission and normal CRP values at 12-weeks follow up. Eleven AEs were recorded: 3 SARS-COV2 infections, 1 dental abscess, 4 mild injection site reactions, 1 diffuse urticarial reaction, and 1 new onset of arthralgia. Eight pts (10.3%) discontinued scVDZ: 3 pts for AEs, 3 for disease flare and 2 for pts' preference.

Conclusion: Switching from ivVDZ to scVDZ can be considered a reasonably safe and effective treatment in maintaining remission in IBD pts at 12 weeks. Thus, recent availability of scVDZ can possibly permit an improvement of the quality of life of the pts and an abatement of the health care costs due to less frequent accesses to outpatient department for intravenous infusions.

However, larger real life studies with longer follow up to confirm the long term efficacy, tolerability and safety to scVDZ are needed.

Disclosure: Nothing to disclose.

P0511

RETROSPECTIVE ONE-CENTER STUDY COMPARING SAFETY AND EFFICACY OF IRON FORMULATIONS (FERRIC DERISOMALTOSE AND CARBOXYMALTOSE) IN GASTROENTEROLOGICAL PATIENTS

E.M. Tulewicz-Marti¹, G. Rydzewska^{1,2}

¹Central Clinical Hospital of Ministry of Interior and Administration, Department of General Medicine and Gastroenterology with Inflammatory Bowel Disease Subdivision, Warsaw, Poland, ²Jan Kochanowski University, Collegium Medicum, Kielce, Poland

Contact E-Mail Address: e.tulewicz@gmail.com

Introduction: Iron deficiency anaemia (IDA) and iron deficiency (ID) are common medical problems in gastroenterology departments. However, the choice of iron formula often depends on the concern in the case of the safety of these drugs for patients, especially women during pregnancy.

Aims & Methods: The aim of this study was to evaluate security profile and the efficiency of iron formulations ferric carboxymaltose (FCM, Ferinject®) and ferric derisomaltose (DIM, Monover®) among gastrointestinal patients.

The present retrospective study examined data of the patients who received IV iron between January 2020 and December 2021 at the Central Clinical Hospital, Warsaw, Poland. Patients demographic data, dosage, adverse drug reactions (ADR) and haemoglobin follow-up were collected from electronic medical records, studied and finally compared.

Results: We analysed data from 241 scheduled iron administrations. In total 183 patients had IV iron administered (53.6% (98) had Crohn's disease, 41% (75) ulcerative colitis, 1.1% (2) Inflammatory Bowel Disease (IBD) unclassified and 4.4% (8) had anaemia caused by Gastric Antral Vascular Ectasia (GAVE), celiac disease or iron deficiency anaemia during the study; what is more 2 patients with IBD were pregnant). 37% (68) of patients had previous history of the form of allergy.

Mean age was 35.6 (SD=12.0). DIM was applied in 80.5% (194 infusions) and FCM in 19.5 % (47 infusions). The mean level of ferritin before IV iron administration was 29.8 µg/L (SD=56.6). 10 patients were needed to be given a blood transfusions before IV iron administration because of a severe anaemia.

Mean haemoglobin level in the whole studied group before IV iron was 10.2 g/dL (SD=1.5): 9.3 (1.4) g/dL in FCM and 10.4 (1.4)g/dL in DIM (p=0.001) and after IV iron 12.1 (SD=1.9) g/dL, including after FCM- 11.1 (1.7) g/dL and DIM- 12.2 (1.9) g/dL respectively (p=0.018). 18.8% (22) patients needed another IV iron replacement in 2-3 months - 25% patients (n=4) after FCM and 17.7% (n=17) after DIM; p=0.50). In 2.4% (6 patients) ADR were observed (including one during FCM infusion) and they included dizziness, faintness, skin problems (rash, skin itchiness), sensation of dyspnoea, pressure in the chest, sensation of hot and hypotension, which were successfully recovered after IV antihistamines and corticoids and further hospitalization was not required. None of the patients who suffered from side effects of IV iron had previous history of allergy to medication.

Conclusion: This study supports data that IV iron formulas are safe in all patients including pregnant women with IBD. Iron IV administration achieved optimal haemoglobin levels in most patients, however some of them needed another IV iron infusion.

Moreover, patients after IV iron administration require strict follow-up in order to control and early symptoms of IDA or ID be detected to plan another replacement urgently.

Disclosure: No conflict of interest.

P0512

MEDICAL CANNABIS REDUCES PAIN AND IMPROVES SLEEP QUALITY IN CROHN'S DISEASE PATIENTS. A PROSPECTIVE OBSERVATIONAL STUDY

A. Hirsch¹, N. Fliss-Isakov¹, L. Werner², D. Meiri³, C. Seidenberg⁴, N. Maharshak^{5,6}

¹Tel Aviv Sourasky Medical Center, Gastroenterology, Tel Aviv, Israel, ²Tel Aviv Sourasky Medical Center Dept. of Gastroenterology, Tel Aviv, Israel, ³Technion-Israel Institute of Technology, The Laboratory of Cancer Biology and Cannabinoid Research, Department of Biology, Haifa, Israel, ⁴Hebrew University of Jerusalem, Department of Pharmacology, Jerusalem, Israel, ⁵Tel Aviv Medical Center, Department of Gastroenterology and Liver Diseases, Tel Aviv, Israel, ⁶Tel Aviv Sourasky Medical Center, Sackler School of Medicine, Tel Aviv, Israel

Contact E-Mail Address: ayal.red@gmail.com

Introduction: Inflammatory bowel disease related symptoms have limiting and often disabling consequences on patients' life. Pain is a predominant symptom in individuals with Crohn's Disease (CD), and in up to 87% of patients with IBD, chronic pain is a growing problem and has a large impact on quality of life. In addition, Poor sleep is associated with adverse health consequences and was shown to be associated with subclinically active inflammatory bowel diseases (IBD). Altered sleep patterns in IBD patients were associated with frequent disease flares and lower quality of life.

The aim of this study was to assess the effect of cannabis use on chronic pain and sleep quality in patients with CD.

Aims & Methods: We conducted a prospective observational cohort study enrolling 127 CD patients who were prescribed medical cannabis. Patients who changed medication during the trial, reported use of cannabis 3 months before the trial, or failed to follow up were excluded from the analysis. Patients filled questionnaires at baseline and after 3 and 6 months of therapy. Sleep quality was measured using the Pittsburgh Sleep Quality Index (PSQI). Pain intensity was measured using pain visual analog scale (VAS).

Results: A total of 127 patients with CD were included, of these x(y%) were male, with a median age of y (range) and a median disease duration of x years (range). The median prescribed cannabis dose was X grams, with a median of x grams of CBD and y grams of THC per month.

Patients reported a reduction in pain intensity with a decrease in mean pain VAS score at 3 months (6.1±0.4 vs 5.2±0.4, p≤0.01) and (6.1±0.4 vs 4.8±0.4, p=) at 6 month, compared to baseline. Pittsburgh Sleep Quality Index (PSQI) for sleep (from 7.7±0.5 to 6.2±0.5, p≤0.001).

Disease severity also decreased significantly according to the Harvey Bradshaw index (HBI, from 8.3±0.7 to 6.5±0.5, p≤0.001).

After 6 months of MC therapy; VAS, PSQI and HBI scores did not change further, in comparison to 3 months therapy (4.8±0.4, 6.5±0.6, and 6.3±0.5; respectively. p=NS).

Conclusion: MC significantly improves how patients perceive their pain, disease severity and sleep quality. Ongoing experiments to determine fecal calprotectin levels will hint to CB's effect on intestinal inflammation.

Disclosure: Nothing to disclose.

P0513

FACTORS INFLUENCING INFLIXIMAB FAILURE IN ANTI-TNF NAIVE CHILDREN WITH ACTIVE ULCERATIVE COLITIS

H. Atta¹, R. Muhammed¹¹Birmingham Children's Hospital, Gastroenterology, Birmingham, United Kingdom

Contact E-Mail Address: huda.atta@nhs.net

Introduction: Infliximab is an effective treatment for moderate to severe ulcerative colitis in children. We aimed to identify factors that influence remission at week 52

Aims & Methods: Aim: To evaluate predictors at diagnosis and post IFX induction for achieving/maintaining remission at week 52

Methods: Retrospective study of 50 consecutive children with ulcerative colitis managed with Infliximab at Birmingham Children's Hospital with follow-up for at least one year after commencing Infliximab treatment. All patients had Infliximab level and antibody levels documented as requested by the clinician.

Clinical remission was assessed using by Paediatric Ulcerative Colitis Activity Index (PUCAI). Steroid-free remission was defined as patients in clinical remission without the need for any forms of steroid therapy in the previous 3 months. Statistical analysis was done using SPSS Statistics 28.0.1

Results: 50 patients treated with Infliximab (biosimilar Infliximab) as their primary biological treatment for active ulcerative colitis. One patient had infusion reaction after one infusion of Infliximab. Clinical remission was achieved in 31/49 (63%) patients at week 12. 38/49 (78%) were in steroid-free clinical remission at week 52.

Table 1 shows the comparison between patients who remained in steroid-free clinical remission at week 52 and patients not in steroid-free remission at week 52 or discontinued Infliximab before week 52.

	Patients in steroid-free clinical remission at week 52 (n=38)	Patients not in steroid-free clinical remission at week 52 or discontinued Infliximab before week 52 (n= 11)	P value
Age at diagnosis in years (mean)	10.9	11.36	0.34
PUCAI at diagnosis (mean)	49.3	58.18	0.078
CRP (mg/L) at diagnosis	7.4	26.87	0.022*
Patients on Combined Therapy (n)	30	7	0.29
PUCAI at week 12 (mean)	6.71	20.45	0.003*
Patients in clinical remission at week 12 (n)	27 (71%)	4 (36%)	0.036*
IFX level (µg/mL) category			
<5	8	0	0.23
5-10	7	2	
>10	23	9	
Anti-infliximab antibodies (AU/mL) at week 12(Mean)	10.2	4.9	0.076
Number of patients with anti-infliximab antibodies	5	0	0.2
Patients needed modification of IFX dose	32 (84%)	6 (55%)	0.09

Table 1.

Of the 31 patients in clinical remission at week 12, 27 continued to remain in steroid-free remission at week 52. 4/31 had secondary loss of response to Infliximab (1 changed to adalimumab, 1 had re-induction with infliximab, 1 had treatment with budesonide and 1 had added treatment with mesalazine).

Of the 18 patients not in clinical remission at week 12, 11 (61%) achieved steroid-free clinical remission by week 52. 2/18 needed colectomy and another 2 patients were switched to different treatment (1 to cyclosporine and 1 to adalimumab). 3/18 remained on Infliximab till week 52, however did not achieve steroid-free remission by week 52.

Factors influencing steroid-free remission at week 52 were elevated CRP at diagnosis ($p = 0.022$) and clinical remission at week 12 ($p = 0.036$). Combination therapy with immunomodulators or Infliximab levels or anti-infliximab antibody levels did not correlate with steroid-free remission at week 52.

Conclusion: Infliximab treatment failure is uncommon in children with ulcerative colitis and is predicted by high CRP levels at diagnosis and failure to achieve clinical remission at week 12 after commencing Infliximab treatment.

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P0514

PROACTIVE INFLIXIMAB IS MORE EFFECTIVE THAN VEDOLIZUMAB IN INDUCING FECAL CALPROTECTIN REMISSION IN INFLAMMATORY BOWEL DISEASE

I. Botto¹, S. Bronze¹, I. Rodrigues¹, J. Serrazina¹, S.R. Fernandes¹, S. Bernardo¹, A.R. Gonçalves¹, A.I. Valente¹, P. Moura Santos¹, L. Correia¹, R.T. Marinho¹¹Centro Hospitalar Universitário Lisboa Norte, Serviço de Gastreenterologia e Hepatologia, Lisboa, Portugal

Contact E-Mail Address: sergiobronze@campus.ul.pt

Introduction: Current evidence suggests that vedolizumab (VDZ) may be as effective as infliximab (IFX) in inflammatory bowel disease. It is unknown if proactive therapeutic drug monitoring (PTDM) of IFX may improve these results.

Aims & Methods: Case-control study including consecutive patients with primary response to conventional IFX (n=70), proactive IFX (n=148), and VDZ (n=95). PTDM was performed at week 14 and every other infusion, aiming at a trough level between 5-10 µg/mL. The primary outcome was fecal calprotectin (Fc) remission (<250 µg/g) at 1 year of treatment. Secondary outcomes included Fc remission at week 14 (proactive IFX/VDZ), and clinical remission, treatment discontinuation, hospitalization, and surgery at 1-year of follow-up.

Results: Proactive IFX was superior to conventional IFX and VDZ in inducing Fc remission at 1-year (69.4% vs 47.1% vs 37.9%, $P=0.003$ and $P<0.001$). Results remained significant in biologic naïve patients (70.8% vs 44.4% vs 51.4%, $P=0.001$ and $P=0.043$) but comparisons between conventional IFX and VDZ were not significant ($P=0.265$ and $P=0.664$). In multivariate analysis correcting for prior biologic exposure, proactive IFX was more effective than conventional IFX (OR 2.480 95%CI[1.367-4.499], $P=0.003$) and VDZ (OR 3.467 95%CI[1.578-7.617], $P=0.002$) in inducing Fc remission. Amongst secondary outcomes, only clinical remission was significant between proactive IFX and VDZ in the overall cohort (80.4% vs 55.8%, $P<0.001$) and in biologic naïve patients (80.2% vs 62.9%, $P=0.043$). Fc remission at 1-year was associated with better results in most secondary outcomes.

Conclusion: Proactive IFX was superior to VDZ in inducing Fc remission at 1-year, which associated with improved clinical outcomes.

Disclosure: Nothing to disclose.

P0515

EFFECTS OF REPEAT INFLIXIMAB TO STEADY STATE ON BLOOD PROINFLAMMATORY BIOMARKERS TNFA, IL-6, IFN γ AND NITRITE/NITRATE IN CROHN'S DISEASE

A. Touny¹, D.-L. Webb¹, P.M. Hellström¹

¹Uppsala University, Medical Sciences/Gastroenterology, Uppsala, Sweden

Contact E-Mail Address: per.hellstrom@medsci.uu.se

Introduction: Crohn's disease is an incurable gastrointestinal inflammation causing a significant burden for patients. It is a heterogeneous disease derived by a cascade of inflammatory reactions. Currently, biological agents are promising and achieving optimum disease management.

The aim of the study was to longitudinally follow the biomarker response to infliximab in order to differentiate the most adequate therapeutic marker.

Aims & Methods: A total of 46 patients with moderate-to-severe Crohn's disease were investigated for their response to infliximab. They received infliximab (5 mg/kg) throughout multiple time points of infusion visits which were coupled with subsequent follow-up visits one week post each infusion. Harvey-Bradshaw Index (HBI), a questionnaire assesses the degree of the disease activity, was reported by patients before and after treatment. Patients' serum samples that were drawn during infusion and follow-up visits were analyzed for the major disease-driving inflammatory biomarkers.

Analysis involved measurement of nitrite/nitrate (NOx) concentration by the nitrite/nitrate assay, in addition to, measurement of TNF α , IL-6, and IFN γ by MesoScale ELISA technique. As controls, 63 healthy subjects were used and their serum samples were analyzed for the same biomarkers.

Results: The analysed biomarkers displayed different response patterns to infliximab. Whereas TNF α reflected the treatment with infliximab, IFN γ displayed a short-term passing response to infliximab, and IL-6 a more protracted response.

NOx levels decreased significantly throughout the infliximab infusions approaching the concentration range of healthy controls. NOx showed a superior stable response to infliximab compared with the other studied proinflammatory cytokines. HBI scores dropped significantly after infliximab treatment.

Infliximab is efficacious in maintaining NOx levels downregulated over time. NOx could be useful as a main diagnostic biomarker and in monitoring therapeutic response. The drop in HBI scores post treatment demonstrates the inhibition of disease activity with remission and improvement of patients' quality of life.

Conclusion: Infliximab treatment is efficacious in maintaining NOx levels downregulated over time, while other biomarkers were found to show variable responses in parallel with infliximab treatments. NOx could be useful as a main diagnostic biomarker and in monitoring a long-standing therapeutic response. The drop in HBI scores post treatment demonstrates the inhibition of disease activity with remission and improvement of patients' quality of life.

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P0516

NEED FOR VEDOLIZUMAB INTENSIFICATION IN REAL LIFE CLINICAL PRACTICE

T. Alexopoulos¹, E. Ionas², S. Kartsoli³, P. Karatzas¹, G. Michalopoulos², S. Vrakas³, V. Delis², V. Xourgias³, G. Papatheodoridis¹

¹Laiko General Hospital of Athens, Academic Gastroenterology Clinic, Athens, Greece, ²General Hospital of Athens G. Gennimatas, Gastroenterology, Athens, Greece, ³General Hospital of Piraeus Tzaneion, Gastroenterology, Piraeus, Greece

Contact E-Mail Address: sbrakas@yahoo.gr

Introduction: Loss of response in vedolizumab has not been extensively studied, but the estimated annual risk is around 13%. In the majority of cases empirical dose intensification every 4 weeks rather than therapeutic drug monitoring is used as a measure to regain response. According to the literature almost 50% of patients can regain response with this approach. Aim of this study was the recording of the percentage of patients receiving intensified regimen of vedolizumab as well as the basic characteristics of these patients.

Aims & Methods: This is a retrospective study with recording of patients currently in vedolizumab treatment from 3 tertiary centers. Data regarding disease extension, location, behavior, reason of intensification, duration of treatment before intensification were recorded.

Results: A total of 59 patients with inflammatory bowel disease (IBD) under vedolizumab therapy were enrolled; 22 with Crohn's disease (CD) and 37 with ulcerative colitis (UC). Six of the CD patients were classified as L1, 2 as L2 and 14 as L3. 20 of the UC patients were classified as extended colitis, 17 with left-sided colitis and none with proctitis. Out of the 59 patients with IBD, 13 were receiving vedolizumab every 4 weeks and one patient every 6 weeks. Intensified dosing was used in 9 (24.3%) of the 37 patients with UC and in 4 (18.2%) of those with CD. The reason for dosing intensification was primary non-response in 2 patients, partial response in 9 patients and disease exacerbation in 2 patients. Only in 1 case vedolizumab was returned to the initial dosing scheme of every 8 weeks. Seven patients received corticosteroids before dose-intensification, whereas six patients did not.

Conclusion: Approximately 20% of IBD patients under vedolizumab therapy need intensified dosing scheme to maintain response.

Disclosure: Nothing to disclose.

P0517

THE USE OF NUTRITION AS A THERAPEUTIC STRATEGY IN CHILDREN AND ADOLESCENTS WITH CROHN'S DISEASE IN BELGIUM

G. Veereman¹, A. Sajed¹, E. Degreef¹, F. Smets², A. Bobarnac³, P. Bontems⁴

¹UZBrussels, Pediatric Gastroenterology, Brussels, Belgium,

²Hopital St Luc, UCL, Pediatric Gastroenterology, Brussels,

Belgium, ³CHC Liège, Pediatric Gastroenterology, Liege, Belgium,

⁴Hopital Reine Fabiola, ULB, Brussels, Belgium

Contact E-Mail Address: gveereman@gmail.com

Introduction: Enteral nutrition (EN) is increasingly used for treating pediatric Crohn's disease (CD). We retrospectively studied the use of EN in Belgium and to assess the effect of diet on disease activity and growth. The Belgian Society for Pediatric Gastroenterology and Nutrition (BESPGHAN) is currently implementing the Improve Care Now (ICN) registry for Belgian CD patients. The ICN registry collects clinical data at each outpatient visit, including nutritional and growth status and the use of EN.

Aims & Methods: The medical files of Belgian pediatric patients (<18 yrs old) diagnosed with CD and identified to be included in the newly implemented ICN registry were analyzed from 2015 to 2020 for disease classification, use of EN, growth delay and BMI. Eleven variables were selected from the dataset. The response variable was BMI (kg/m²). The predictor variables were Modulife program diet, exclusive enteral nutrition (EEN), any specific diet (milkfree, lactosefree, glutenfree, meat free, excluding processed foods, including supplements), dietician involved, treatment, age at diagnosis, disease location and behavior, growth delay.

Statistical analysis was conducted using the SPSS software v.28. Pie plots with %, mean and SD were calculated for BMI. Independent samples t-tests were used to compare BMI based on variables with 2 groups or ANOVA for more than 2 groups. A p-value < 0.05 was considered significant. Effect size was calculated for each variable as well as power analysis.

Results: Data were collected from the databases of UZ Brussel, ULB, UCL and CHC Liège during the period 2015 – 2020.

The final dataset consisted of 124 patients (39.5% UZBrussel, 43.5% UCL and 17% CHC Liege). We found no association between disease location or behavior and BMI (p 0.566 & 0.864 respectively). Growth delay was significantly associated with BMI (p < 0.05).

Patients not needing biological treatment had a statistically higher BMI (p-value < 0.001). A large proportion of patients (81%) received EEN but results showed no statistical significance between those who were exposed or not (p-value = 0.667 > 0.05).

In contrast, the Modulife program led to a significantly better BMI (19.8 ± 3.8 vs. 17.5 ± 3.9 p = 0.004) and patients on any type of specific diet had a mean BMI 19.7 ± 3.9 compared to the others with BMI 17.3 ± 3.1 (p = 0.005). Involving a dietician showed a trend for better mean BMI (20.1 ± 3.9) compared to not (mean BMI 18.9 ± 3.9).

Conclusion: Results indicate no relationship between using a diet and age, disease location, behavior or growth, indicating the lack of criteria for implementing nutritional therapy. However, the use of Modulife program or any specific diet were associated with improved BMI.

Disclosure: Nothing to disclose.

P0518

RESTORATION OF MICROBIOME COMPOSITION AND INCREASED BUTYRATE PRODUCTION ARE ASSOCIATED WITH RESPONSE TO SYSTEMIC CORTICOSTEROIDS IN PATIENTS WITH ACTIVE ULCERATIVE COLITIS

A. Blesl¹, P. Wurm¹, S. Waschina², H.-P. Gröchenig³, G. Novacek⁴, C. Primas⁴, W. Reinisch⁴, M. Kutschera⁴, C. Illiasch⁵, B. Hennlich⁵, P. Steiner⁶, A.R. Moschen⁷, R. Koch⁸, W. Tillinger⁹, T. Haas¹⁰, G. Reicht¹¹, A. Mayer¹², O. Ludwiczek¹³, W. Miehsler¹⁴, K. Steidl¹⁵, L. Binder¹, S. Reider⁷, S. Fürst¹, P.K. Kump¹, K. Aden¹⁵, G. Gorkiewicz¹⁶, C. Högenauer¹

¹Medical University of Graz, Division of Gastroenterology and Hepatology, Graz, Austria, ²Christian-Albrechts-University Kiel, Institute for Human Nutrition and Food Science, Nutriinformatics, Kiel, Germany, ³Barmherzige Brüder, St. Veit an der Glan, Austria, ⁴Medical University of Vienna, Vienna, Austria, ⁵Hospital Landstraße, Vienna, Austria, ⁶Hospital Wels-Grieskirchen, Wels, Austria, ⁷Johannes Kepler University Linz, Linz, Austria, ⁸Medical University of Innsbruck, Innsbruck, Austria, ⁹Franziskus Hospital, Wien, Austria, ¹⁰Darmpraxis, Salzburg, Austria, ¹¹Barmherzige Brüder, Graz, Austria, ¹²University Hospital, St. Pölten, Austria, ¹³Hospital Hall, Hall, Austria, ¹⁴Barmherzige Brüder, Salzburg, Austria, ¹⁵Christian-Albrechts-University and University Hospital, Institute of Clinical Molecular Biology and Department of Internal Medicine I, Kiel, Germany, ¹⁶Medical University of Graz, Institute of Pathology, Graz, Austria

Contact E-Mail Address: andreas.blesl@medunigraz.at

Introduction: Corticosteroid therapy is still widely used to treat active ulcerative colitis (UC). The composition of the intestinal microbiome has been shown to influence treatment response to biologics in UC. We therefore investigated microbiome composition and metabolic processes during systemic corticosteroid therapy in patients with active UC and its association to treatment response.

Aims & Methods: Investigator-initiated, prospective, multi-centre study. UC patients were eligible if suffering from active disease (Lichtiger score ≥ 4) and scheduled for treatment with systemic corticosteroids. Patient characteristics and clinical scores were assessed and serum and stool samples collected at the time of steroid initiation (V1) and after one month (V2).

Patients were divided into responders (decrease of Lichtiger score ≥ 50%) and non-responders to corticosteroids at V2. 16s rRNA sequencing was performed from fecal samples, data were analysed with QIIME 2 and microbial community metabolic processes were predicted using parsimonious flux balance analysis.

Results: 93 patients (45% females) with active UC were included in the analysis. 69 patients (74%) responded to corticosteroid treatment, 24 patients (26%) did not respond. Before treatment initiation, both groups could not be distinguished by microbiome composition or function. Responders longitudinally experienced varied beta diversity and an increase of the beneficial genera *Blautia*, *Anaerostipes* and *Bifidobacterium* as well as an increase of predicted butyrate production. Non-responders had only minor longitudinal taxonomic changes with an increase of *Streptococcus salivarius*. After one month of corticosteroid therapy, responders had lower alpha diversity, distinct microbiome composition with higher abundance of the genus *Anaerostipes* and a trend to increased predicted butyrate synthesis compared to non-responders.

Conclusion: Response to systemic corticosteroids in active UC is characterized by microbiome restoration and enhanced butyrate production, probably as an indirect effect of reduced intestinal inflammation.

We were however unable to find specific predictive microbiome makers that could forecast response to therapy.

References: None.

Disclosure: Nothing to disclose.

P0519 WITHDRAWN

P0520

CUTANEOUS MANIFESTATIONS IN BIOLOGICAL-TREATED PEDIATRIC INFLAMMATORY BOWEL DISEASE: A 10 YEARS' EXPERIENCE FROM A TERTIARY CENTER

Z. Shchomak¹, S. Azevedo¹, L. Rodrigues¹, A.S. Cordeiro Fernandes dos Santos¹, H. Loreto¹, P. Mourato¹, A.I. Lopes¹

¹Centro Hospitalar Lisboa Norte, Department of Pediatrics, Gastroenterology Unit, Lisbon, Portugal

Contact E-Mail Address: zakhar.shchomak@gmail.com

Introduction: The advent of biological therapy has greatly improved the treatment of inflammatory bowel disease (IBD). However, biological agents, particularly anti-tumor necrosis factor-alpha (TNF-α) agents, can induce a wide variety of skin eruptions, including eczema, paradoxical psoriasis, cutaneous infections, among others.

It is important to recognize and treat these conditions appropriately and in the case of severe lesions, the biological may need to be discontinued. Only few data have been so far reported in pediatric population.

Aims & Methods: The aim of this study is to describe the cutaneous manifestations associated with biologic treatment of pediatric IBD within the last ten years in a tertiary center. A retrospective chart review (period between 2011-2022) was performed concerning patients ≤ 18 years with newly IBD diagnosis who developed new-onset lesions while treated with biological therapy.

Results: Eleven children from a total of 33 (33%) (25 with Crohn's disease, 7 with ulcerative colitis and 1 with IBD unclassified) developed cutaneous manifestations. The median age was 13,6 years (range 0,5-17,1), 6 (45%) were male and the median time from the start of biological treatment to development of lesions was 8,7 months (range 1,8-26,1).

The skin manifestations included 9 cases of paradoxical psoriasis (2 with associated folliculitis and 1 with eczema) and 2 cases of recurrent folliculitis. 9/11 (82%) were observed in dermatology outpatient clinic and 3/9 (33%) of these have required a biopsy.

The most frequently associated agents were adalimumab (7) and infliximab (4). The severity of lesions led to biologic agent discontinuation in 4 patients, all of them treated with adalimumab. In all patients, severe paradoxical psoriasis was observed and IBD was in remission at the time of onset of the skin lesions. In three of these 4 patients, a switch to another biological agent was required and in one patient to azathioprine.

Clinical improvement was observed in 2 patients that switched to ustekinumab and in one who switched to azathioprine. In two patients (1 treated with infliximab who developed recurrent folliculitis, and another treated with adalimumab who developed paradoxical psoriasis) the switch to another biological agent was due to IBD control failure.

Both, experienced subsequent clinical improvement of clinical lesions (vedolizumab and ustekinumab, respectively). Five of the remaining patients have responded to standard dermatological care.

Conclusion: Cutaneous manifestations associated with biological treatment were common in our series and led to biologic agent discontinuation in 12% of the patients, similarly to other recent series. The agent most frequently associated with cutaneous lesions was adalimumab and the

most common lesion was paradoxical psoriasis. In the most severe cases, the switch to alternative class biological agent may be effective in controlling the skin lesions and maintaining disease remission. The pathogenic mechanisms of paradoxical psoriasis are still poorly understood, but our preliminary findings suggest that cutaneous manifestations do not seem to be associated with the severity of IBD.

Disclosure: Nothing to disclose.

P0521

IMPACT OF BIOLOGIC ERA ON COLECTOMY RATE OF ULCERATIVE COLITIS; ASSESSMENT OF 22 YEAR IN A TERTIARY REFERRAL CENTER COHORT FROM A DEVELOPING COUNTRY

B. Tukek¹, O.K. Bakkaloglu¹, İ. Hatemi¹, A.F. Celik¹, Y. Erzin¹
¹Istanbul University Cerrahpasa, Istanbul, Turkey

Contact E-Mail Address: o.k.bakkaloglu@gmail.com

Introduction: We aimed to evaluate the effect of biologic era on colectomy rates and determine colectomy-related factors in our 22-year-old ulcerative colitis (UC) cohort.

Aims & Methods: Our tertiary referral center UC cohort was retrospectively evaluated. Biologic therapy in UC was reimbursed in our country in 2009 whereas its use was more frequent in our center since 2012 [first anti-TNF's than followed by vedolizumab (2017) and ustekinumab (2018)]. The patients were grouped and compared considering 2012 as a turning point of pre and post biologic era. Two patient subgroups were selected from the cohort: one consisted of patients whose follow-up finished before 2012 and the other consisted of patients with follow-up starting at/after 2012. Patients with less than 6 months of follow-up were excluded.

Results: The total number of patients of our cohort was 1058 with a median follow-up of 4 years. %35 of patients had pancolitis and half of the whole group required steroid at any point. Among steroid users, frequency of unresponsiveness was 4% and dependence was 28%.

	Pre-2012 Patient Group (n=205)	Post-2012 Patient Group (n=633)	p value
Sex (Female, %)	42	47	0.149
Age at Diagnosis (Mean ± SD years)	37 ± 13	35 ± 13	0.220
Follow-up Duration (median, month) (minimum>6 months)	31	37	0.08
Smoking (ever, %)	42	24	<0.001
Active Smoker	20	18	0.175
Ex-Smoker	22	7	<0.001
Initial extension (Paris) E1/E2/E3/E4 (%)	12/49/11/28	16/40/14/30	0.704
Maximum extension (Paris) E1/E2/E3/E4 (%)	11/46/9/34	13/37/15/36	0.245
Extension progressed during follow-up (%)	7	11	0.164
Steroid course need (ever) (%)	50	51	0.784
Steroid unresponsiveness (%)	3	2	0.560
Steroid dependency (%)	19	11	0.004
Steroid course/year (median)	1,1	0,6	0.025
Maximal treatment (%)			
5-ASA	71	56	<0.001
Immunomodulatory	28	19	0.004
Biologic	-	26	-
Minimum CRP under max. treatment step (median, mg/L)	3	1.4	<0.001
Mucosal remission under max. treatment (%)	46	57	0.048
Disease duration at colectomy (median, month)	46	38	0.404
First Year Colectomy Rate (%)#	5	0.3	<0.001
Total Colectomy rate (%)	12	2	<0.001

Table 1: Comparison of clinical features and colectomy rates of two non-overlapping independent patient sub-groups.

For the whole group: 38% of the patients received immunomodulatory therapy and 20% received biologics (of which were 64% Infliximab, 59% Adalimumab, 15% Vedolizumab, 4% Ustekinumab). Before 2012 biological therapy was less than 1%, but increased up to 25% after 2012. Total colectomy rate (including malignancy related cases) was 5.8% and disease activity related colectomy was 4.8% (n=51) in the whole group. Colectomy rate before and after 2012 was 6% (n=28) and 2.7% (n=23) respectively showing significant difference ($p<0.001$).

Table 1 shows the comparison of pre- and post-biologic era patients. Both total and 1st year colectomy rates were lower in the biologic era patients. Disappearance of this significance^{#(Table 1)} at the 4th year of disease duration suggests that biological era delay or rescue early colectomies. In the Cox regression analysis of the whole group, failure to achieve mucosal remission, a best achieved CRP value $>3\text{mg/L}$ under maximal treatment, steroid dependency, steroid unresponsiveness, and an increased number of steroids needing relapses per year were found to be independently associated with colectomy.

Conclusion: To our best knowledge, our current study discloses the colectomy decreasing effect of biologic era from a developing country for the first time. Although achievement of mucosal remission and/or (as a novel target) CRP $<3\text{mg/L}$ under were associated with reduced colectomy risk in the whole cohort, the frequency of colectomy was particularly decreased in the biological era. Treatment, modalities, and cessation of smoking between each era, as well as the effect of biological therapy, may have influence on this result.

Disclosure: Nothing to disclose.

P0522

LOSS OF RESPONSE AND DOSE ESCALATION OF INFLIXIMAB AND ADALIMUMAB IN ULCERATIVE COLITIS PATIENTS: A SYSTEMATIC REVIEW AND META-ANALYSIS

E. Savelkoul¹, P. Thomas², L. Derikx², N. Den Broeder², T.E.H. Römkens³, F. Hoentjen⁴

¹Radboudumc, Gastroenterology, Nijmegen, Netherlands,

²Radboudumc, Gastroenterology and Hepatology, Nijmegen, Netherlands, ³Jeroen Bosch Hospital, Den Bosch, Netherlands,

⁴University of Alberta, Edmonton, Canada

Contact E-Mail Address: Edo.Savelkoul@radboudumc.nl

Introduction: Loss of response to infliximab or adalimumab in ulcerative colitis occurs frequently and dose escalation may aid in regaining clinical benefit. This study aimed to systematically assess the annual loss of response and dose escalation rates for infliximab and adalimumab in ulcerative colitis.

Aims & Methods: A systematic search was conducted from January 2000 to July 2021, for studies reporting loss of response and dose escalation during infliximab and/or adalimumab use in ulcerative colitis patients with primary response. Annual loss of response and dose escalation rates and clinical benefit after dose escalation were calculated. Subgroup analyses were performed for studies with one-year follow-up (cut-off ≤ 65 weeks).

Results: We included 50 unique studies assessing loss of response (infliximab: n=24, adalimumab: n=21) or dose escalation (infliximab: n=21, adalimumab: n=16). The pooled annual loss of response for infliximab was 10.1% (95% CI [7.1-14.3]) and 13.6% (95% CI [9.3-19.9]) for studies with one-year follow-up.

The pooled annual loss of response for adalimumab was 13.4% (95% CI [8.2-21.8]) and 23.3% (95% CI [15.4-35.1]) for studies with one year follow-up. Annual pooled dose escalation rates were 13.8% (95% CI [8.7-21.7]) for infliximab and 21.3% (95% CI [14.4-31.3]) for adalimumab, regaining clinical benefit in 72.4% and 52.3%, respectively.

Conclusion: Annual loss of response was 10% for infliximab and 13% for adalimumab, with higher rates during the first year. Annual dose escalation rates were slightly higher than loss of response, with clinical benefit 72% (infliximab) and 52% (adalimumab). Uniform definitions are needed to provide more robust evaluations.

Disclosure: PT, ES, and NdB report no conflicts of interest. LD has served as speaker or on advisory boards of Sandoz, Janssen and Dr Falk. TR has served as speaker, or consultant for Ferring, Janssen, Takeda. FH has served on as speaker or consultant for Abbvie, Takeda, and has received unrestricted grants from Janssen-Cilag, Abbvie.

P0523

LONG-TERM COLECTOMY RATES IN ULCERATIVE COLITIS OVER DIFFERENT ERAS – A POPULATION-BASED STUDY FROM WESTERN HUNGARY BETWEEN 1977–2020, DATA FROM THE VESZPREM COUNTY COHORT

L. Gonczi¹, L. Lakatos², P.A. Golovics³, T. Pandur⁴, G. Dávid², Z. Erdelyi², I. Szita², P.L. Lakatos⁵

¹Semmelweis University, Department of Internal Medicine and Oncology, Budapest, Hungary, ²Ferenc Csolnoky County Hospital, Department of Gastroenterology, Veszprem, Hungary, ³Hungarian Defence Forces Medical Centre, Department of Gastroenterology, Budapest, Hungary, ⁴Grof Eszterhazy Hospital, Department of Gastroenterology, Papa, Hungary, ⁵McGill University Health Center, Division of Gastroenterology, Montreal, Canada

Contact E-Mail Address: lorantgonczi@gmail.com

Introduction: Few population-based studies have investigated the long-term colectomy rates of ulcerative colitis (UC). The present study is a continuation of the Veszprem IBD population based cohort with a follow-up of the incidence and disease course for over 40 years.

Aims & Methods: Our aim was to analyze the long-term colectomy rates over different therapeutic eras in a prospective population-based database from Veszprem Province, including incident UC patients.

Data of 1,370 incident UC patients were analyzed (male/female: 702/668; median age at diagnosis: 37 years(y) [IQR: 26-51]), with a median of 17y (IQR 9-24) follow-up. Patient inclusion lasted between January 1, 1977 and December 31, 2018. Patient follow-up ended December 31, 2020.

Both in-hospital and outpatient records were collected and comprehensively reviewed at diagnosis and during clinical follow-up. Disease extension was evaluated based on the Montreal classification. Colectomy rates were examined in three different eras based on time of diagnosis: cohort-A, 1977-1995; cohort-B, 1996-2008; and cohort-C, 2009-2018.

Results: The overall colectomy rate was 76/1,370 patients during the total follow-up. The cumulative probability of colectomy in the total population was $4.1\pm 0.6\%$ after 10 years, $6.3\pm 0.8\%$ after 20 years, and $8.8\pm 1.2\%$ after 30 years. Disease phenotype at diagnosis was similar in the three cohorts (extensive colitis: 24.2% / 24.3% / 34.9% in cohorts A/B/C). Overall immunosuppressive therapy use was increasing in the cohorts (11.3% / 20.9% / 34.4%), as well as the probability of biological therapy initiation within 5 years of diagnosis ($0.0\pm 0\%$ / $3.3\pm 0.7\%$ / $13.9\pm 1.8\%$).

There were no statistically significant differences in the cumulative probability of colectomies between cohorts A/B/C: $1.7\pm 0.7\%$ / $2.2\pm 0.6\%$ / $3.7\pm 1.0\%$ after 5 years; $3.5\pm 1.0\%$ / $3.9\pm 0.8\%$ / $4.5\pm 1.2\%$ after 10 years; and $6.9\pm 1.4\%$ / $5.3\pm 1.0\%$ (cohorts A/B) after 20 years [Log Rank=0.447].

Conclusion: No differences in colectomy risk have been observed in incident UC patients over the 40 years of this population-based study, despite the increasing use of immunosuppressive and biological therapies.

Disclosure: Nothing to disclose.

P0524

INFLUENCE OF DIABETES MELLITUS ON INFLAMMATORY BOWEL DISEASE COURSE AND TREATMENT OUTCOMES.A SYSTEMATIC REVIEW WITH META-ANALYSIS

G. Fuschillo¹, V. Celentano^{2,3}, M. Rottoli^{4,5}, G. Sciaudone¹, A.G. Gravina⁶, R. Pellegrino⁶, R. Marfella¹, M. Romano⁶, F. Selvaggi¹, G. Pellino¹

¹Università degli Studi della Campania "Luigi Vanvitelli", Department of Advanced Medical and Surgical Sciences, Naples, Italy, ²Chelsea and Westminster Hospital NHS Foundation Trust, London, United Kingdom, ³Imperial College London, Department of Surgery and Cancer, London, United Kingdom, ⁴Alma Mater Studiorum University of Bologna, Department of Medical and Surgical Sciences, Bologna, Italy, ⁵IRCCS Azienda Ospedaliero Universitaria di Bologna, Surgery of the Alimentary Tract, Bologna, Italy, ⁶Division of Hepatogastroenterology, University of Campania "Luigi Vanvitelli", Department of Precision Medicine, Naples, Italy

Contact E-Mail Address: gipe1984@gmail.com

Introduction: Inflammatory bowel disease (IBD) may be associated with other immune-mediated conditions, both as a consequence of medical treatment and because of complex etiologic interactions. Diabetes Mellitus (DM) may occur in patients with IBD and influence the disease progression.

Aims & Methods: The aim of this study was to compare the course and outcomes of treatment in IBD patients with and without DM.

This is a PRISMA- and MOOSE- compliant systematic review with meta-analysis recorded on PROSPERO (ID CRD42022315509). Only studies comparing patients with IBD plus DM with patients with IBD only were included.

Primary endpoints were: need for surgery, IBD-related complications, IBD-related hospitalizations, sepsis, and mortality.

Secondary endpoints were risk of infection, quality of life, and healthcare costs.

Results: Five studies including 71,216 IBD patients, 36,248 patients (50.9%) without vs. 34,968 patients (49.1%) with DM, were included in the meta-analysis. The risk for IBD-related complications (OR=1.12 95%CI 0.52-2.45 P 98% $p=0.77$), mortality (OR=1.52 95%CI 0.61-3.81, P 98% $p=0.37$) and IBD-related surgery (OR=1.20 95%CI 0.88-1.63, P 81% $p=0.26$) did not differ between groups.

The risk of IBD-related hospitalizations (OR=2.52 95%CI 2.17-2.98, I^2 0% $p<0.00001$) and sepsis (OR=1.56 95%CI 1.06-2.29, I^2 88% $p=0.0003$) was higher in the IBD+DM group.

The risk of pneumonia and urinary tract infections (UTIs) was higher in the IBD+DM group (OR=1.72 95%CI 1.38-2.14, P 0% $p<0.00001$ vs OR=1.93 95%CI 1.51-2.47 P 8% $p<0.00001$ respectively), while the risk of *C. Difficile* infection did not differ (OR=1.22 95%CI 0.78-1.90 P 88% $p=0.37$).

The mean Short Inflammatory Bowel Disease Questionnaire (SIBDQ) score was lower in the IBD+DM group than in the IBD group (38.9 vs. 47, respectively $p=0.03$). Mean health care costs per year were \$10,598.2 [IQR 37,808.4] vs \$3,747.3 [IQR 20,182.9] ($p<0.001$).

In order to reduce heterogeneity, a sensitivity analysis has been conducted: for surgical interventions related to IBD an OR of 1.21 was found (95%CI 1.00-1.46, P 0% $p=0.05$), as for sepsis, the OR was 1.92 (95%CI 1.56-2.37, P 0% $p<0.00001$).

Finally, an analysis was conducted on patients with Crohn's disease (CD) that reported an OR on surgery CD-related of 3.03, 95%CI 0.92-9.99, I^2 76% $p=0.07$.

Outcomes	IBD+DM vs IBD				CD+DM vs CD		
	Before sensitivity analysis		After sensitivity analysis				Relative effect (95% CI)
	N of patients (studies)	Relative effect (95% CI)	I^2	N of patients (studies)	Relative effect (95% CI)	I^2	
IBD related hospitalizations	3026 (2)	OR 2.54 (0.52 to 2.45)	0	-	-	-	-
Mortality	70225 (2)	OR 1.52 (0.61 to 3.81)	98%	-	-	-	-
Sepsis	70435 (3)	OR 1.56 (1.06 to 2.29)	88%	2695 (2)	OR 1.92 (1.56-2.37)	0%	-
IBD-related surgery	71006 (4)	OR 1.20 (0.88 to 1.63)	81%	3026 (2)	OR 1.21 (1.00-1.46)	0%	OR 3.03 (0.92 to 9.99)
Pneumonia	2695 (2)	OR 1.71 (1.38 to 2.14)	0%	-	-	-	-
Urinary tract infections	2695 (2)	OR 1.93 (1.51 to 2.47)	8%	-	-	-	-
C. difficile	70225 (2)	OR 1.22 (0.79 to 1.90)	88%	-	-	-	-

Conclusion: DM appears to negatively affect the course of IBD by increasing the risk of hospitalization and infections (pneumonia, UTIs and sepsis), while it does not appear to influence IBD-related complications and mortality.

Disclosure: Nothing to disclose

P0525

DEFINITIVE SURGICAL MANAGEMENT OF PERIANAL FISTULAS IN ADULTS WITH CROHN'S DISEASE: A CROSS-SECTIONAL ANALYSIS OF LOCAL PRACTICE IN AUSTRALIA AND NEW ZEALAND

M. De Gregorio^{1,2}, A. Sidhu³, C. Behrenbruch³, G. Guerra³, M.J. Johnston^{2,3}, J.O. Keck³, E.J.S.K. Ong³, A.J. Thompson^{1,2}, R. Woods³, B. D'Souza (co-senior author)^{3,4}, N.S. Ding^{1,2}

¹St Vincent's Hospital Melbourne, Gastroenterology, Fitzroy, Australia, ²University of Melbourne, Medicine, Parkville, Australia, ³St Vincent's Hospital Melbourne, Colorectal Surgery, Fitzroy, Australia, ⁴Northern Health, Colorectal Surgery, Epping, Australia

Contact E-Mail Address: mdegregorio@live.com.au

Introduction: Perianal fistulas are a morbid and often treatment refractory manifestation of Crohn's disease. Combination treatment with biologics and definitive surgical closure have shown the highest rates of sustained fistula healing. Multiple surgical drainage and closure techniques can be used, with variable efficacy. Furthermore, there is a paucity of data evaluating real-world colorectal surgeon practice.

Aims & Methods: In an investigator-initiated cross-sectional study we evaluated the preferred definitive surgery of colorectal surgeons in Australia and New Zealand for managing adults with Crohn's perianal fistulas. Data was collected using an anonymous survey developed by a working group of colorectal surgeons and gastroenterologists specialising in inflammatory bowel disease. Twelve questions covered: surgeon characteristics; preferred definitive surgery in adults with Crohn's perianal fistulas with a seton *in situ* and quiescent disease; and factors influencing decision making.

Questions relating to preferred surgery and influential factors used a 100-point continuous visual analogue scale (0 = *never or not influential*; 100 = *always or extremely influential*). Registered colorectal surgeons with *Colorectal Surgical Society of Australia and New Zealand* membership were invited to participate. Ordinal scale data was presented as a median and

interquartile range (IQR). Correlation between preferred surgery and surgeon characteristics and influential factors was assessed using univariate and multivariable logistic regression analysis; presented as an odds ratio (OR) and 95% confidence interval (CI).

Results: Of the 288 colorectal surgeons invited to participate, 129 completed the survey; 54% were registered as colorectal surgeons for >10 years, 84% practiced in public hospitals, 64% had multi-disciplinary meeting access, and 47% performed ≤ 5 definitive surgeries per year, with only 9% performing >20 cases.

Most surgeons preferred to manage fistulas with setons alone, either long-term placement without removal (median score 65; IQR 50-80) or with removal (median score 50; IQR 22-70). The remaining definitive surgical options had median scores <50, including fistulotomy or fistulectomy, mucosal advancement flap, ligation of intersphincteric fistula tract, biomaterial plug, simple closure of internal opening, fibrin glue, video-assisted anal fistula treatment, fat graft injection, and laser closure.

Previous training and experience were rated as the most influential factors on the choice of definitive surgery performed, followed by guidelines and expert opinions, publications and conferences, and multi-disciplinary meetings. Sepsis control was rated as the most influential factor on the timing of definitive surgery, followed by active proctitis, medical therapy optimisation, patient symptom burden, tract maturation, and gastroenterologist agreement.

On multivariable analysis, preference for placement of a long-term seton positively correlated with prioritisation of active proctitis (OR 3.68; CI 1.07-12.67; $P = .039$). No correlations were identified for preference to perform seton removal only.

Conclusion: Despite evidence supporting combination treatment with biologics and definitive surgical closure techniques for sustained fistula healing in patients with Crohn's disease, long-term seton placement is still the preferred practice by colorectal surgeons. Previous training and experience had the highest influence on the choice of surgery performed. Further studies evaluating why colorectal surgeons prefer long-term seton placement as opposed to fistula closure techniques are needed.

Disclosure: No conflicts of interest to disclose.

P0526

HAS BODY IMAGE IMPROVED AMONGST INDIVIDUALS WITH INFLAMMATORY BOWEL DISEASE IN THE MODERN ERA?

S. Madigan¹, I. Prichard², C. Smart¹, C.L. Wang^{3,4}, R. Prosser¹, R. Mountfield¹

¹Southern Adelaide Local Health Network, Department of Gastroenterology, Flinders Medical Centre, Bedford Park, Australia, ²Flinders University, College of Nursing and Health Science, Bedford Park, Australia, ³University of Adelaide, Adelaide Nursing School, Faculty of Health and Medical Sciences, Adelaide, Australia, ⁴Flinders Medical Centre, Surgical and Perioperative Medicine, Bedford Park, Australia

Contact E-Mail Address: shaunamadigan@gmail.com

Introduction: IBD is known to adversely affect patient body image due to negative cosmetic effects of disease and the medical and surgical treatments required.[1] This has historically been associated with female sex, previous IBD surgery, and impaired QoL. [2] The introduction of biologic therapies and modern IBD care in Australia in 2007 has improved disease control and endoscopic outcomes, but it is unclear if body image has improved in parallel with this.

Aims & Methods: To determine whether body image and QoL have improved amongst IBD patients with modern IBD care and to determine the relationship between modern IBD surgery and body image.

Individuals with known history of IBD cared for via SALHN IBD service (a tertiary hospital specialist clinic) were offered inclusion in the study both in 2006 by postal survey (historical era), and in 2021 by electronic survey (modern era).

All participants completed surveys which included demographics and history of IBD surgery. In the historical era body image dissatisfaction (BID) and QoL were assessed using a patient reported yes/no question as no validated IBD tools were available. In the modern era the modified Body Image Scale (BIS) and Short Inflammatory Bowel Disease Questionnaire (SIBDQ) were used. The modified BIS is a validated tool for assessing body image in IBD. [3] A score of greater than 10 was considered BID. The SIBDQ is a validated tool that measures QoL and a score of less than 50 was considered impaired QoL. [4]

Results: The modern era included 135 patients, 59% female, mean age 45.9. The historical era included 215 patients, 66% female and mean age 35.5. Historical era had 40% reporting IBD surgery vs 36% in modern era ($P=0.489$). BID was observed in 67% vs 39% of the historical and modern eras respectively ($p<0.00001$). In both eras females were affected to a greater extent with 75% BID compared with 52% of males in the historical era ($p<0.001$), and 50.5% versus 22% of males in the modern era ($p<0.001$). In the historical era patients reporting surgical intervention for their IBD had higher rates of BID than those without surgery (81% vs 58%, $p<0.001$). Interestingly this association between surgery and BID was not observed in the modern era (47% vs 34.9%, $p=0.168$).

In the historical era 89% patients reported impaired QoL compared with 71% in the modern era ($p<0.001$). Females again demonstrated higher rates of impaired QoL than males in the modern era (68% vs 49%, $p=0.03$). Whilst surgical intervention in the historical era was associated with greater QoL impairment than no surgery (94% vs 85%, $p=0.042$), this association was not observed in the modern era, with surgical and non-surgical patients reporting similar QoL (67% vs 57% $p=0.278$).

In the historical era those with BID were significantly more likely to report impaired QoL (97% vs 71%, $p<0.0001$). This association persisted with time with modern era patients with BID also having higher rates of QoL impairment compared to those without BID (85% vs 45% $p<0.0001$). Comparison of the eras demonstrated significant reduction in QoL impairment over time ($p=0.003$).

Conclusion: Whilst the rate of BID has decreased with modern IBD treatment; it remains a common problem for those with IBD, and is associated with impaired QoL. Whilst females remain disproportionately affected, the historically observed association between IBD surgery and impaired body image was not demonstrated in the modern era. This may reflect improved surgical techniques and biologic down staging prior to surgery. However, body image remains an important Patient Reported Outcome in IBD and warrants further attention.

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P0527

FACTORS ASSOCIATED WITH RESECTION IN ISOLATED ILEAL CROHN'S DISEASE IN AN ASIAN COHORT

Y.Y. Tan¹, C.K. Tan², T.T. Tey³, T.-E.C. Lionel⁴, W.C. Teoh⁵, S.X.K. Shawn⁶, S.W. Tay⁷, C.T. Lim⁷, E. Salazar⁸, W.P.W. Chan⁷, M. Tan⁷

¹Singapore General Hospital, Gastroenterology and Hepatology, Singapore, Singapore, ²Changi General Hospital, Department of Gastroenterology and Hepatology, Singapore, Singapore, ³Sengkang General Hospital, Gastroenterology and Hepatology, Singapore, Singapore, ⁴Singapore General Hospital, Radiology, Singapore, Singapore, ⁵Changi General Hospital, Radiology, Singapore, Singapore, ⁶Sengkang General Hospital, Radiology, Singapore, Singapore, ⁷Singapore General Hospital, Department of Gastroenterology and Hepatology, Singapore, Singapore, ⁸Singapore General Hospital Department of Gastroenterology and Hepatology, Gastroenterology, Singapore, Singapore

Contact E-Mail Address: yiyuan.tan@gmail.com

Introduction: There is growing consensus that ileal Crohn's disease (iCD) should be considered fundamentally distinct from colonic Crohn's. Montreal classification of L1 encompasses ileal disease but does not provide additional descriptors for anatomical distribution. The ileum is about 3 meters, the terminal ileum is accessible via colonoscopy but not the distal or proximal ileum. Proximal and terminal ileum disease would be classified as L1 but could have varied clinical implications.

We aimed to describe our cohort of iCD patients and factors associated with surgery. Our secondary aim was to determine if the anatomical distribution of iCD at diagnosis predicts a higher likelihood of unplanned ileal resection.

Aims & Methods: This was a retrospective, study conducted across 3 large hospitals in Singapore. Patients were identified from a prospectively maintained registry of inflammatory bowel disease (IBD) patients.

We enrolled patients between Jan 2001 to Sep 2021 with endoscopic, histological and cross-sectional imaging at diagnosis and excluded patients with colonic involvement.

Cross-sectional images were reviewed by IBD radiologists. Lengths of discrete diseased segments were measured. We used the following anatomical definitions for different ileal segments:

- Terminal ileum (TI): continuous 15cm segment before the ileocaecal valve
- Distal ileum (DI): mid ileum to proximal end of TI
- Proximal ileum (PI): distal end of jejunum to mid ileum

Analysis was done with SPSS version 23.0

Results: From a period between Jan 2001 to Sep 2021, there were 534 patients with CD. We identified 74 patients with iCD. 59 patients were included for analysis, 15 patients were excluded as index cross-sectional images at diagnosis were not available.

The median time to surgery was 337 days. 15 patients required ileal resection for which the indications were: perforation (n=6), obstruction (n=4), medical failure (n=5); 2 patients had concomitant intra-abdominal abscesses. Of these, 7 had immunomodulator, 1 had biologic monotherapy, 6 had combination therapy and 1 was untreated.

iCD with B3 phenotype (p<0.05) and positive smoking history (p=0.013) were associated with higher risks of surgery. Most of the patients who underwent surgery were in the A2 category of the Montreal classification (ages 17 to 40). Of interest, 11 out of 15 (73.3%) patients who underwent resection had multiple diseased segments.

When stratified into isolated TI involvement vs DI/PI involvement in a survival curve, there was trend to ileal resection in the DI/PI group (Log Rank p=0.145). Of note, while not significant, there was DI involvement in 13 out

of 15 patients who underwent resection (86.7%, p=0.085). Gender, Race, Perianal involvement, treatment exposure, total length of ileal disease involvement were not associated with ileal resection.

Conclusion: In iCD, smoking and B3 phenotype are poor prognostic factors in iCD, with most patients having surgery within the 1st year. Although not statistically significant due to few events, involvement of DI/PI at diagnosis tended towards a higher risk of ileal resection compared to isolated TI involvement. Further studies are required to corroborate our findings.

Disclosure: Nothing to disclose.

P0528

MRI EVOLUTION AND EFFICACY OF BONE MARROW-DERIVED MESENCHYMAL STEM CELLS IN PERIANAL FISTULAE IN CROHN'S DISEASE: RESULTS FROM A PROSPECTIVE MONOCENTRIC STUDY

C. Reenaers¹, R. Gillard², C. Coimbra³, S. Vieujean¹, R. Gillard², P. Meunier², C. Lechanteur⁴, E. Baudoux⁴, L. Boutaffala¹, Y. Beguin⁴, E. Louis¹

¹Liege University, CHU Sart Tilman, Gastroenterology, Liège, Belgium, ²Liege University, CHU Sart Tilman, Radiology, Liège, Belgium, ³Liege University, CHU Sart Tilman, Abdominal surgery, Liège, Belgium, ⁴Liege University, Laboratory of Cell and Gene Therapy LTCG, Liège, Belgium

Contact E-Mail Address: catherine.reenaers@chuliege.be

Introduction: Local injection of adipose tissue-derived mesenchymal stem cells (MSC) is effective in fistulizing perianal Crohn's disease (CD) although it is currently hampered by the cost and the logistics of administration of centrally-produced MSC. Less is known about bone marrow-derived MSC and little is known about predictive factors of response and MRI evolution of the fistulae after MSC injection.

Aims & Methods: Our aims were to evaluate the safety and efficacy of bone marrow-derived MSC injection for perianal fistulizing CD, to evaluate the MRI evolution of the fistulae and to identify factors associated with fistula closure.

A prospective interventional uncontrolled study was performed in the CHU of Liège from October 2019 till October 2021. All CD patients with perianal fistula and appropriate drainage with a seton without abscess at MRI were eligible. Clinical examination, biomarkers and pelvic MRI were performed at weeks 0, 12 and 48. MAGNIFI-CD and Van Assche Index were calculated for each MRI. The evolution of the % of fibrosis of the fistula tract was evaluated.

Efficacy was defined as closure of all treated external openings at clinical examination without abscess at MRI. Super closure was defined as closure without discharge reported by the patient the week before examination and partial closure by the closure of some, but not all, external openings.

Results: Sixteen patients with a median age of 49 years old and a median duration of perianal CD of 8 months were included. At baseline, 10 (62.5%) and 6 patients (37.5%) had 1 and 2 external openings at clinical examination respectively. At week 12 and 48, 9/16 and 8/16 patients had fistula(e) closure respectively, 6/16 patients had super closure at week 12 and 48 whereas 11/16 patients had at least partial closure. Fistula closure at week 12 was predictive of fistula closure at week 48 (p=0.024, OR=21). The MAGNIFI-CD index did not change significantly overtime. At MRI, the degree of fibrosis significantly increased after MSC injection and it was associated with fistula closure at week 48 (p=0.036, OR=4.5). Eighty-six % of patients with >80% of fibrosis of the fistula tract at week 48 had fistula closure.

The enhancement of the part of the fistula close to the external opening significantly decreased at week 48 compared to baseline (p=0.002). Several items of the MAGNIFI-CD and Van Assche index at week 48 were

associated with super closure at week 48: number of fistula tracts, hyperintensity of primary tract on post-contrast T1-weighted images, fistula length, hyperintensity T2-weighted images, hyperintensity on T1 post-contrast.

Conclusion: Open-label injection of bone marrow-derived mesenchymal stem cells was safe and effective in half of the patients in fistulizing perianal CD and induced significant MRI changes associated with favorable clinical outcome.

This study might be a first step to define targets in perianal CD to implement a treat-to-target strategy in perianal CD.

Disclosure: Nothing to disclose.

P0529

CZECH EXPERIENCE WITH TREATMENT OF CROHN'S DISEASE PERIANAL FISTULAS BY ALLOGENIC MESENCHYMAL STEM CELLS

Z. Serclová¹, P. Zusková¹, A. Tremerová¹, M. Lengálová¹, L. Hrdlicka¹

¹NH Hospital, Surgical Department, Horovice, Czech Republic

Contact E-Mail Address: sercl@seznam.cz

Introduction: Perianal complex fistulas in Crohn's disease (CD) are difficult to treat by both surgical and conservative methods. Administration of allogenic, adipose-derived mesenchymal stem cells (darvadstrocel) was studied in a prospective randomised trial (PRS) with a success rate of more than 50%¹.

The aim of our study was prospectively evaluate results of commercial treatment of perianal fistulas in CD patients by darvadstrocel in Czech Republic.

Aims & Methods: We prospectively followed 56 consecutive patients treated commercially by darvadstrocel since August 2019 till November 2021. Complete healing was considered as: no secretion from the external opening, no infiltration perianally, no pain; treatment failure: clear perianal secretion, painful infiltration and / or the need for surgery; partial response: anamnestic mild secretion from one external opening, infiltration around the fistula without pain and without the need for surgical intervention.

56 prospectively monitored patients (33F/23M), average age 40,5 years (range; 21-71 years) underwent darvadstrocel treatment in 2 Czech mesenchymal stem cell (MSC) therapy centers (53 pp in NH Hospital, 3 in ISCARE center).

Patients suffered from intestinal CD for an average of 14.5 years (2-43 years), perianal CD for 8 years (2-23 years) and underwent an average of 7.5 (3-25) minor perianal surgeries before the treatment. 41% (23) of patients had anorectal stenosis at the time of the treatment.

Patients were treated on average 19 months (1-120) by stable immunosuppressive and/or biologic therapy. Fistulas characteristic: High transfincteric in 52 (92,8%) pts with 1-3 external openings (EO) (72%; 40 pp had 1 EO) and with 1-2 internal openings (IO) (12.5%; 7 pp had 2 IO).

Results: Median follow-up was 12 months (5-31 months). Complete healing occurred in 78,5% patients (44), partial response in 10.7% (6pp) and treatment failure in 6 patients (10.7%). PDAI before MSC surgery was on average 5.8 (3-13), 3 months after surgery 2.4 (0-13) and 6 months after surgery 2.1 (0-13) in healed and unhealed patients.

Conclusion: The treatment was more successful in real life than in PRS, which may be due to the relatively short follow-up period. Another reason for better outcome could be proper selection of patients with long term stable conservative treatment, which demonstrates stable CD.

In our conditions, this treatment is similarly effective as eradication of the fistula using Advancement Flap, but it can also be used in difficult conditions such as anorectal stenosis or chronic inflammatory changes of rectal mucosa.

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Disclosure: Consultant - Takeda.

P0530

MESENCHYMAL STEM CELLS INJECTION INTO COMPLEX PERIANAL FISTULAS IN CROHN'S DISEASE: PRELIMINARY REAL-LIFE RESULTS

N. Fathallah¹, L. Siproudhis², M. Akaffou¹, A. Landemaine², E. Pommaret¹, L. Spindler¹, C. Brochard², G. Bouguen², V. de Parades¹

¹GH Paris St Joseph, Proctology, Paris, France, ²CHU de Rennes, Gastroenterology and Proctology, Rennes, France

Contact E-Mail Address: laurent.siproudhis@gmail.com

Introduction: The available data about expanded allogeneic adipose-derived mesenchymal stem cells (darvadstrocel) in Crohn's disease fistulas are limited.

Aims & Methods: The main objective of this study was to evaluate the real-life clinical and radiological efficacy of darvadstrocel injection.

Secondary objectives were to assess safety and predictors of therapeutic response.

We conducted a prospective study including all consecutive treated patients in two French centers.

Complete clinical response was defined as complete closure of all external openings (EOs) with no discharge on pressure. Partial response was defined as not closure of all EO's but with no discharge and no pain on pressure. Failure was defined as no closure of any of the EO's with persistent spontaneous or on pressure discharge ± occurrence of an abscess.

Complete radiological response (MRI), evaluated at least after 6 months of follow up, was defined as fibrous sequelae with no inflammatory enhancement and no abscess. Partial response was defined as a decrease in inflammatory signal ± length ± diameter of tracts without abscess. Failure was defined by the occurrence of new tracts ± abscess.

Results: Forty-six patients were included (F = 23, mean age = 37 ± 13 years). At the time of the procedure, 12 patients (26%) were active smokers. Mean duration of Crohn's disease and anal fistula(s) were 131 ± 114 and 82 ± 81 months respectively. Fistula tracts were multi-branched in 31 patients (67%) including 16 horseshoe fistulas.

The patients underwent a mean of 4 ± 2 drainage procedures and 15 (32%) failed at least one sphincter-saving technique. The last seton was placed 7 ± 8 months before the injection.

On MRI, the fistulous tracts were inflammatory in 42 (91%) patients.

All patients were on biologic treatment (optimized in 50% of cases) and on combination therapy in 75% of cases. Complete clinical and endoscopic remission has been achieved in 37 patients (80%), the others had signs of mild activity.

After a mean follow-up of 10 ± 5 months, 40 patients (87%) improved and 28 patients (61%) had no more perineal symptoms (pain and discharge). There was a significant improvement in the mean PDAI (2,3 ± 3 vs. 6,4 ± 2,5; p<0.0001).

Finally, 74% of patients responded clinically (50 % completely and 24 % partially).

Concerning the 41 patients/46 who had an MRI, 88 % responded radiologically (39% completely and 49% partially).

No significant adverse events were noted except mild to moderate pain in the days following the injection which was adequately managed with simple analgesics.

In univariate analysis, only young age (< 37 years) ($p = 0.049$) and inflammatory disease phenotype (B1) ($p = 0.046$) were associated with complete clinical response. In multivariate analysis, only the inflammatory phenotype remained significant and independently associated with clinical response ($p = 0.046$).

Conclusion: In our series, darvadstrocel injection resulted in 74% clinical response (50 % completely and 24 % partially) and 88% radiological response (39% completely and 49% partially). The inflammatory disease phenotype was the only independent predictor of clinical success.

Disclosure: Takeda, Abbvie, Janssen, Biogen, Amgen, MSD, Gilead, Tillots.

P0531

PREHABILITATION STRATEGIES PRIOR TO ILEOCOLIC (RE-)RESECTION IN PATIENTS WITH CROHN'S DISEASE: A MISSED WINDOW OF OPPORTUNITY?

M.T.J. Bak¹, M.F.E. Ruiterkamp¹, J. Arkenbosch¹, L. Stassen², G. Dijkstra³, M. Campmans-Kuijpers³, M. Romberg-Camps⁴, S. van der Marel⁵, F. Hoentjen^{6,7}, K.W. van Dongen⁸, R. West⁹, C.J. van der Woude¹, O. van Ruler^{10,11}, A. De Vries¹

¹Erasmus University Medical Center Rotterdam, Department of Gastroenterology and Hepatology, Rotterdam, Netherlands,

²Maastricht University Medical Centre, Department of Surgery, Maastricht, Netherlands, ³University Medical Center Groningen, Department of Gastroenterology and Hepatology, Groningen, Netherlands, ⁴Zuyderland Medical Center, CO-MIK, Amstenrade, Netherlands, ⁵Haaglanden Medical Center, Department of Gastroenterology and Hepatology, Den Haag, Netherlands, ⁶Radboud University Medical Center, Department of Gastroenterology and Hepatology, Nijmegen, Netherlands, ⁷University of Alberta, Department of Gastroenterology, Edmonton, Canada, ⁸Pantein Hospital, Department of Surgery, Boxmeer, Netherlands, ⁹Sint Franciscus Gasthuis, Department of Gastroenterology and Hepatology, Rotterdam, Netherlands, ¹⁰IJsselland Hospital, Department of Surgery, Capell a/d IJssel, Netherlands, ¹¹Erasmus University Medical Center Rotterdam, Department of Surgery, Rotterdam, Netherlands

Contact E-Mail Address: m.bak@erasmusmc.nl

Introduction: Studies on prehabilitation strategies (PS) to improve post-operative outcomes of patients with Crohn's disease (CD) are scarce and guidelines lack recommendations on tailored management.

Aims & Methods: This study aimed to explore the implementation of PS prior to ileocolic (re-)resection (ICR) in patients with CD.

Patients with CD who underwent an elective ICR, from 2017 to 2021, with a window from surgery indication to ICR of ≥ 2 weeks were included. Data concerning the preoperative management, surgery-related characteristics and -outcomes were retrospectively collected. Primary endpoint was the implementation of PS in patients with CD prior to ICR on several modifiable domains (e.g., nutrition). In addition, early postoperative complications (<30 days) according to the Clavien-Dindo classification were reported.

Results: In total, 124 patients were included. Median window from surgery indication to ICR comprised 7.9 weeks (IQR: 5.0 – 11.5). Preoperative weight was assessed in 39% of the patients. Active smoking and alcohol consumption were reported in 22% and 28%. Malnutrition was diagnosed in 26% of whom 53% consulted a dietician. Consultation of a dietician, psychologist and physiotherapist were reported in 36%, 7% and 3%. Pre-operative anemia was diagnosed in 42% and corrected in 6%. Exposure to a biological or corticosteroid, at time of ICR, was reported in 41% and 28%. Corticosteroids were weaned off in 3% Hand-grip strength was assessed in none of the patients. Overall early postoperative complications rate comprised 39%.

Window from surgery indication to ICR (in weeks), median (IQR)	7.9 (5.0 – 11.5)
Assessment of pre-operative weight, n(%)	48 (38.7)
Malnutrition, n(%) [*]	32 (25.8)
Preoperative weight loss, n (%)	1 (0.8)
Hypoalbuminemia (<30 g/dL)	3 (2.4)
BMI < 18.5	9 (7.3)
BMI > 30.0	19 (15.3)
Active smoking at time of surgery, n (%)	27 (21.8)
Alcohol consumption, n(%)	35 (28.2)
Dietician consultation, n(%)	45 (36.3)
Nutritional intervention, n(%)	41 (91.1)
Enteral support	33 (80.5)
Parenteral support	0
Exclusive enteral nutrition	6 (14.6)
Total parenteral nutrition	2 (4.9)
Micronutrients supplementation, n(%)	39 (31.5)
Psychologist consultation, n(%)	8 (6.5)
Physiotherapy consultation, n(%)	4 (3.2)
Assessment of hand-grip strength, n (%)	0
Assessment of laboratory values, n(%)	
Albumin level	30 (24.2)
CRP	53 (42.7)
Blood count [*]	65 (52.4)
Hemoglobin	84 (67.7)
Hematocrit	70 (56.5)
Leukocyte count	79 (63.7)
Thrombocyte count	44 (35.5)
Vitamin B12	12 (9.7)
Vitamin D	9 (7.3)

Abbreviations: BMI = body mass index; CRP = C-reactive protein level; ICR = ileocolic resection.

^{*}Combination of multiple causes of malnutrition is possible

^{*}Assessment of blood count includes combination of hemoglobin level, hematocrit level, leukocyte and thrombocyte count

Table 1. Prehabilitation strategies prior to ICR

Conclusion: PS are not routinely applied and not individually tailored in the preoperative setting prior to elective ICR in patients with CD. Since early postoperative complications occur frequently, future research on PS is necessary.

Disclosure: Nothing to disclose.

P0532

EFFICACY AND SAFETY OF MESENCHYMAL STEM CELL THERAPY WITH DARVADSTROCEL FOR COMPLEX PERIANAL FISTULIZING CROHN'S DISEASE: MULTICENTRIC EXPERIENCE IN THE BASQUE COUNTRY AND NAVARRE

A. Elorza¹, T. Arzallus Marco², A. Izagirre Arostegi², M. Vicuña³, C. Rodríguez Gutiérrez³, I. Badiola⁴, G. Elorza⁵, J. Suárez⁶, J.L. Cabriada Nuño¹, I. Rodríguez-Lago¹

¹Hospital Universitario Galdakao, Gastroenterology, Galdakao, Spain, ²Hospital Universitario Donosti, Gastroenterology, Donosti, Spain, ³Complejo Hospitalario de Navarra, Gastroenterology, Pamplona, Spain, ⁴Hospital Universitario Galdakao, Surgery, Galdakao, Spain, ⁵Hospital Universitario Donosti, Surgery, Donosti, Spain, ⁶Complejo Hospitalario de Navarra, Surgery, Pamplona, Spain

Contact E-Mail Address: elorzainara@gmail.com

Introduction: Perianal fistulizing Crohn's disease has a negative impact on patients' quality of life and despite advances in medical and surgical treatment, high rates of recurrence are still reported. Mesenchymal stem cell therapy has recently been authorized for the treatment of complex perianal fistulas in adult patients with Crohn's disease, and it may be an

effective and safe option. The aim of this study was to evaluate the results of efficacy, defined as combined clinical and radiological remission, and safety after administration of darvadstrocel in clinical practice.

Aims & Methods: All patients with complex perianal disease treated with darvadstrocel were prospectively evaluated at three centers in Spain. The inclusion criteria and the surgical technique followed the predefined indications from Spanish Ministry of Health.

Follow up visits were performed at baseline, 6 and 12 months after the treatment. All visits included a clinical evaluation of perianal disease activity (digital compression and PDAI). Pelvic MRI was performed at baseline and at 6 months, with some cases undergoing also the examination at month 12.

The response variable to be assessed is combined remission, clinical and radiological, which is defined as clinical closure of all treated fistula (absence of discharge despite gentle finger compression) and absence of abscesses larger than 2 cm confirmed by MRI.

Results: From November 2020 to March 2022, 17 patients (mean age 43 years, IQR, 33-53, 66% males) were treated with darvadstrocel. The most common type of fistulas were transsphincteric (70%), high intersphincteric (24%) and the suprasphincteric (12%), the latter associated with other types of fistulas.

All patients had failed anti-TNF treatment and received concomitant biologic therapy with either anti-TNF (70%), ustekinumab (24%) or vedolizumab (6%). Fourteen patients (82%) have reached the 6-month follow up, 7 (50%) of them achieved combined remission, two patients (14%) had radiologic remission, one patient (7%) was in clinical remission, and four (29%) had no response. Seven patients (41%) have reached the 12-month follow up, five (71%) of them showed clinical remission and two patients (28%) have had no response.

The rate of adverse events related to therapy was 18%: two patients developed a new fistula or abscess, one of them underwent a surgical intervention with seton placement, one patient had rectal bleeding and one patient had anal pain.

CHARACTERISTICS	FREQUENCY (N=17)
Mean age	43 (IQR 33-53)
CD extent (n,%)	
L1	11 (65)
L2	1 (6)
L3	5 (29)
Type of fistula (n%)	
Transsphincteric	12 (70)
High intersphincteric	4 (24)
Suprasphincteric	2 (12)
Concomitant treatment (n, %)	
Anti-TNF	12 (70)
Ustekinumab	4 (24)
Vedolizumab	1 (6)
Previous surgical treatment (n, %)	
Seton placement	14 (82)
Abscess drainage	5 (29)
Fistulotomy	1 (6)

Table.

Conclusion: Mesenchymal stem cell therapy shows promising results in terms of effectiveness and safety in the short term in complex perianal disease. A longer follow-up period is still needed to confirm these promising data.

Disclosure: The authors declare no conflict of interest in this article.

Poster presentations

Other lower GI disorders

Poster Presentations Other lower GI disorders

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P0533

THE ORAL TISSUE TRANSGLUTAMINASE INHIBITOR ZED1227 PREVENTS GLUTEN-INDUCED ENTEROPATHY IN A HUMANIZED MOUSE MODEL OF CELIAC DISEASE

M. Encalada¹, H. El Mard¹, A. Pesi¹, K. Sajko¹, F. Röhr¹, F. Fitriasari¹, R. Krini¹, R. Surabattula¹, M. Hils², B. Tewes³, R. Pasternack², R. Greinwald⁴, S. Steven⁵, V.F. Zevallos⁶, E. Verdu⁷, D. Schuppan⁸

¹University Medical Center of Mainz, Institute for Translational Immunology, Mainz, Germany, ²Zedira GmbH, Darmstadt, Germany, ³Dr. Falk Pharma GmbH, Research and Development, Freiburg im Breisgau, Germany, ⁴Dr. Falk Pharma GmbH, Research and Development, Freiburg, Germany, ⁵University Medical Center of Mainz, Center for Cardiology I, Mainz, Germany, ⁶University of Mainz, Institute of Translational Immunology, Mainz, Germany, ⁷McMaster University, Hamilton, Canada, ⁸Medical University Mainz, Institute of Translational Immunology, Mainz, Germany

Contact E-Mail Address: Helmarde@uni-mainz.de

Introduction: Celiac disease (CeD) is triggered by gluten peptides that escape intestinal digestion and are bound to HLA-DQ2 or -DQ8 in the small intestinal lamina propria. The CeD autoantigen tissue transglutaminase (TG2) converts certain glutamines in these peptides, which improves their binding to both HLAs, enhancing the gluten-specific T cell response, resulting in villous atrophy and intraepithelial (cytotoxic) lymphocytosis (IEL).

Aims & Methods: We developed and tested ZED1227, an oral inhibitor of TG2, in a mouse model of small intestinal inflammation induced by poly-IC and in humanized transgenic CeD mice model (NOD-DQ8 mice) that develop mild features of human CeD.

Therefore mice received intraperitoneal poly-IC together with 50 or 150 mg oral ZED1227/kg vs vehicle 2 h before sacrifice. Gluten-sensitized NOD DQ8 mice fed a gluten-containing or gluten-free diet for 3 weeks received daily oral gavages of ZED1227 vs vehicle for the last week.

Results: ZED1227 completely blocked TG2 activity in the poly:IC model. In NOD-DQ8 mice, ZED1227 prevented gluten-induced villous atrophy, IEL, increases in CD45, CD3, CD8, CD68 and Ki67 positive cells, and decreased pro-inflammatory transcripts and serum levels of CeD specific antibodies.

Conclusion: 1.Oral ZED1227 effectively blocked TG2 activity in vivo and attenuated CeD in our transgenic NOD-DQ8 mouse model.

2.The NOD-DQ8 model predicted therapeutic efficacy of ZED1227 that was later demonstrated in a phase 2a clinical trial of 160 CeD patients in remission who were challenged with gluten (Schuppan et al, NEJM 2021).

References: Schuppan et al, A Randomized Trial of Transglutaminase 2 Inhibitor for Celiac Disease, *The New England Journal of Medicine*, 2021, 385;1, 35-45

Disclosure: Nothing to disclose.

P0534

MULTIDISCIPLINARY BELGIAN POSITION STATEMENT ON THE MANAGEMENT OF IMMUNE CHECKPOINT INHIBITOR ASSOCIATED COLITIS

A. Jauregui Amezaga¹, V. Desmedt², L. Fierens³, S. Aspeslagh⁴, J. Dekervel⁵, E. Wauters⁶, M. Peeters⁷, J. Sabino⁵, L. Crapé⁸, M. Somers¹, A. Hoorens⁹, J. Dutre¹⁰, T. Lobaton Ortega²

¹University Hospital Antwerp, Gastroenterology and Hepatology, Edegem, Belgium, ²University Hospital Ghent, Gastroenterology and Hepatology, Ghent, Belgium, ³KU Leuven, Chronic Diseases, Metabolism and Ageing, Leuven, Belgium, ⁴University Hospital Brussels, Medical Oncology, Jette, Belgium, ⁵University Hospital Leuven, Gastroenterology and Hepatology, Leuven, Belgium, ⁶University Hospital Leuven, Pneumology, Leuven, Belgium, ⁷University Hospital Antwerp, Oncology, Edegem, Belgium, ⁸ASZ Aalst, Gastroenterology and Hepatology, Aalst, Belgium, ⁹University Hospital Ghent, Pathology, Ghent, Belgium, ¹⁰ZNA Jan Palfijn, Gastroenterology and Hepatology, Merksem, Belgium

Contact E-Mail Address: aran.jauregui@gmail.com

Introduction: The use of immune checkpoint inhibitors (ICIs) in cancer immunotherapy has shown increased overall survival in a wide range of cancer types with the associated risk of developing severe gastrointestinal immune-mediated adverse events, mainly colitis.

Aims & Methods: The aim of this position statement is to provide an updated practice advice to the Belgian gastroenterologist and oncologists on the diagnosis and management of ICI-induced colitis. Consensus was reached using a 3-round modified Delphi methodology and approved by the members of the Belgian Inflammatory Bowel Disease Research and Development Group (BIRD), Belgian Society of Medical Oncology (BSGO), Belgian group of Digestive Oncology (BGDO), and BeRS (Belgian Respiratory Society).¹

In total 42 physicians agreed for participation of which 34 completed the questionnaire. The accepted statements were those showing an agreement score from 7 to 10 on a 10-point Likert scale (median [IQR]). The percentage after the score showed at Results illustrates the proportion of agreement among the participants.

Results: It is recommended to discuss patients with a suspicion of ICI-induced colitis in a multidisciplinary meeting at an early phase (8,0 [7,00-9,00]; 85,3%). Early endoscopic evaluation with biopsies (even if endoscopically normal) is recommended in patients with grade ≥2 diarrhea (9,0 [8,00-10,00]; 100,0%), being a total ileocolonoscopy the preferred procedure (8,00 [6,00-10,00]; 73,5%).

The first-line therapy for ICI-induced colitis are systemic corticosteroids such as prednisone 1–2 mg/kg/day or an equivalent (10,0 [9,00-10,00]; 94,1%). Biological agents should be considered, after discussion in a multidisciplinary team, as an escalation therapy in non-responders to corticosteroids, after 3–5 days of high-dose corticosteroids (9,00 [9,00-10,00]; 100,0%) and as an early treatment in patients with high-risk endoscopic findings such as presence of deep ulcerations or extensive colitis (8,00 [6,75-9,25]; 76,5%).²

In patients with partial but not complete response after the first dose of biological agent, the standard induction infusion interval of 0–2–6 weeks might be advisable (8,00 [7,00-9,00]; 92,2%). In patients without response to the first biological agent, and after excluding other complications, a second line treatment with vedolizumab (in case of non-response to in-

fliximab) or infliximab (in case of non-response to vedolizumab) can be considered (8,00 [8,00-9,25]; 91,2%).^{3, 4} Resumption of anti-PD(L)-1 and anti-CTLA-4 therapy was evaluated for the different grades of diarrhea. In patients in clinical remission in which the resumption is being discussed, endoscopy should be considered in order to confirm endoscopic remission (8,00 [7,75-8,00]; 85,3%).

Conclusion: The management of ICI-induced colitis requires an early multidisciplinary approach. Early endoscopic assessment is recommended. Even if corticosteroids are still considered the first-line therapy, biologics are recommended as an escalation therapy and as early treatment in patients with high-risk endoscopic findings.

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P0535

GENETIC FEATURES OF GLUTEN-RELATED DISORDERS IN UKRAINIAN PATIENTS

O. Gubska¹, A. Kuzminets¹, V. Bashynska², O. Naumova³, Y. Zaplatnikov⁴, V. Moseiko^{2,5}, A. Koliada^{2,5}, O. Dolko¹, Y. Borysovykh⁴, O. Zahorodnia⁴

¹Bogomolets National Medical University, Therapy, Infectious Diseases and Dermatology Postgraduate Education, Kyiv, Ukraine, ²Molecular Genetic Laboratory Diagen, Kyiv, Ukraine, ³A.I. Kolomiychenko Institute of Otolaryngology of the National Academy of Medical Sciences of Ukraine, Center of Allergic Diseases of the Upper Respiratory Tract, Kyiv, Ukraine, ⁴Taras Shevchenko National University of Kyiv, Kyiv, Ukraine, ⁵Dmitry F. Chebotarev Institute of Gerontology of the National Academy of Medical Sciences of Ukraine, Laboratory of Epigenetics, Kyiv, Ukraine

Contact E-Mail Address: gubskao@gmail.com

Introduction: Celiac disease is a disease that develops in genetically predisposed individuals. Despite numerous studies dedicated to the prevalence of disease haplotypes in different countries and regions, we found no data on the prevalence of these haplotypes in Ukraine.

Aims & Methods: To study and compare the prevalence of HLA-DQ2.5 and HLA-DQ8 haplotypes, DQA1*05, DQB1*02, DQA1*03, DRB1*04 alleles in patients with celiac disease (CD), non-celiac gluten sensitivity (NCGS) and healthy people in Ukraine.

We investigated 80 persons with previously established diagnoses of celiac disease or NCGS and 68 healthy volunteers for the prevalence of HLA-DQ2.5 and HLA-DQ8 haplotypes, DQA1*05, DQB1*02, DQA1*03, DRB1*04 alleles, or their absence, using the PCR-SSP method.

Results: Haplotype DQ2.5 appeared to be significantly more prevalent in patients with CD than in NCGS patients (OR = 2.77; 95% CI 1.12-6.87, p = 0.022) and in healthy people (OR = 3.99; 95% CI 1.73-9.20, p = 0.0009). Simultaneously the absence of haplotype DQ2.5 was less frequently detected in CD group than in NCGS group (OR = 0.19; 95% CI 0.066 - 0.55, p = 0.0014) and in CD group comparing to the control group (OR = 0.19; 95% CI 0.068 - 0.49, p = 0.0003), without the significant difference between the NCGS and control groups (p > 0.1). The difference in the prevalence of DQ8 haplotype was statistically insignificant - p = 0.052 when comparing the CD and NCGS groups; there was no difference in the frequency of haplotype DQ8 detection between the groups (p > 0.05).

We obtained a higher prevalence of DQA1*05 allele in CD group patients (OR = 2.40, 95% CI 1.03-5.58, p = 0.031) comparing the control group. Simultaneously DQA1*03 allele was detected significantly more often in CD group than in the NCGS group (OR = 2.87; 95% CI 1.05 - 7.81, p = 0.031).

Conclusion: Among the Ukrainian population, patients with CD have a higher detection rate of DQ2.5. Among NCGS and control, the DQ2.5 and DQ8 haplotypes were absent more frequently than in the CD group. The difference in the prevalence of the DQ8 haplotype did not reach the significance level. The DQA1*05 allele is more prevalent in the CD patients than in the control group, and the DQA1*03 allele is more prevalent in the CD than in the NCGS group.

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Disclosure: Nothing to disclose.

P0536

ISOLATED TERMINAL ILEITIS: THE NATURAL COURSE OF DISEASE

J. Doherty¹, A. O Keeffe², K. Sheehan², R. Geraghty², E. McDermott¹
¹St Vincent's Hospital, Dublin, Ireland, ²St Vincent's University Hospital, Dublin, Ireland

Contact E-Mail Address: jaynedohertie@hotmail.com

Introduction: Isolated terminal ileitis is a frequently encountered clinical conundrum. Existing literature provides limited guidance on management or subsequent development of Crohn's disease (CD).

Aims & Methods: To evaluate the natural course of terminal ileitis and factors predictive of CD.

Retrospective review of patients with confirmed histological diagnosis of ileitis from 2015-2020. Patient's characteristics, endoscopic, markers of inflammation including C-reactive protein (CRP) and faecal calprotectin levels (FCP) and outpatient findings were collected. Patients with a previous diagnosis of IBD were excluded from analysis.

Results: 393 patients had histologically confirmed ileitis. 289 were excluded due to a prior diagnosis of IBD. 104 had isolated terminal ileitis. 52.4% were male. Median age 46 years. Median follow-up was 5years. Reasons for endoscopy were as follows; diarrhoea (26%), abdominal pain (18.3%), diarrhoea and abdominal pain (10.6%), weight loss (3.8%), anaemia (7.7%), other causes (29.8%).

32% (n=34) of patients developed CD over a 5-year period. 56% of patients without a subsequent diagnosis of IBD were booked for follow-up outpatient appointments. Patients who had ulceration in the ileum were more likely to develop CD compared to those without ulceration (54% versus 25%, p = 0.006). Median FCP was significantly higher in patients with a subsequent diagnosis of CD (425µg/mg versus 24µg/mg, p = <0.001) and similar results were seen with CRP (19mg/dL versus 6mg/dL, p = < 0.001). On regression analysis, younger age (p = 0.02) and male gender (p = 0.019) were associated with subsequent development of CD.

Conclusion: Isolated terminal ileitis has a general benign course. Factors associated with subsequent development of CD include younger age, male gender and elevated biomarkers, which could help guide clinical follow-up and avoid unnecessary outpatient follow-up.

Disclosure: Nothing to disclose.

P0537

ALTERATIONS OF GUT MICROBIOTA IN FUNCTIONAL DIARRHEA - A RETROSPECTIVE SINGLE-CENTER STUDY

C.L. Pugliano^{1,2}, F. Di Pierro², V. Gerardi^{2,1}, S. Piccirelli^{2,1}, D. Salvi^{2,3}, C. Spada⁴

¹Policlinico Universitario Agostino Gemelli, Medicina Interna e Gastroenterologia, Roma, Italy, ²Fondazione Poliambulanza Istituto Ospedaliero, Medicina, Gastroenterologia ed Endoscopia Digestiva, Brescia, Italy, ³Policlinico Universitario Agostino Gemelli, Medicina Interna e Gastroenterologia, Roma, Italy, ⁴Catholic University Rome, Digestive Endoscopy Unit, Rome, Italy

Contact E-Mail Address: cecilia.pugliano@poliambulanza.it

Introduction: Functional diarrhea is an invalidant condition affecting many patients referred to Gastroenterology clinics. Available evidences suggest a link between functional diarrhea and dysbiosis. Changes in biodiversity and taxonomy of gut microbiota are associated with impaired gut homeostasis and changes in stool frequency and consistency.

Aims & Methods: Aim of this study was to analyze the gut microbiota composition of 40 out of 153 patients referred for microbiota evaluation who reported diarrhea as the main symptom (30 IBS-D patients and 10 patients with functional diarrhea). Gut microbiota analysis of these patients was compared to that of the remaining 113 patients without diarrhea. Alpha-biodiversity and taxonomy were analyzed using 16S rRNA sequencing. Statistical significance was calculated using the Wilcoxon two-sample test (p<0.05).

Results: Alpha-biodiversity by rarefaction curve demonstrated lower values for patients with diarrhea compared to patients without diarrhea. Bacteroidetes were significantly higher in the diarrhea group (p-value 0.0101), while Firmicutes were lower (p-value 0.0082).

Furthermore, our analysis confirmed a gram negativity gut microbiota composition in patients with chronic diarrhea, with a decreased gram +/- ratio (p-value 0.00191).

Regarding taxa analysis, a reduction in butyrate-acetate producer bacteria was observed. *Eubacterium hallii*, *Eubacterium xylanophilum*, *Lachnospira*, *Ruminococcus* and *Blautia* were significantly decreased, while *R. torques* and *Lachnospiridium* were increased.

Conclusion: These preliminary results suggest a reduction of rarefaction curve, Firmicutes, and grams +/- ratio and a corresponding increase in *R. torques* and *Lachnospiridium* (recognized markers of dysbiosis and gut disease), could constitute a possible marker of functional diarrhea.

Disclosure: Nothing to disclose.

P0538

A PROBIOTIC FORMULA FOR MODULATION OF COLORECTAL CANCER RISK VIA REDUCING CRC-ASSOCIATED BACTERIA

J.Q. Liang¹, Y. Zeng¹, Z. Xu¹, S.C. Ng¹, F.K.L. Chan¹

¹Faculty of Medicine, The Chinese University of Hong Kong, Department of Medicine and Therapeutics, Hong Kong, Hong Kong, China (SAR)

Contact E-Mail Address: jessieqy@cuhk.edu.hk

Introduction: Gut microbiota dysbiosis with increased pathogenic bacteria and decreased beneficial bacteria is associated with colorectal cancer (CRC) development. Specifically, some pathogenic bacteria, such as *Fusobacterium nucleatum* (Fn), have been shown to play important roles in CRC development.

Therefore, it is anticipated that reducing or eliminating pathogenic bacteria associated with CRC can reduce the risk for CRC development. Whether pathogenic bacteria involved in CRC development can be inhibited by

specific probiotic bacteria and their mechanisms of action have not been investigated. We hypothesize that bacteria associated with CRC development can be altered by microbiota modulation via a targeted probiotic formula.

Aims & Methods: This study aimed to examine the effect of a newly developed probiotic formula in modulating CRC-related bacteria. We developed a probiotic formula (SMT04) containing 3 Bifidobacteria (*B. adolescentis*, *B. longum* and *B. bifidum*) based on the identification of bacterial species that showed significant correlations with CRC-related bacteria, including *Fn*, *Lachnoclostridium* sp. m3, *Clostridium hathewayi* (Ch), and *Bacteroides clarus*(Bc). We co-cultured *Fn* with each Bifidobacterium or the combined formula and examined the growth of *Fn* by qPCR. We further examined the effect of SMT04 in a pilot study of 48 subjects (40 on SMT04; 8 no intervention) for 4 weeks and followed up for another 8 weeks.

We quantified levels of the bifidobacteria in SMT04 and CRC-related markers (*Fn*, m3, Ch and Bc) by qPCR in stool samples before and after the intervention. We also assessed the effect of the intervention on the combined CRC risk score (4Bac; *Fn*, m3, Ch and Bc) as established in our previous study (Liang et al, Gut 2020).

Results: *In vitro* co-culturing of individual bifidobacteria in SMT04 significantly inhibited the growth of *Fn* compared with control treatment (24~65% inhibition; all $P<0.001$). The combination of the 3 Bifidobacteria showed a greater inhibitory effect on *Fn* growth (70% inhibition) than individual bifidobacteria (all $P<0.05$).

Subjects treated with SMT04 showed significantly increased levels of the individual Bifidobacterium species from week 2 to week 5 compared with baseline ($P<0.05$) and dropped to baseline levels after cessation of treatment. There was a significant decrease in levels of CRC-related bacteria (*Fn* and m3) and CRC risk score (4Bac) from week 2 to week 12 compared with baseline levels ($P<0.05$) in the SMT04 intervention group but not the control group.

Conclusion: A novel probiotic formula SMT04 was effective in inhibiting the growth of *Fusobacterium nucleatum* *in vitro* and improved the gut microbial environment against CRC development.

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Liang JQ, Li T, Nakatsu G, et al. A novel faecal *Lachnoclostridium* marker for the non-invasive diagnosis of colorectal adenoma and cancer. Gut 2020;69:1248-1257.

Disclosure: Liang JQ provides consultancy to GenieBiome Ltd. Ng SC and Chan FK are scientific co-founders of GenieBiome Ltd.

P0539

INTRODUCTION OF THE PROBIOTIC STRAIN, E COLI NISSE 1917, REDUCES MICROBIAL DIVERSITY, PARTIALLY MEDIATED BY HOST-ACTIVATED TYPE VI SECRETION SYSTEM

H. Bar-Yoseph^{1,2}, A. Serapio Palacios¹, B.B. Finlay¹

¹University of British Columbia, Michael Smith Laboratories, Vancouver, Canada, ²Rambam Health Care Campus, Gastroenterology, Haifa, Israel

Contact E-Mail Address: haggaiy@gmail.com

Introduction: *Escherichia coli* Nisse 1917 (EcN) has been suggested as a safe probiotic intervention to fight enteric pathogens and treat other intestinal disorders. Still, not much is known regarding the effect EcN bare on the intestinal microbiome. Type VI secretion system (T6SS) has been suggested as crucial bacterial machinery used for inter-bacterial competition.

Although typically described in bacterial pathogens, evidence suggests that commensals utilize this system as well. EcN has a T6SS cluster, but its structure and functionality remain to be elucidated.

Aims & Methods: We aimed to investigate the impact that EcN has on the intestinal microbiome and its use of T6SS in this context.

Results: We first characterized EcN's T6SS *in-silico* and showed that it is functional *in-vitro*. A T6SS deletion mutant strain (Δ tssM) was then constructed. To test the effect of EcN and its T6SS on the murine intestinal microbiota, we treated C57BL/6J mice obtained from Jackson Laboratories with either wild-type EcN (WT-EcN), the T6SS mutant (Δ tssM) or PBS (control) (n=30; 10 mice per group). After the treatment, alpha-diversity indices (Chao1, Simpson and Shannon) in mice treated with EcN were significantly lower compared to baseline ($p<0.001$ for all indices).

Interestingly, this effect was not observed in mice treated with Δ tssM or control ($p=NS$ for all indices). Furthermore, post-intervention alpha diversity was lower in the EcN group compared with the control and Δ tssM groups for Chao1 and Shannon indices ($p=0.07$ and 0.08 , respectively). Significant differences were seen between the samples before and after intervention in the Bray-Curtis index (a beta-diversity metric) in the EcN group ($p<0.001$), but not in the control or Δ tssM groups ($p=NS$).

These findings were confirmed using mice originating from a different vendor (Charles River Laboratories), which harbors a different microbiome community (n=15; 5 mice per group).

To better understand EcN's T6SS effect on the microbiota, we co-cultured human commensal *E. coli* and adherent-invasive *E. coli* (AIEC) strains originating from patients with inflammatory bowel disease with either WT-EcN or Δ tssM.

Surprisingly, there was no difference in the commensals/AIECs' growth between the wild-type and the mutant under different co-culture conditions. Since EcN's T6SS induced microbiota changes with no apparent direct bacterial effect on commensals, we hypothesize that this effect is mediated by the host in the intestinal environment. By using a T6SS reporter EcN strain, we found that the T6SS is preferentially activated under gut-mimicking conditions (lower PH, presence of conjugated bile acids and mucin).

Furthermore, in a co-culture with two different human intestinal cell lines (Caco2/TC7 and HT29), we observed that the direct interaction with host cells or its secretome induced T6SS activation. Lastly, we showed that WT-EcN adheres better to human intestinal cells *in-vitro* and outcompetes the Δ tssM mutant strain in *an in vivo* colonization murine model.

Conclusion: Taken together, our findings suggest that EcN reduces the diversity of the normal intestinal microbiome, an effect that is partially mediated by the T6SS in the context of the host. As a common probiotic prescribed to treat gastrointestinal disorders, our data provide further evidence for the need to cautiously use this probiotic in patients, and the importance of the T6SS in the host-microbiome-probiotic interaction.

Disclosure: Nothing to disclose.

P0540

DIET-MICROBIOME INTERACTIONS AND THEIR POTENTIAL IMPACT ON THE HUMAN HEALTH

D. Safina^{1,2}, M. Markelova¹, S. Abdulkhakov^{1,3}, T.V. Grigoryeva¹, M. Siniagina¹, D. Kamaldinova¹, G. Synbulatova¹, R.A. Abdulkhakov³

¹Kazan Federal University, Kazan, Russian Federation, ²IQVIA, Moscow, Russian Federation, ³Kazan State Medical University, Kazan, Russian Federation

Contact E-Mail Address: diliarik@yandex.ru

Introduction: Diet is a major modifiable factor that could alter composition and metabolism of the human gut microbiota. However, data regarding certain food types and their impact on the gut microbiota are very limited.

Aims & Methods: The aim of the study was to determine the association between the gut microbiota taxonomic composition and specific food group's consumption of the healthy volunteers. Six food groups – vegetables/fruits, meat/high-protein foods, fatty foods, dairy, bakery products, digestible carbohydrates (sugars) – were identified.

A total of 66 healthy subjects were included into the study, food consumption was assessed using a special questionnaire. Subjects stool samples were analyzed using shotgun metagenomic sequencing technology (SOLiD 5500 Wildfire platform) to identify the gut microbiota composition.

Correlations between specific food groups consumption and the microbiota composition were analyzed using the R “psych” package based on Spearman's rank correlation coefficient, p-values were adjusted with the Benjamini–Hochberg method (p-value<0.05 was considered significant).

Results: Only weak and moderate ($0 < r < 0.5$ or $-0.5 < r < 0$) statistically significant correlations were identified in this study. There were the following positive correlations: dairy and bakery foods intake correlated with relative abundance of *Firmicutes* phyla ($r=0.33$ and $r=0.27$, respectively), meat/high-protein foods –with *Spirochaetes* phyla ($r=0.27$); negative correlations were found between dairy intake and *Bacteroidetes* phyla ($r=-0.34$).

Also some statistically significant correlations were revealed between specific food consumption and relative abundance of bacterial genera: bakery consumption positively correlated with *Methanospaera* (Archaea, $r=0.33$), *Clostridium* (*Firmicutes*, $r=0.37$), *Megasphaera* (*Firmicutes*, $r=0.3$) and negatively correlated with *Bacteroides* (*Bacteroidetes*, $r=-0.33$), *Barnesiella* (*Bacteroidetes*, $r=-0.25$), *Coprobacter* (*Bacteroidetes*, $r=-0.29$), *Oscilibacter* (*Firmicutes*, $r=-0.27$), *Sutterella* (*Proteobacteria*, $r=-0.36$).

Consumption of vegetables/fruits positively correlated with *Weissella* (*Firmicutes*, $r=0.28$), *Butyrivibrio* (*Firmicutes*, $r=0.24$), *Haemophilus* (*Proteobacteria*, $r=0.28$) and *Methanospaera* (Archaea, $r=0.32$) and negatively – with *Alistipes* (*Bacteroidetes*, $r=-0.37$), *Sutterella* (*Proteobacteria*, $r=-0.24$) genera.

Dairy intake positively correlated with *Lactobacillus* (*Firmicutes*, $r=0.255$), *Lactococcus* (*Firmicutes*, $r=0.27$) and negatively – with *Bacteroides* (*Bacteroidetes*, $r=-0.29$) bacterial genera.

Fatty food consumption positively correlated with bacterial genera of *Firmicutes* phyla (*Clostridium* ($r=0.27$), *Peptostreptococcaceae* ($r=0.25$), *Mitsuokella* ($r=0.29$)), with archaea *Methanospaera* ($r=0.35$), *P22likevirus* ($r=0.31$) and negatively with *Barnesiella* (*Bacteroidetes*, $r=-0.33$), *Roseburia* (*Firmicutes*, $r=-0.26$), *Sutterella* (*Proteobacteria*, $r=-0.33$).

Meat/high-protein foods usage positively correlated with *Prevotella* (*Bacteroidetes*, $r=0.38$), *Dorea* (*Firmicutes*, $r=0.32$), *Enterobacter* (*Proteobacteria*, $r=0.26$) and *Haemophilus* (*Proteobacteria*, $r=0.36$) bacteria.

In addition, sugars intake positively correlated with *Haemophilus* genus (*Proteobacteria*, $r=0.25$) and negatively with *Blautia* ($r=-0.34$), *Holdeman* ($r=-0.33$) corresponding to *Firmicutes* phyla.

Conclusion: Thus, some associations between the gut microbiota taxonomic composition and specific food groups consumption were identified. So potentially, specific dietary changes could be implemented in the future to develop personalized therapeutic strategies aimed to modify gut microbiome composition.

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P0541

BAY3295079 BENEFICIALLY MODULATES HUMAN MICROBIAL COMPOSITION AND ACTIVITY IN VITRO

R.M. Ammar¹, M.R. Pausan², C. Duysburgh³, M. Govaert³, T. Van de Wiele³, L. Van Meulebroek³, L. Verstrepen³, O. Kelber², S. Rabini¹

¹Bayer Consumer Health, Global Medical Affairs, Darmstadt, Germany, ²Bayer Consumer Health, Research and Development, Darmstadt, Germany, ³ProDigest BV, Zwijnaarde, Belgium

Contact E-Mail Address: ramy.ammar@bayer.com

Introduction: Stress has become nearly unavoidable in today's world. Chronic stress causes allostatic overload and dysregulation, leading to gastrointestinal problems and digestive discomfort. BAY3295079 is a combination of *Lactobacillus acidophilus*-14, lemon balm extract and vitamin B2 that helps in relaxation and digestive comfort.

Aims & Methods: Since dysbiosis is one of the pathomechanisms proposed for both stress and digestive discomfort, in this study we investigated the impact of BAY3295079 on human gut microbiome composition and function. Low grade inflammation and leaky gut are associated with stress induced digestive discomfort therefore we evaluated the impact of BAY3295079 on gut permeability and its immuno-modulatory effects.

A standardized *in vitro* simulation of the colonic environment of six healthy adult donors was used to assess the impact of BAY3295079 on microbial composition (quantitative deep shotgun sequencing) and microbial metabolic activity (gas chromatography). Moreover, Caco-2/THP1 co-culture assay was used to test the effect of colonic incubates on gut barrier integrity (Trans Epithelial Electrical Resistance) and immune functions (cytokine profiles).

Additionally, to assess the potential metabolic alterations that may occur upon treatment with the test product, a strategy of untargeted metabolic fingerprinting was applied using ultra-high performance liquid-chromatography coupled to high-resolution mass spectrometry to map both the polar and lipid fraction of the metabolome.

Results: BAY3295079 was efficiently fermented by the gut microbiota, in a process that started early within 3h and was paralleled by increased levels of short chain fatty acids (SCFAs), mainly propionate and butyrate. BAY3295079 selectively and consistently increased the abundance of lactate-producing Lactobacillaceae and Streptococcaceae.

Furthermore, levels of the butyrate-producing Lachnospiraceae and propionate-producing Veillonellaceae families slightly increased for most of the donors tested. Fermentation of BAY3295079 exerted a protective effect on inflammation-induced barrier disruption as confirmed by the significant increase in TEER and donor-dependent immuno-modulatory effects.

The most pronounced beneficial effects were the trend to increase the level of the anti-inflammatory cytokine IL-10, and decreased level of pro-inflammatory cytokine IL-6. Upon performing untargeted metabolic fingerprinting, both the polar and lipid fraction of the metabolome were mapped, rendering fingerprints that enclosed, respectively, 8749 and 10,499 compounds. Multivariate analysis of these metabolic data revealed significant alterations that occurred upon treatment with the test product.

Selection and subsequent identification of the discriminating compounds suggested relevant shifts in pyrimidine metabolism (i.e. orotic acid, glutamine, and thymine), phenylalanine metabolism (i.e. phenylpropionic acid, phenyllactic acid, and hydrophenylpropionic acid), protein degradation (i.e. leucylglycine), bile acid metabolism (i.e. lithocholic acid), and methionine metabolism (i.e. methionine sulfoxide and methionine).

Conclusion: The synbiotic potential of BAY3295079 formula combining both probiotic and plant-based prebiotic (lemon balm) has been confirmed in this study by the positive modulation of gut microbiome and the

generation of health-related metabolites. This could justify its positioning in the area of stress relief and digestive comfort via modulating the microbiome and immune pathways of the gut brain axis.

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Ramy M. Ammar, Manuela Pausan, Olaf Kelber, and Sabine Rabini are employed by Bayer Consumer Health.

P0542

ROLE OF GUT MICROBIOME AND SHORT CHAIN FATTY ACIDS IN MEDIATING STW 5-II EFFECT ON GUT EPITHELIAL AND IMMUNE REGULATION: AN IN VITRO STUDY

R.M. Ammar¹, E.-M. Pferschy-Wenzig^{2,3}, P. Van den Abbeele⁴, L. Verstrepen⁴, J. Ghyselinck⁴, T. Thumann^{2,3}, R. Bauer^{2,3}

¹Bayer Consumer Health, Global Medical Affairs, Darmstadt, Germany, ²Institute of Pharmaceutical Sciences, University of Graz, Department of Pharmacognosy, Graz, Austria, ³BioTechMed, Graz, Austria, ⁴ProDigest BV, Zwijnaarde, Belgium

Contact E-Mail Address: ramy.ammar@bayer.com

Introduction: Recent investigations have revealed that gut microbiota could be a pharmacological target for herbal medicines. STW 5-II, a combination of 6 herbal extracts, is a clinically proven treatment for functional dyspepsia (FD) and irritable bowel syndrome (IBS).

Aims & Methods: Since dysbiosis is one of the pathomechanisms proposed for both FD and IBS, we aimed to explore the bidirectional interaction between this herbal formula and human gut microbiome as a novel mechanism of action. A standardized *in vitro* simulation of the colonic environment of five healthy donors was used to assess the impact of STW 5-II on microbial composition (quantitative 16S rRNA-based Illumina sequencing), pH, gas production, and microbial metabolic activity (Gas chromatography). Moreover, Caco-2/THP1 co-culture assay was used to test the effect of colonic incubates on gut barrier integrity (Trans Epithelial Electrical Resistance) and immune functions (cytokine profiles). Additionally, the impact of gut microbiome on STW 5-II metabolism was evaluated using an established UHPLC-HRMS method.

Results: STW 5-II was efficiently fermented by the gut microbiota, in a process that started early (within 3h) as evidenced by consistent changes in pH and gas production. Fermentation of STW 5-II was paralleled by increase in the level of short chain fatty acids (SCFAs), acetate, propionate, and butyrate. Most of the major classes of secondary compounds in STW 5-II were fermented by the gut microbiota. UHPLC-HRMS analysis allowed identification of 109 compounds that significantly changed: 62 compounds were identified as STW 5-II constituents that significantly decreased, 22 compounds as intermediate metabolites, and 25 compounds as final metabolites. Major stable metabolites were davidigenin, 18-b-glycyrrhetic acid, and 3-hydroxy-phenylpropionic acid. The majority of metabolic reactions were very similar in the five donor samples, indicating that the microbial functions required for conversion of these constituents were present in all donors' microbiome. STW 5-II selectively and consistently increased the abundance of acetate, lactate, butyrate-producing microorganisms including but not limited to *Bifidobacteriaceae*, *Eggerthellaceae*, *Ruminococcaceae* and specific families belonging to the *Bacteroidetes* phylum. While *E. coli/Shigella sonnei* was inhibited in four of five donors. Fermentation of STW 5-II exerted a protective effect on inflammation-induced barrier disruption as confirmed by the significant increase in TEER and donor-dependent immuno-modulatory effects. The most pronounced beneficial effects were the increased secretion of the anti-inflammatory cytokine IL-10, increased NF- κ B activity, and decreased secretion of MCP-1.

Conclusion: The current study shows the two-way interactions between STW 5-II and human gut microbiome indicating that the human gut microbiome could be a novel extra target for STW 5-II. This could explain, at least in part, the clinically proven efficacy of STW 5-II and provides a new basis for better understanding of the pharmacology of STW 5-II.

Disclosure: This study was supported by a grant from Bayer Consumer Health

Ramy M. Ammar is employed by Bayer consumer health.

P0543

CHANGES IN THE GUT MICROBIOME ASSOCIATED WITH MURINE MC38 COLON TUMORS BY ANTI-PD-L1 ANTIBODY AND 17 β -ESTRADIOL TREATMENT

C.-H. Song¹, N. Kim^{1,2}, R.H. Nam¹, S.I. Choi¹, J.Y. Jang¹

¹Seoul National University Bundang Hospital, Department of Internal Medicine, Seongnam, Korea (Republic of), ²Seoul National University College of Medicine, Department of Internal Medicine and Liver Research Institute, Seoul, Korea (Republic of)

Contact E-Mail Address: chinheesong@gmail.com

Introduction: The composition of the gut microbiota is affected by sex hormones, immune checkpoint inhibitor therapies, and colorectal cancer (CRC) development. Previously, we reported that 17 β -estradiol (E2) administration before MC38 cell injection inhibits MC38 tumor growth by downregulating PD-L1 expression and regulating tumor-associated cell populations in male mice. Furthermore, E2 boosted the effect of anti-PD-L1 antibody in the MC38 tumor model.

Aims & Methods: Here, we investigated the gut microbiota as a potential biomarker regulated by E2 and/or anti-PD-L1 antibodies in the MC38 tumor model as a secondary outcome of a previous study. A total of 5 x 10⁵ MC38 cells (passage no. 8) resuspended in 100 μ l DPBS were injected subcutaneously into the right flank of 8-weeks-old C57BL/6 male and female mice. E2 (10 mg/kg) was intraperitoneally administered to male mice three days before injection of MC38 cells for one week. The tumor (50–100 mm³) bearing male and female mice were selected and injected with anti-PD-L1 or isotype control antibodies intraperitoneally at a dose of 10 mg/kg every three days for a total of three injections.

Mice were sacrificed at day 26 after injection of MC38 cells and collected feces were used for 16S rRNA sequencing. The composition of the gut microbiota evaluated by means of 16S rRNA metagenomics sequencing of stool DNA extracted from feces.

Results: Microbial diversity (ACE, Chao1 and Jackknife) was increased in the anti-PD-L1 antibody, E2, and anti-PD-L1+E2 groups compared to the MC38 male controls without statistical significance. Similar to males, MC38 female mice also showed a tendency to increase microbial diversity by anti-PD-L1 treatment compared to the control group.

The change in microbial diversity by anti-PD-L1 treatment was strongly increased in males than in females. At the taxonomic family level, *Muribaculaceae* was enriched only in the MC38 male control group among the male and female groups. As a result of LEfSe analysis at the species level in male mice, the four microorganisms were commonly regulated in all treatment groups including anti-PD-L1, E2, and anti-PD-L1+E2; decrease of PAC001068_g_uc and PAC001070_s (family *Muribaculaceae*) and increase of PAC001716_s and PAC001785_s (family *Ruminococcaceae*).

Interestingly, in the anti-PD-L1 and E2 combination treatment group, a decrease in opportunistic pathogen (*Enterobacteriaceae* group) and increase in commensal bacteria (*Lactobacillus murinus* group and *Parabacteroides goldsteinii*) were observed. Furthermore, the abundance of *Parabacteroides goldsteinii* was commonly increased in the anti-PD-L1 group regardless of sex.

Conclusion: Our results suggest that estrogen may contribute to improving anti-PD-L1 therapeutic efficacy by alleviating the dysbiosis of gut microbiota associated with colon tumors in mice.

Disclosure: Nothing to disclose

P0544

ALTERATION OF GUT MICROBIOTA BY ENDOGENOUS AND EXOGENOUS ANDROGENS IN AZOXYMETHANE/DEXTRAN SULFATE SODIUM-INDUCED COLON CANCER MOUSE MODEL

N. Kim^{1,2}, C.-H. Song¹, R.H. Nam¹, S.I. Choi¹, J.Y. Jang¹

¹Seoul National University Bundang Hospital, Department of Internal Medicine, Seongnam, Korea (Republic of), ²Seoul National University College of Medicine, Department of Internal Medicine and Liver Research institute, Seoul, Korea (Republic of)

Contact E-Mail Address: nakim@snubh.org

Introduction: Sex hormones are known to affect the gut microbiota. Previously, we reported that endogenous and exogenous testosterone are associated with colorectal cancer (CRC) development and submucosal invasion.

Aims & Methods: In the present study, we investigated whether the gut microbiota is affected by orchiectomy (ORX) and testosterone propionate (TP) administration using an azoxymethane/dextran sulfate sodium (AOM/DSS)-induced CRC mouse model. Seven-week-old male and female C57BL/6 mice were used in this study. The orchiectomy (ORX) group of male mice underwent surgical orchiectomy. TP supplementation was initiated on the day of the surgery. Gut microbiota was evaluated by means of 16S rRNA gene sequencing of stool DNA extracted from feces that were obtained at 13 weeks after AOM injection (from 22-weeks old animals) and stored in a gas-generating pouch.

Results: The increase in microbial diversity (Chao1 and Phylogenetic Diversity index) and Firmicutes/Bacteroidetes (F/B) ratio upon AOM/DSS treatment in ORX mice was significantly decreased by TP supplementation. The ratio of commensal bacteria to opportunistic pathogens was lower in the TP-administered females and ORX mice than in the AOM/DSS group. Opportunistic pathogens (*Mucispirillum schaedleri* or *Akkermansia muciniphila*) were identified only in the TP group. In addition, microbial diversity and F/B ratio were higher in male controls than in female and ORX controls. *Flintibacter butyricus*, *Ruminococcus bromii*, and *Romboutsia timonensis* showed similar changes in the male control group as those in the female and ORX controls.

Sex	Group	ACE	Chao1	Jackknife	Shannon	Phylogenetic Diversity
Female	Con (n=4)	1161.93	1068.37	1214.25	1.64	552.25
	AOM/DSS (n=7)	1941.47	1766.54^a	1966.76	1.94	704.86^a
	AOM/DSS+TP (n=4)	1545.72	1473.22	1638.25	1.98	689.75
Male	Con (n=4)	2875.33	2683.75	3063.75	2.63	865.50
	AOM/DSS (n=10)	1700.83^a	1567.51^a	1776.17^a	1.92^a	698.00^a
	AOM/DSS+TP (n=8)	1499.86	1405.00	1581.75	1.84	647.00
ORX	Con (n=4)	1604.73	1502.82	1703.00	1.70	706.75
	AOM/DSS (n=10)	2431.72^a	2299.48^a	2592.70^a	2.41^a	778.70^a
	AOM/DSS+TP (n=6)	1014.46^b	931.09^b	1036.55^b	1.39^b	547.83^b

Data are presented as the medians. *p*-value < 0.05 was considered to be significant and was presented as boldface. Mann-Whitney U-test for comparison difference between independent two groups was performed. ^a*p*-values between Con vs AOM/DSS; ^b *p*-values between AOM/DSS vs AOM/DSS+TP. Con, control; AOM, azoxymethane; DSS, dextran sulfate sodium salt; TP, testosterone propionate; ORX, orchiectomized.

Table 1. Alpha diversity of microbiota from fecal contents.

Conclusion: In conclusion, testosterone determines the dysbiosis of gut microbiota, which suggests that it plays a role in the sex-related differences in colorectal carcinogenesis.

Disclosure: Nothing to disclose.

P0545

INHIBITION OF IN VITRO CLOSTRIDIODES DIFFICILE BIOFILM FORMATION BY THE PROBIOTIC YEAST SACCHAROMYCES BOULARDII CNCM I-745 THROUGH MODIFICATION OF THE EXTRACELLULAR MATRIX COMPOSITION

S. Bouttier¹, A. Simons², P.-A. Lacotte¹, J. Malet-Villemagne¹, V. Nicolas³, C. Janoir¹

¹Micalis Institute, Châtenay-Malabry, France, ²Laboratoire Eau, Environnement et Systèmes Urbains, Créteil, France, ³UMS IPSIT Université Paris-Saclay-US 31 INSERM-UAR 3679 CNRS, Châtenay-Malabry, France

Contact E-Mail Address: sylvie.bouttier@universite-paris-saclay.fr

Introduction: *Clostridioides difficile* is a Gram-positive, strictly anaerobic, spore-forming bacillus. In Western countries, *C. difficile* is the leading cause of healthcare-associated intestinal infections in adults, and the number of community *C. difficile* infections (CDI) has been steadily increasing for a couple of years [1].

The CDI's clinical signs range from self-resolutive mild- to severe diarrhea to life-threatening pseudomembranous colitis. Furthermore, rare complications such as fulminant colitis may occur, requiring urgent medico-surgical management. A major challenge encountered with CDI is the occurrence of recurrences, most of them being relapses related to the persistence in the colonic niche of the strain responsible for the initial episode [2].

Multiple recurrences can be considered chronic infections. The role of biofilm formation in CDI recurrences is now widely considered and strategies that hinder *C. difficile* biofilm formation or disrupt pre-formed biofilm may be a promising alternative to fight against CDI and/or recurrent CDI [3].

Aims & Methods: This study aimed to explore if the probiotic yeast *Saccharomyces boulardii* CNCM I-745 (Biocodex, Gentilly, France), already known to exert some antagonistic effects against *C. difficile* diarrhea and colitis [4], could impact the biofilm formation of *C. difficile* *in vitro*.

We compared the quality and integrity of single-species biofilms formed by *C. difficile* alone to dual-species biofilms formed by *C. difficile* in presence of *S. boulardii* after different incubation durations and at different bacteria:yeast ratios, using crystal violet staining, quantification of viable bacterial cells and confocal laser scanning microscopy.

Results: Combining these approaches revealed that live *S. boulardii* exerts an antagonistic effect on the biofilm formation by three different *C. difficile* strains, including the 027 PCR-ribotype R20291 strain. In a time- and yeast-concentration-dependent manner, *S. boulardii* significantly reduced biomass and viable bacteria count. Confocal laser scanning microscopy observation confirmed a weakening and an average thickness reduction of the biofilm structure when *C. difficile* was co-incubated with *S. boulardii*, compared to the single-species biofilm structure. These effects were neither observed with a genetically close yeast, *S. cerevisiae*, nor with the supernatant of *S. boulardii* cultures, suggesting they are specific to the probiotic yeast and require direct contact between the yeast and *C. difficile*. We also analyzed the composition of the extrapolymeric matrix of single- and dual-species biofilms, by quantification of polysaccharides, proteins, and eDNA and showed that the matrix of *C. difficile* biofilm produced in presence of live *S. boulardii* comprised significantly less eDNA, an essential structural component of the *C. difficile* biofilm matrix. This observation was further confirmed by biofilm analysis after DNase treatment.

Conclusion: *S. boulardii* CNCM I-745 exerts an antagonistic effect on the formation of the *C. difficile* biofilm, in terms of the biomass produced, on bacterial viability and architecture of the biofilm structure. A modulation of the matrix composition probably mediated this effect.

This could in part explain the preventive effect of this probiotic yeast in recurrent CDI. Further studies investigating the efficacy of various antibiotics associated with *S. boulardii* CNCM I-745 could provide new insights into the management of patients with recurrent CDI.

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P0546

INTESTINAL MICROBIOTA TRANSPLANT FOR RECURRENT CLOSTRIDIODES DIFFICILE INFECTION RESTORES MICROBIAL ARYLSULFATASES AND SULFATIDE DEGRADATION: A NOVEL MECHANISM OF EFFICACY?

B.H. Mullish¹, P. Paizs¹, J. Alexander¹, E. Verigos¹, J.A.K. McDonald², L. Ford¹, S. Maneta-Stavarakaki¹, M. Sani¹, L.A. Roberts¹, D. Chrysostomou¹, J. Kinross³, T. Monaghan⁴, J.R. Marchesi¹, D. Kao⁵, Z. Takats¹

¹Imperial College London, Department of Metabolism, Digestion and Reproduction, London, United Kingdom, ²Imperial College London, MRC CMBI, London, United Kingdom, ³Imperial College London, Department of Surgery And Cancer, London, United Kingdom, ⁴NIHR Nottingham Digestive Diseases, Biomedical Research Unit, Nottingham, United Kingdom, ⁵University of Alberta, Division of Gastroenterology, Department of Medicine, Edmonton, Canada

Contact E-Mail Address: b.mullish@imperial.ac.uk

Introduction: Key mechanisms of the efficacy of intestinal microbiota transplant (IMT) for recurrent *Clostridioides difficile* infection (rCDI) relate to changes in gut microbiome-related metabolites, and alterations of host serum glycan profile (1).

The gut lipidome may be relevant to rCDI pathogenesis; for instance, the cytotoxic action of toxins in other Clostridial diseases depends upon their binding to sulfatides in mucous membranes. As such, we explored the impact of IMT for rCDI upon the gut lipidome and gut microbiota members related to it.

Aims & Methods: Ultra high performance liquid chromatography (UHPLC-MS) and high-throughput laser desorption-rapid evaporative ionisation mass spectrometry (LD-REIMS) was performed on paired pre-/ post-IMT (>4 weeks post-) for patients successfully treated with IMT for rCDI (n=16) and on samples from an *in vitro* artificial gut model (aka “chemostat” model) of IMT/rCDI to compare lipidomic profiles; univariate and multivariate analysis was performed on identified lipid species. 16S rRNA gene sequencing was performed on chemostat samples; shotgun metagenomic

analysis and a functional sulfatase enzyme assay was performed on donor and serial patient stool samples (collected pre-FMT, and weeks 1, 4 and 12 post-IMT) from a separate cohort of rCDI patients treated successfully with IMT (patients: n=17 for shotgun analysis, n=34 for enzyme assay; donors: n=9).

Results: On lipidomic analysis of stool samples (n=16; mean age 69.8 years, female 69%), 6483 molecular features species were found, of which 1873 were significantly different (false discovery rate (FDR) corrected, $p < 0.01$) between pre- and post-IMT; particularly noteworthy was the finding that all 14 identified sulfatide moieties were significantly reduced in human stool in post-IMT samples compared to pre-IMT.

A comparable pattern was observed on analysis of artificial gut culture samples from an IMT/rCDI model, suggesting that the reduction in sulfatides reflected microbial degradation; relative abundance of the glycan-degrading gut commensal *Bacteroides fragilis* showed a strong negative correlation with that of most sulfatides.

Analysis of stool shotgun metagenomic data of the key microbial arylsulfatase EC:3.1.6.1 demonstrated a significant increase in read counts of this gene at weeks 1 and 12 post-IMT versus pre-IMT ($p < 0.05$, Wilcoxon rank sum). Pre-IMT faecal sulfatase activity was significantly reduced compared to that of donors, and of patients post-IMT at all assessed timepoints up to week 12 ($q < 0.01$, Kruskal-Wallis with Benjamini-Hochberg FDR).

Conclusion: Successful IMT for rCDI is associated with restoration of microbial arylsulfatase gene count and enzyme activity, and degradation of sulfatides. *Bacteroides* members with glycan-degrading ability may be responsible for this activity. Restoration of this functionality by IMT may disrupt *C. difficile* toxin binding and may contribute to established changes in host glycan profile after IMT.

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P0547

THE PECULIARITIES OF INTESTINAL MICROBIOME IN PATIENTS WITH OSTEOARTHRITIS

O. Gubska¹, A. Kuzminets¹

¹Bogomolets National Medical University, Therapy, Infectious Diseases and Dermatology Postgraduate Education, Kyiv, Ukraine

Contact E-Mail Address: andrewkuzminets@gmail.com

Introduction: Osteoarthritis (OA) requires frequent nonsteroidal anti-inflammatory drugs (NSAIDs), harmful to the gastrointestinal tract. Intestinal microbiome (IM) disturbance can result from NSAID use, amplifying NSAID-enteropathy, but some evidence shows that IM disturbance can relate to OA directly.

Aims & Methods: To study the peculiarities of the intestinal microbiome in patients with OA. We investigated 91 patients with OA of different localizations and degrees divided into three subgroups depending on NSAIDs use and their selectivity. 30 people without OA were recruited as a control group (CG).

We studied major phyla of intestinal bacteria (*Bacteroidetes*, *Firmicutes*, *Actinobacteria*), then calculated the *Firmicutes/Bacteroidetes* (F/B) ratio and content of “other” in feces; PCR-SSP method. Among “others,” we determined the content of *Gamma-proteobacteria* class and *Akkermansia muciniphila* species.

Results: There was a negative correlation between *Firmicutes* content and the stage of OA ($p=0.521$); the *F/B* ratio correlated with the body mass index (BMI) ($p=0.455$) and patient's age ($p=0.562$); a negative correlation in *Actinobacteria* content with the patient's age was found ($p=0.300$); $p<0.05$.

The *Gamma-proteobacteria* content was 1.44% (IQR 0.81-2.03) in "non-NSAIDs", 1.96% (IQR 1.52-2.57) in non-selective NSAIDs ($p<0.01$), and 2.19% (IQR 1.08-2.51) in selective NSAIDs ($p>0.05$). A correlation between the bacteria content and stage of OA ($p=0.526$) and BMI ($p=0.356$), $p<0.05$, was found. *Akkermansia muciniphila* content was, respectively, 2.55% (IQR 1.63-4.30), 1.35% (IQR 1.20-1.64), 1.22% (IQR 0.99-1.50), $p<0.001$ in NSAIDs vs "non-NSAIDs" subgroups. The difference was between NSAIDs-intake and "non-NSAIDs" subgroups ($p<0.001$). Its content correlated with the patient's age ($p=0.402$; $p<0.05$).

Phyla content	OA	OA subgroups			CG
		"non-NSAIDs"	non-selective NSAIDs	selective NSAIDs	
<i>Firmicutes</i>	51.80% (IQR 45.37-58.64) [§]	51.47% (IQR 48.11-56.21) [§]	57.21% (IQR 49.98-69.05) ^{**}	47.83% (IQR 32.24-52.92) [§]	66.66% (IQR 58.57-73.66)
<i>Bacteroidetes</i>	15.86% (IQR 8.25-20.54) [§]	15.08% (8.03-29.21) [§]	18.04% (IQR 9.36-17.75) [§]	13.50% (IQR 9.24-17.75) [§]	6.06% (IQR 3.23-8.57)
<i>F/B</i> ratio	3.32 (IQR 2.18-5.47) [§]	3.33 (IQR 1.79-6.74) [§]	3.27 (IQR 2.65-5.25) [§]	3.65 (IQR 1.63-4.84) [§]	11.60 (IQR 6.56-20.76)
<i>Actinobacteria</i>	9.99% (IQR 6.55-13.61) [*]	8.41% (IQR 5.59-10.02) ^{§§}	7.75% (IQR 5.51-10.56) ^{§§}	13.66% (IQR 13.26-14.56)	12.16% (IQR 8.09-16.54)
"other"	22.33% (IQR 13.39-33.95)	25.04% (IQR 19.51-34.48) [§]	17.00% (IQR 12.54-25.69) [§]	25.02% (IQR 12.85-36.16) [§]	15.12% (IQR 12.10-19.57)

§- a significant difference from CG ($p<0.0001$)

*- a significant difference from CG ($p<0.05$)

§- a significant difference from CG ($p<0.01$)

§- a significant difference from selective NSAIDs ($p<0.01$)

§- a significant difference from selective NSAIDs ($p<0.0001$)

§- a significant difference from "non-NSAIDs" ($p<0.05$)

Table.

Conclusion: There is a significant difference in the IM composition among subjects with OA and without this disease. Patients with OA have higher levels of *Bacteroidetes* and "other" bacteria and lower *Firmicutes* and *Actinobacteria* content. The *F/B* ratio is the most sensitive indicator of the difference. The NSAIDs intake and its selectivity affect some bacterial taxonomical units, but we did not find apparent regularity. The most explicit changes were found in *Akkermansia muciniphila* content: NSAIDs intake decreased it, regardless of NSAID's selectivity.

Disclosure: Nothing to disclose.

P0548

S. BOULARDII CNCM I-745 STIMULATES IMMUNITY BY INCREASING INTRACELLULAR BACTERICIDAL ACTIVITY AGAINST SALMONELLA TYPHIMURIUM IN MACROPHAGES

D. Czerucka¹, R. Pontier-Bres¹

¹Centre Scientifique de Monaco, Ecosystèmes & Immunité, Monaco, Monaco

Contact E-Mail Address: dczerucka@centrescientifique.mc

Introduction: During bacterial infection, macrophages act as "professional phagocytes". *Salmonella typhimurium* (ST) escape from host immune system innate- and humoral- mediated killing, by being internal-

ized into specialized vacuoles in the macrophage that constitute niches for ST protection and bacterial replication. Thus, enhancing intracellular antimicrobial responses of infected macrophages may be determinant for the outcome of the infection. Nitric oxide (NO) is an antimicrobial effector produced by inducible nitric oxide synthetase (iNOS). iNOS expression is controlled by cytokines: produced upon interferon IFN- γ stimulation and repressed by interleukin IL-10. The probiotic yeast *S. boulardii* CNCM I-745 (Biocodex, Gentilly) has been shown to protect mice from infection by ST via various mechanisms, including promoting the differentiation of monocytes that infiltrate the lamina propria into macrophages, which acquire properties to phagocyte ST (Pontier-Bres R et al. *Frontier in Immunology* 2019).

Aims & Methods: The aim of our study was to investigate the effect of *S. boulardii* on bactericidal activity of macrophages.

This study was conducted on the murine macrophages RAW 264.7 cells. The cells were seeded in six well plate and incubated with *S. boulardii* CNCM I-745 (10^6 CFU/ well) overnight before infection with ST (MOI 10 CFU/ cell). After one hour, non-adherent ST were removed by repeated washes and cells exposed to gentamycin 100 μ g/ml, a membrane-impermeant antibiotic, for one hour followed by gentamycin 10 μ g/ml during 22 hours. The number of adherent bacteria (estimated after one hour of infection) and the number of intracellular bacteria (estimated after 24h of infection) were determined by colony forming units (CFU) enumeration. iNOS-, IFN- γ - and IL-10-mRNA were quantified by qPCR.

Results: In this specific model, *S. boulardii* CNCM I-745 didn't modify the number of adherent bacteria but decreased by 5-fold the number of intracellular ST when compared to unexposed macrophages infected with ST. These data suggest that the yeast induces a bactericidal activity in the macrophage.

This bactericidal action of the yeast was confirmed by the 12-fold increase of iNOS expression in cells exposed to *S. boulardii* CNCM I-745 before infection when compared to unexposed cells infected by ST. Interestingly, this induction of iNOS expression in yeast pretreated cells before infection was correlated with the up-regulation of IFN- γ and downregulation of IL-10 as compared with unexposed cells infected with ST.

Conclusion: This study demonstrates that *S. boulardii* CNCM I-745 stimulates intracellular bactericidal activity of macrophages infected by *Salmonella*. This effect is correlated with a stimulation of the expression of iNOS and changes in the expression of cytokines involved in its induction.

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P0549

ECONOMIC AND CHRONOLOGIC OPTIMIZATION OF FECAL DONOR RECRUITMENT IN THE BACTERIOTHERAPY CLINIC. ANALYSIS OF 5 YEARS OF ACTIVITY

B. Levy^{1,2}, L. Werner^{1,2}, N. Fliss-Isakov^{1,2}, T. Ziv-Baran², M. Leshno³, N. Maharshak^{1,2}

¹Tel Aviv Medical Center. Dept. of Gastroenterology, Tel Aviv, Israel,

²Tel Aviv University, Sackler School of Medicine, Tel Aviv, Israel, ³Tel Aviv University, School of Management, Tel Aviv, Israel

Contact E-Mail Address: wernerlael@gmail.com

Introduction: Fecal microbial transplantation (FMT) is the delivery of microbes, isolated from a healthy donor's feces, into a patient's gastrointestinal tract. FMT is the most efficient treatment for recurrent *Clostridioides difficile* infection (CDI). During the past decade, FMT is under vast investigation as a potential therapeutic option for various conditions and diseases.

Fecal donors undergo a strict screening process to avoid transmission of infections and microbiome-related disease conditions. This consists of several blood and stool tests, which are performed in a conditional, multi-stage process, which may be very costly and time-consuming.

Aims & Methods: Our aim was to review the process of donor recruitment at our Bacteriotherapy Clinic in the Tel Aviv Medical Center, during the past 5 years. We performed a cost-minimizing analysis to find the optimal order in which the tests should be performed, without jeopardizing results, and yet making the process more cost-effective and efficient, without increasing the number of visits of donors.

Methods: This study reviews the economic and chronologic aspects of screening FMT stool donors, description of the etiology of donor disqualification, the number of donors who were disqualified at each stage and the average cost for each screening failure.

In order to study the most cost-effective order of tests, we allocated the screening tests into 14 groups of tests (chemistry, virology, serology, fecal tests etc.). Performance analysis was implemented, and an algorithm for the order of the tests to minimize the cost was defined and proven mathematically. This algorithm takes into account the cost of each test and the probability for it to be abnormal.

Results: A total of 87 volunteers were screened as potential stool donors for CDI treatment. Of these, 53 were not eligible according to their questionnaire, physical examination, or inability to complete the donation process. Thirty-four potential donors (Age- 31.0±6.6 years, 59 % male, mean BMI 21.9±1.9 kg/m²), were screened by laboratory tests. Ten volunteers were disqualified due to abnormal lab tests. Finally, 24 potential donors were qualified as stool donors.

In the current order of tests, according to our data, the average cost of screening of each of the 34 subjects was \$2290±175, and \$3243 to qualify a single donor.

Applying our algorithm to optimize the order of the group of tests, reduced the average cost for screening a potential donor to \$1,150±1,030 and the average cost to qualify a single donor decreased to \$2,550. This resulted in a potential saving of 49.9% of the cost of screening a potential donor and a 21.3% of the cost to qualify a single donor.

Conclusion: Improving the order and timing of the screening tests of potential FMT stool donors can decrease the costs by about 50% per subject.

Disclosure: Nothing to disclose.

P0550

DOT-BLOT HYBRIDIZATION FOR THE RAPID AND SIMULTANEOUS DETECTION OF *CAMPYLOBACTER JEJUNI* AND *CAMPYLOBACTER COLI*

B. Bakhshi¹, S. Shams²

¹Tarbiat Modares University, Medical Bacteriology, Tehran, Iran (Islamic Republic of), ²Qom University of Medical Sciences, Cellular and Molecular Research Center, Qom, Iran (Islamic Republic of)

Contact E-Mail Address: sshamsmed@gmail.com

Introduction: Campylobacteriosis is acute bacterial diarrhea that is mainly caused by the genus *Campylobacter*. These are gram-negative, spiral, microaerophilic bacteria and consist of about 25 species. Among them, *C. jejuni* and *C. coli* are known as the main causes of campylobacteriosis worldwide with 90% and 10% of cases, respectively. The disease is common in developed and developing countries, and in many countries, it is about 2 to 3 times more common than salmonellosis.

These bacteria can colonize asymptotically in the intestinal tract of most mammals and birds. It is estimated that 50 to 70% of human *Campylobacter* infections are due to the consumption of contaminated poultry meat products. Cases of Guillain-Barré syndrome (GBS) and reactive arthritis have been reported following *C. jejuni* infection. Therefore, the importance of this disease, especially in children, is very important.

Aims & Methods: Our aim was to develop a dot-blot technique for detecting both *C. jejuni* and *C. coli* simultaneously. The *cadF* gene of *Campylobacter jejuni* and *Campylobacter coli* was selected as the target gene. The sequences were downloaded from GenBank and multiple alignments were done using CLC Sequence Viewer 7.6 software to determine conserved regions among members of both species. GeneRunner and CLC software were used for designing the probe/primers. Dig Oligonucleotide 3-End Labeling Kit was used to synthesize Dig-Probes. TA cloning was also performed to produce a recombinant plasmid (pTG19-T/*cadF*) as a positive control. Dot blot hybridization was performed according to the instructions on DNAs extracted from *C. jejuni* ATCC 29428 and nine laboratory-confirmed campylobacters, including 7 *C. jejuni* and 2 *C. coli* strains. A limit of detection (LOD) was detected using prepared plasmid and different concentrations of the probe (500, 250, 100, 50, and 5 µg/ml).

To evaluate the specificity, a list of intestinal bacteria such as *E. coli*, *Vibrio cholerae*, *Aeromonas hydrophila*, *Enterobacter cloacae*, *Shigella sonnei*, *C. jejuni*, *C. coli*, and *Salmonella enterica* was also used.

Results: A 95-bp fragment of the *cadF* gene was selected, and bioinformatics analyses showed that this region is conserved among campylobacters, so that, in theory, the designed probe can detect these bacteria simultaneously. Hybridization with recombinant plasmid created a black spot on the nylon membrane, which confirmed that the probes were synthesized correctly.

All standard and clinical strains were also identified by the dot-blot technique. The sensitivity of the test was determined at the concentration of 50 µg/ml and no visible spot with other bacteria (100% specificity) was observed.

Conclusion: The designed assay can be useful for the detection of the target bacteria with high specificity and sensitivity, inexpensive, and rapid detection of both bacteria.

Disclosure: Nothing to disclose.

P0551

CLINICAL CHARACTERISTICS AND OUTCOMES OF CLOSTRIDIODES DIFFICILE INFECTION IN THE INTENSIVE CARE UNIT

J.E. Baek¹, I.H. Choi¹, Y.W. Cho¹, Y.-S. Cho¹

¹Seoul St. Mary's Hospital, College of Medicine, The Catholic University of Korea, Department of Internal Medicine, Seoul, Korea (Republic of)

Contact E-Mail Address: bje310@naver.com

Introduction: *Clostridioides difficile* infection (CDI) is one of the leading causes of hospital-associated infectious diarrhea. Despite of the growing clinical and economic burden of CDI, data on intensive care unit (ICU) related CDI is lacking in Asia-Pacific region. The purpose of our study was to assess patient characteristics and clinical outcomes of CDI treated in the intensive care unit (ICU).

Aims & Methods: Ninety-eight patients with CDI in intensive care unit of Seoul St. Mary's Hospital from January 2017 to May 2021 were analyzed retrospectively. Backward-stepwise multiple logistic regression model was used to analyze factors influencing response to treatment and mortality.

Results: The median age of patients was 70.5 years (IQR 57.8–78.0) and 36 patients (36.7%) were considered immunocompromised. The mean Charlson Comorbidity Index was 5.40±2.44 (10-year survival rate of 21%), APACHE II 18.87±8.16 (predicted mortality rate of 25%), ATLAS score 5.45±1.59 (predicted cure rate of 75%), and SOFA score 8.66±3.83 (predicted mortality rate of 33%), respectively. According to SHEA/IDSA 2017 guideline, 43 cases (43.9%) were mild to moderate CDI, 22 cases (22.4%) with severe CDI, and 33 cases (33.7%) with fulminant CDI.

Oral metronidazole was the most frequently used regime as first-line treatment (n=36; 36.7%), followed by oral vancomycin (n=23; 23.5%), intravenous metronidazole (n=21; 21.4%) and combination of oral vancomycin and intravenous metronidazole (n=18; 18.3%). However, there were no statistically significant differences in the cure rate and all-cause mortality between different treatment groups.

The cure rate after 10 days was 45.9% and the 30 day recurrence rate was 14.3%. Fulminant CDI (OR 0.164; 95% CI 0.053–0.507; p=0.002), high SOFA score (OR 0.207; 95% CI 0.050–0.866; p=0.031), and increment in APACHE II score (OR 0.844; 95% CI 0.727–0.980; p=0.026) were associated with poorer treatment response.

Overall mortality at 60 days was 43.9%, and CDI related mortality 9.1%. Immunocompromised patients (OR 0.240; 95% CI 0.077–0.744; p=0.013), high APACHE II score (OR 0.222; 95% CI 0.064–0.774; p=0.018), and high ATLAS score (OR 0.717; 95% CI 0.514–1.000; p=0.050) were associated with death.

Conclusion: In this study, high-risk patients in ICU have higher mortality and lower cure rate of CDI. Types of antibiotics do not significantly influence the treatment of CDI in ICU patients. Further research is required to provide more accurate prediction scoring systems and better clinical outcomes of CDI in ICU.

Disclosure: Nothing to disclose.

P0552

PERFORMANCE OF COMBINED STOOL AND SERUM CYTOMEGALOVIRUS REAL-TIME POLYMERASE CHAIN REACTION IN DIAGNOSING CMV COLITIS

O. Sattayalertyanyong¹, N. Horthongkham², M. Chayakulkeeree³, A. Pongpaibul⁴, N. Angkathunyakul⁴, N. Pausawasdi³, P. Phaophu³, N. Subdee³, J. Limsrivilai³

¹Mahidol University, Siriraj GI Endoscopy Center, Siriraj Hospital, Bangkok, Thailand, ²Mahidol University, Department of Microbiology, Siriraj Hospital, Bangkok, Thailand, ³Mahidol University, Department of Medicine, Siriraj Hospital, Bangkok, Thailand, ⁴Mahidol University, Department of Pathology, Siriraj Hospital, Bangkok, Thailand

Contact E-Mail Address: onuma.gimed@gmail.com

Introduction: Colonoscopy with tissue biopsy is the gold standard for diagnosing cytomegalovirus (CMV). However, the invasive nature of this technique limits its use in some patients. An alternative non-invasive test, serum CMV real-time polymerase chain reaction (rt-PCR), has insufficient diagnostic performance. Stool CMV-PCR could be an alternative or complementary.

Aims & Methods: This study aimed to assess the diagnosis performance of stool CMV-PCR. This prospective study included 117 consecutive patients with 122 consecutive colonoscopies who had clinically suspected CMV colitis, and 20 asymptomatic healthy volunteers. All participants underwent colonoscopy with tissue biopsy for both H&E stain and immunohistochemistry for CMV as the definite diagnosis. The number of infected cells was counted. Quantitative stool CMV-PCR (CMV R-gene[®] kit, Biomerieux) and quantitative serum CMV-PCR (Cobas[®] CMV, Roche) were collected within 7 days of colonoscopy. The positive test was defined as the detection of virus. The diagnostic performance of the stool and serum CMV-PCR tests were analyzed.

Results: Of 117 patients, 27 (23.1%) were diagnosed with CMV colitis. The stool and serum CMV-PCR performance are shown in Table 1.

Total test (n=122)	Sensitivity(%) (95% CI)		Specificity(%) (95% CI)		PPV(%) (95% CI)		NPV(%) (95% CI)	
Stool CMV-PCR	70.4 (53 – 87)		91.6 (86 – 97)		70.4 (53 – 87)		91.6 (86 – 97)	
Serum CMV-PCR	66.7 (49 – 84)		94.7 (90 – 99)		78.3 (61 – 95)		90.9 (85 – 96)	
Both stool and serum positive	55.6 (36 – 74)		96.8 (92 – 99)		79 (61 – 97)		88.3 (82 – 94)	
Either stool or serum positive	81.5 (67 – 96)		90.5 (84 – 96)		71 (55 – 87)		94.5 (90 – 99)	
Subgroup analysis	IMT	IMP	IMT	IMP	IMT	IMP	IMT	IMP
Stool CMV-PCR	91 (74 – 100)	56 (32 – 81)	95 (88 – 100)	89 (80 – 97)	83 (62 – 100)	60 (35 – 86)	97 (93 – 100)	87 (78 – 96)
Serum CMV-PCR	82 (59 – 100)	56 (32 – 81)	98 (93 – 100)	93 (86 – 99)	90 (71 – 100)	69 (44 – 94)	95 (89 – 100)	88 (79 – 96)
Both stool and serum positive	73 (46 – 99)	44 (19 – 68)	98 (93 – 100)	94 (88 – 100)	89 (68 – 100)	70 (41 – 98)	93 (85 – 100)	85 (76 – 94)
Either stool or serum positive	100 (100 – 100)	69 (46 – 91)	95 (88 – 100)	87 (78 – 96)	85 (65 – 100)	61 (38 – 84)	100 (100 – 100)	90 (82 – 98)
IMT, Immunocompetent (n=52); IMP, Immunocompromised (n=70)								

IMT, Immunocompetent (n=52); IMP, Immunocompromised (n=70)

Table 1. Diagnostic performance of stool and serum CMV PCR

The sensitivity and specificity was 0.70 and 0.91 for stool CMV-PCR and 0.67 and 0.95 for serum CMV-PCR. No significant difference was observed. When both test results were combined, the specificity of the posi-

tive of both tests was 0.97, significantly higher than the stool test alone ($P=0.045$). Furthermore, the sensitivity of the positive of either test was 0.81, significantly higher than the serum CMV-PCR alone ($P=0.045$). In subgroup analysis, diagnostic performance was better in immunocompetent patients (Table 1).

We found a good and significant correlation between stool CMV-PCR and serum CMV-PCR ($r=0.71$, $p<0.01$), and each test with cytomegalic cell count ($r=0.63$, $p<0.01$ for stool CMV-PCR and 0.68 , $p<0.01$ for serum CMV-PCR). There were no positive results for stool and serum CMV-PCR tests among healthy volunteers.

Conclusion: Stool CMV-PCR had a good diagnostic performance for CMV colitis. Combining stool and serum CMV-PCR could improve diagnostic value. Positive both tests had high specificity and can be used for ruling in, while negative results of both tests can exclude CMV colitis.

Disclosure: Nothing to disclose.

P0553

CHARACTERISATION OF THE MUCOSAL IMMUNE RESPONSE IN COLONIC SPIROCHAETOSIS

K. Fan¹, M. Gottstein¹, A. Carrozzi², G. Burns¹, M.M. Walker², E. Hoedt¹, N.J. Talley², S. Keely¹

¹University of Newcastle, School of Biomedical Sciences & Pharmacy, New Lambton Heights, Australia, ²University of Newcastle, Faculty of Health & Medicine, New Lambton Heights, Australia

Contact E-Mail Address: kening.fan@uon.edu.au

Introduction: Human colonic spirochaetosis (CS) is an infection caused by the *Brachyspira* genus. Although considered as commensal, recent evidence suggests *Brachyspira* are associated with gastrointestinal symptoms and irritable bowel syndrome [1].

Increased eosinophils, mast cells and lymphocyte aggregates have been reported in CS [2,3], however, little is known about immune cell localization or activation status. We aim to characterize the distribution and activation of mucosal immune responses in patients with CS compared to controls.

Aims & Methods: Formalin fixed, paraffin-embedded colonic biopsy samples from 20 CS patients (mean age $\pm$ SEM 44.50 $\pm$ 4.32, 70% male) were examined; 20 age/sex and date of colonoscopy-matched patients (45.65 $\pm$ 4.06, 70% male) who did not have CS were recruited as matched controls. Patient demographic and clinical information were collected and the associations with CS were compared (Fisher exact test with odd ratios (OR) and 95% confidence intervals (CI)). Spirochaete infection was confirmed by cross-reactive *Treponema pallidum* antibody immunohistochemistry (IHC) staining. Intra-epithelial lymphocytes (IEL) /150 colonic enterocytes were identified by H&E staining, eosinophils were identified by Congo-red staining, and mast cells were identified by CD117 IHC staining. Tissue sections were visualised using the Aperio AT2 digital pathology scanner. Peak cell numbers were counted in 3 fields of intra-epithelial, intra-crypt and lamina propria areas.

Results: CS patients had a significantly higher risk of faecal incontinence (OR: 14.37, 95%CI: 0.67 to 307.4) and mucus in the stool (OR: 14.37, 95%CI: 0.67 to 307.4) compared to matched controls. Patients with CS also had an increased likelihood of abdominal pain (OR: 3.75, 95%CI: 0.79 to 15.26), diarrhea (OR: 4.33, 95%CI: 1.00 to 16.74), vomiting (OR: 5.09, 95%CI: 0.19 to 135.5), blood in the stool (OR: 9.00, 95%CI: 1.054 to 114.9), defecation urgency (OR: 9.29, 95%CI: 0.41 to 211.9) and nocturnal defecation (OR: 5.09, 95%CI: 0.19 to 135.5). CS patients had a significantly higher eosinophil count and degranulated eosinophil count in the lamina propria, intra-epithelial and intra-crypt regions compared to matched controls (Table 1).

CS patients had a significantly higher mast cell count and degranulated mast cell count in the lamina propria, intra-epithelial but not in intra-crypt regions compared to matched controls (Table 1). CS patients had significantly higher IELs compared to matched controls (Table 1).

Cell count (Mean $\pm$ SEM)	CS (n=20)	Matched control (n=20)	P value
Lamina propria eosinophils	46.84 $\pm$ 4.78	30.69 $\pm$ 3.29	0.0123
Lamina propria degranulated eosinophils	35.81 $\pm$ 3.70	19.11 $\pm$ 2.30	0.0004
Lamina propria CD117+ mast cells	62.77 $\pm$ 3.24	46.21 $\pm$ 1.97	<0.0001
Lamina propria degranulated CD117+ mast cells	50.74 $\pm$ 3.08	37.08 $\pm$ 1.84	0.0002
Intra-epithelial eosinophils	4.68 $\pm$ 0.55	2.82 $\pm$ 0.33	0.0121
Intra-epithelial degranulated eosinophils	4.44 $\pm$ 0.53	2.47 $\pm$ 0.31	0.0045
Intra-epithelial CD117+ mast cells	3.33 $\pm$ 0.38	1.88 $\pm$ 0.28	0.0032
Intra-epithelial degranulated CD117+ mast cells	2.70 $\pm$ 0.32	1.46 $\pm$ 0.24	0.003
Intra-crypt eosinophils	2.21 $\pm$ 0.32	1.07 $\pm$ 0.22	0.01
Intra-crypt degranulated eosinophils	2.10 $\pm$ 0.32	0.67 $\pm$ 0.18	0.0005
Intra-epithelial lymphocytes	14.38 $\pm$ 1.29	6.71 $\pm$ 0.58	<0.0001

Table 1. Summary of immune cell count comparisons between CS patient and matched controls

Conclusion: Patients with CS had increased eosinophils, mast cells count and activation in the lamina propria and intra-epithelial regions, as well as increased IELs, suggesting these cells that play important roles in anti-bacterial defence may be induced by spirochete infection. CS patients also have a higher risk of GI symptoms. These data suggest that CS infection provokes a mucosal immune response and GI symptoms, and that *Brachyspira* species may be a group of underappreciated intestinal pathogens.

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Disclosure: Nothing to disclose.

P0554

CHANGES OF CLOSTRIDIODES DIFFICILE INFECTION RATE DURING FIRST STAGES OF COVID-19 PANDEMIC ERA -A RETROSPECTIVE STUDY FROM A ROMANIAN TERTIARY CENTER

M. Chirvase¹, O. Mocanu¹, R. Stefan¹, S. Bucurica^{1,2}, F. Ionita-Radu^{1,2}

¹Central University Emergency Military Hospital, Bucharest, Romania, ²'Carol Davila' University of Medicine and Pharmacy, Internal Medicine and Gastroenterology, Bucharest, Romania

Contact E-Mail Address: mirela_chereja@yahoo.com

Introduction: Clostridioides difficile infection (CDI) is generally one of the most frequent health care-associated infections (HAI) all around the world, with variations between different medical systems.

The Covid-19 pandemic radically changed our medical practice, with implications in the healthcare-associated infections (HAI) incidence secondary to the enhancement of the measures meant to reduce SARS-CoV-2 spreading. Gut dismicrobism induced by SARS-COV-2 infection, long hos-

pital stay, empirical antibiotic therapy and immunomodulating agents used as treatment for Covid-19 could change CDI incidence during the pandemic.

Aims & Methods: The aim of this study was to evaluate if there is a change in *Clostridioides difficile* infection rates due to Covid-19 pandemic impact in medical system. In this retrospective study we analyzed the rate of new CDI cases diagnosed in the Central Military Hospital of Bucharest from september 1 2020 to march 31 2021 (6 months) in full pandemic time, using the hospital database system. We included 96 hospitalized patients in this study with established diagnosis of CDI by enzyme immunoassay detection of antigen GDH and toxins A and or by positive *Clostridioides difficile* PCR from stool sample.

Also, we studied the CDI diagnosis and death rates of patients diagnosed with CDI during 6 months of Covid-19 pandemic compared to a non-pandemic 6 months time interval (1 sept 2016- 1march 2017).

Results: In our study group of patients with CDI the mean age at diagnosis was 62.52 years old, 52% of patients being over 65 years old, with small difference between genders (53% males vs 47% females).

Most of the patients suffered from chronic comorbidities (87%) and 59.3% of them presented history of SARS-COV-2 infection.

Regarding risk factors, 89.58% of the patients were exposed to 2 or more risk factors for CDI infection (advanced age, antibiotic therapy, proton pump inhibitor administration and immunosuppressive drugs were the most common CDI risk factors).

The infection with *Clostridioides difficile* was significantly higher in Covid-19 infection patients with RR =12.059 (95% CI – Confidence interval, 8.047 to 18.072)

The mortality rate of patients diagnosed with CDI was 15.6%, four times higher than it was found in the pre-pandemic data regarding *Clostridioides difficile* deaths (4%). The number of new CDI cases diagnosed during 6 months of Covid 19 pandemic was almost twice higher (96 vs 54) compared with 4 years ago in a study conducted in the same hospital.

Conclusion: During the Covid-19 pandemic, not only the incidence, but the death rate of CDI was found to be much higher, patients with comorbidities, exposed to one or more risk factors being most common affected. Coronavirus may contribute to worsening the prognosis of CDI patients through dismicrobism (gut specific receptors for SARS-CoV-2), longer hospitalization, empirical antibiotic therapy and immunomodulating agents used as treatment for Covid-19.

Disclosure: Nothing to disclose.

P0555

RISK FACTORS FOR TREATMENT FAILURE AFTER FECAL MICROBIOTA TRANSPLANTATION IN *CLOSTRIDIoidES DIFFICILE* INFECTION

J.-H. Lee¹, S.J. Lee², J. Shin², S.-H. Park², B. Cha², K.S. Kwon², Y.-W. Shin²

¹Inha University Hospital, Hospital Medicine, Incheon, Korea (Republic of), ²Inha University Hospital, School of Medicine, Incheon, Korea (Republic of)

Contact E-Mail Address: endlesmile@naver.com

Introduction: Recently, Fecal Microbiota Transplantation (FMT) was introduced as an effective treatment option for *Clostridioides difficile* Infection (CDI). However, risk factors associated with treatment failure of FMT were not well-demonstrated in the previous study, So we aimed to investigate risk factors to affect treatment failure or recurrence after FMT for CDI.

Aims & Methods: In this retrospective study, (140)patients with CDI received FMT at the microbiome center in Inha University Hospital from November 2017 to August 2021. Among them, (124) who could follow up until 8 weeks after FMT for signs or symptoms of CDI were excluded. FMT

Failure was defined as recurrence of diarrhea or a positive stool test. We collected the risk factors of treatment failure including comorbidities using Charlson Comorbidity Index (CCI), antibiotics usage before and after FMT, and the number of CDI episodes before FMT.

Results: Ninety-three patients (93/124, 75 %) experienced an improvement in symptoms after FMT within 1 week. Treatment failure occurred in 40 patients (40/124, 32.3%) related to unresolving symptoms or positive stool tests.

In multivariate analysis, the rate of symptom improvement within 1 week after FMT was marginally lower in the group with male patients (Odd ratio[OR]: 0.43, 95% confidence interval [CI], 0.179-0.996, P=0.049). The group using antibiotics after FMT showed significantly high recurrence or treatment failure within 8 weeks (Odd ratio[OR]: 2.41, 95% confidence interval [CI], 1.08-5.40, P=0.032).

Conclusion: Patients who need to use antibiotics after FMT should be considered for treatment failure of FMT. It should be confirmed by a large and randomized prospective study.

Disclosure: We have no conflict of interest to declare.

P0556

EVALUATION OF THE RECURRENCE RATE OF *CLOSTRIDIoidES DIFFICILE* INFECTION AFTER ADMINISTRATION OF BEZLOTOXUMAB IN A SINGLE CENTER

F. Lopez Romero-Salazar¹, M. Algara San Nicolas¹, M.A. Orellana Miguel², A. Masedo Gonzalez¹, G.J. Gomez Gomez¹, C. Yela San Bernardino¹, B. Casis Herce¹, M.P. Martinez Montiel¹

¹University Hospital 12 de Octubre, Digestive Disease Department, Madrid, Spain, ²University Hospital 12 de Octubre, Microbiology Department, Madrid, Spain

Contact E-Mail Address: fran_8_orgaz@hotmail.com

Introduction: *Clostridioides difficile* infection (CDI) is the leading cause of nosocomial diarrhea. In addition, multiple studies have shown recurrence rates (rCDI) of approximately 25% (1). Bezlotoxumab, a monoclonal antibody targeted against toxin B, has demonstrated a 40% decrease in the rate of rCDI at 12-week follow-up when co-administered with conventional therapy in clinical trials (2). However, there are still few data that reflect these response rates in daily clinical practice. The main objective of this study was to describe the rate of rCDI during the 12 weeks after administration of bezlotoxumab in patients with CDI.

Aims & Methods: This retrospective, observational, single-centre study recorded all patients who received bezlotoxumab infusion during the duration of antimicrobial treatment for CDI between January 2019 and September 2021. Demographic, clinical data, number of CDI episodes prior to administration of bezlotoxumab, antibiotic treatments received in each episode and follow-up time were included. Treatment success was defined as the absence of rCDI 12 weeks after bezlotoxumab infusion.

Results: 53 patients were included in the study, 27 (50.9%) were women, the median age was 67 years, with a median follow-up of 64 weeks. The main risk factors for rCDI in our population are shown in Table 1.

13 patients (24.5%) received bezlotoxumab in the first CDI episode, 16 (30.2%) in the first recurrence, and 24 (45.3%) in the second or later recurrences. No patient had adverse events related to bezlotoxumab.

Oral vancomycin was the most frequent antibiotic treatment (38.5%) in the patients who received bezlotoxumab in the first CDI, tapered vancomycin the most frequent (62.5%) in the patients who received it in the first rCDI and extended regimen fidaxomicin (29.2%) the most frequent antibiotic in patients who received bezlotoxumab in the second or subsequent recurrences. 49 of 53 patients had no rCDI in the first 12 weeks after administration of bezlotoxumab, which was equivalent to a

success rate of 92.5%. When analyzing risk factors for rCDI in our cohort, we found a significant difference when comparing the recurrence rate between patients who received bezlotuxumab in the first CDI or in the first rCDI versus recurrence rate in those who received bezlotuxumab in the second or later rCDI ($p=0.03$), with a relative risk of 1.2 (95% confidence interval 1.003-1.435).

	N=53
Age >65	34 (64.2%)
Chronic Kidney Disease	13 (24.5%)
Active Cancer (solid organ and hematologic tumors)	11 (20.8%)
Liver Cirrhosis	6 (11.3%)
Inflammatory Bowel Disease	12 (22.6%)
Immunosuppressed	34 (64.1%)
Solid Organ Transplant	10 (18.9%)
Proton Pump Inhibitor Use	47 (88.7%)
Previous Antibiotic Treatment	42 (79.2%)

Table 1. Risk factors for recurrent *Clostridioides difficile* infection (CDI).

Conclusion: In our study, the rCDI rate was lower (7.5%) than that obtained in the pivotal clinical trial (17%) (2). Furthermore, this study demonstrated that late administration of bezlotuxumab (second or later recurrences) increased the risk of recurrences in our population. These results suggest that bezlotuxumab should be used before multiple recurrence occurs. Also, bezlotuxumab was a safe drug with no adverse events reported. However, given the small sample size and the retrospective nature of the study, future evidence is needed to confirm these findings.

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P0557

THE EFFICACY AND SAFETY OF HEMOSTATIC POWDER UI-EWD IN PATIENTS WITH LOWER GASTROINTESTINAL BLEEDING

J. Shin¹, B. Cha¹, J.-S. Park¹, K.-S. Kwon¹, H.-K. Kim¹

¹Inha University Hospital, Inha University School of Medicine, Department of Internal Medicine, Incheon, Korea (Republic of)

Contact E-Mail Address: shinjongv@naver.com

Introduction: Acute lower gastrointestinal bleeding (LGIB) is a common cause of hospitalization, and there are many cases of readmission for re-bleeding after endoscopic hemostasis. Recently, endoscopic hemostatic powder (UI-EWD/Nexpowder™ Nextbiomedical, Incheon, South Korea) has been developed and used to manage LGIB.

Aims & Methods: The aim of this study was to evaluate the safety and efficacy of UI-EWD in LGIB. We conducted this retrospective cohort study of LGIB at a tertiary center. A total number of consecutive patients with LGIB who were included in our research was 167. UI-EWD was applied as rescue therapy during endoscopic treatment in 55 patients. we evaluated the success rate of hemostasis, the adverse event related with UI-EWD and the rate of re-bleeding.

Results: All hemostasis with UI-EWD was successful. The rebleeding rate within 28 days in the UI-EWD group was 5.5% (3/55), which was significantly lower than that in the conventional treatment group, 17.0% (19/112) (p -value:0.039). There were no adverse events associated with or without UI-EWD application.

Conclusion: Apply of UI-EWD is considered as a very effective method for hemostasis, and prevention of rebleeding in LGIB patients who are difficult to control with conventional treatment. Based on this results, we suggest that considering the use of UI-EWD for hemostasis in LGIB is useful and safe.

Disclosure: Nothing to disclose.

P0558

CAN HOSPITAL ADMISSIONS FOR LOWER GASTROINTESTINAL BLEEDING BE REDUCED? IMPLEMENTATION OF TWO SCALES FOR THE PREDICTION OF SAFETY DISCHARGE IN A RETROSPECTIVE COHORT

L. Gonzalez Gonzalez¹, I. Iborra², M. Fortuny³, A. Calm Salvans³, F. Cañete^{1,4}, M. Calafat Sard^{4,1}, M. Mañosa^{1,4}, E. Domenech Morral^{4,1}
¹Hospital Universitari Germans Trias i Pujol, Gastroenterology, Badalona, Spain, ²Hospital Universitari Germans Trias i Pujol, Endoscopy, Badalona, Spain, ³Hospital Universitari Germans Trias i Pujol, Badalona, Spain, ⁴CIBEREHD, Madrid, Spain

Contact E-Mail Address: glaug2@gmail.com

Introduction: The incidence of lower gastrointestinal bleeding (LGIB) is increasing due to the population's aging and causes up to 20-30% of all episodes of gastrointestinal bleeding. Most (80-90%) LGIB episodes follow an uncomplicated course with bleeding control without any haemostatic intervention. Conversely, hospital admission can be a cause of morbidity unrelated to the LGIB itself, particularly in elderly or frail patients. Recently, two scales have been developed to predict a "safe discharge" from the emergency room in patients with LGIB.

Aims & Methods: To evaluate the accuracy of two scales (Oakland and SHA₂PE scores) to predict a safe discharge from the Emergency room in a retrospective cohort of patients admitted for LGIB in a tertiary centre. All patients admitted for LGIB between June 2014 and June 2019 in a tertiary care centre were identified. Patients referred from smaller centres for tertiary care and those in whom the reason for admission was not LGIB, were excluded. "Safe discharge" was defined as meeting all the following criteria:

1. No blood transfusion;
2. No haemostatic treatment (endoscopic, radiological, or surgical);
3. No bleeding recurrence;
4. No medical consultation for LGIB within 28 days after discharge; and
5. No death during admission.

Results: A total of 595 admissions due to LGIB were identified, of which 398 episodes were included. The most frequent aetiology was diverticular disease (53%). Among them, 214 episodes (54%) met the criteria for "safe discharge". Among those not meeting the criteria for safe discharge, 42% required blood transfusion, 8.5% haemostatic treatment, 3% had bleeding recurrence, 15.5% seek for medical advice due to LGIB after discharge and 0.9% died. An Oakland score ≤ 8 points was the one with the highest specificity and positive predictive value (PPV) (both 100%), while the Oakland score of ≤ 10 points (specificity 96.7% and PPV of 45.6%) and the SHA₂PE index (specificity of 94.6% and PPV 89.1%) were less accurate. Nine, 42 and 89 admissions would have been avoided in the study period in case of Oakland score ≤ 8 , Oakland score ≤ 10 points and SHA₂PE ≤ 1 point, respectively. However, using Oakland score ≤ 10 points and SHA₂PE ≤ 1 point, 12% and 11% of patients discharged from the Emergency room would have not met the criteria of safe discharge.

Conclusion: With the current admission criteria, almost half of the patients with LGIB meet the “safe discharge” criteria. Nevertheless, the available prediction indices would only avoid a very small proportion of unnecessary admissions. Further research for more accurate prognostic scores is warranted.

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P0559

MANAGEMENT AND OUTCOMES OF LOWER GASTROINTESTINAL BLEEDING IN PATIENTS ON ANTICOAGULATION

L. Gonzalez Gonzalez¹, I. Iborra², M. Fortuny³, A. Calm Salvans³, F. Cañete^{1,4}, M. Calafat Sard^{4,1}, M. Mañosa Ciria^{4,1}, E. Domenech Morral^{4,1}

¹Hospital Universitari Germans Trias i Pujol, Gastroenterology, Badalona, Spain, ²Hospital Universitari Germans Trias i Pujol, Endoscopy, Badalona, Spain, ³Hospital Universitari Germans Trias i Pujol, Badalona, Spain, ⁴CIBEREHD, Madrid, Spain

Contact E-Mail Address: glaug2@gmail.com

Introduction: Lower gastrointestinal bleeding (LGIB) is common, and it is increasing in incidence among the elderly and in people on anticoagulant treatment. The impact of anticoagulation and its optimal management during the bleeding episode are not well established.

Aims & Methods: To describe the management and impact of anticoagulation on the clinical outcomes of patients with LGIB.

Retrospective analysis of all episodes of LGIB admitted in a tertiary care hospital from June 2014 to June 2019.

Results: Among a total of 398 episodes of LGIB, 102 (26%) occurred while on anticoagulant treatment (71% with dicumarinics and 14% with direct oral anticoagulants -DOAC-). Patient on anticoagulation were older (77 vs. 74 years; $p=0.032$) and had a higher Charlson score (9 vs. 6; $p<0.001$). Anticoagulation was discontinued upon arrival in 16% of the episodes and re-started after a median of 5 days (1-40). At discharge, 4% required modification of the anticoagulation drug or regimen, as follows: 53% treatment discontinuation, 18% were switched from dicumarinics to DOAC and in 29% the DOAC's dose/type was changed. The patients on anticoagulation had a significantly lower haemoglobin concentration upon arrival (10.5 vs.

11.6g/dL; $p<0.001$) and minimum haemoglobin during admission (9 vs. 9.9g/dL; $p=0.001$), as well as a significantly higher need for blood transfusion (55% vs. 37%; $p=0.001$), endoscopic treatment (10% vs. 4%; $p=0.043$), re-admission for LGIB (13% vs. 5%; $p=0.009$) and haemorrhage rate in other territories (17% vs. 5%; $p<0.001$).

In contrast, haemodynamic instability in the emergency room, colonoscopy (62% vs. 61%; $p=0.96$), recurrence of LGIB or death during admission were similar in the two groups. Thirty-nine per cent of patients on dicumarinics had an INR >3 on arrival at the emergency room, which was associated with a lower haemoglobin concentration on arrival and a greater need for transfusion compared to those with an INR within the therapeutic range.

Conclusion: Currently, one fourth of LGIB episodes occur in patients on anticoagulation. Anticoagulation is associated with a greater need for transfusion, endoscopic treatment, and readmission for LGIB, even more pronounced in case of dicumarinic overdose. Anticoagulant therapy is modified at discharge in a very low proportion of patients.

Disclosure: Nothing to disclose.

P0560

SAFETY OF PERFORMING LEFT SIDE COLONOSCOPY VERSUS TOTAL COLONOSCOPY IN PATIENTS LESS THAN 45 YEARS OLD AGE PRESENTED WITH FEATURES SUGGESTIVE OF PERIANAL DISEASE

M. Al-Shekhani¹, S. Shekha^{2,3}

¹Kurdistan Center for GEH, Gastroenterology, Asulaimaniyah, Iraq,

²Kurdistan center for GEH, Gastroenterology, Sulaimanyah, Iraq,

³Sulaimani University, Gastroenterology, Sulaimanyah, Iraq

Contact E-Mail Address: shaikhanimohammad@gmail.com

Introduction: Background: Colonoscopy and flexible sigmoidoscopy are both recommended tools in diagnosing colorectal diseases, but their relative effectiveness is unclear. Direct comparisons of colonoscopy and sigmoidoscopy in the same population would be helpful to inform patients, providers, and policy makers about CRC screening options.

Aims & Methods: Objectives: To evaluate the ability of each of these two modalities (colonoscopy and sigmoidoscopy) to reach the diagnosis in patients presented with features suggestive of perianal disease and to determine Factors that predict safely performing left sided colonoscopy in patients less than forty five years old age presented with features suggestive of perianal disease.

This retrospective and prospective observational study is conducted between 1st of January 2021 and 1st of January 2022 in department of KCGH / Ferkary- hospital, Sulaimaniyah city, Iraq. Five hundred patients presented with features of perianal disease where subjected to sigmoidoscopy and extended to full colonoscopy (first group) and other five 500 patients aged equal and more than 45 years with same presentation taken (second group).

Results: Among five hundred patients who visited KCGH for colonoscopy in Sulaimaniyah city- Iraq, All patient's age were below 45 years old with the mean age of about 33 years. All patients underwent sigmoidoscopy and total colonoscopy with terminal ileal intubation, in colonoscopy group we have 226 (about 45.2%) patients with normal total colonoscopy findings while in sigmoidoscopy group 265 (about 54.8%) cases have normal findings, Thirty nine patients (about 7.8%) have normal finding in sigmoidoscopy but positive findings in colonoscopy.

Conclusion: Colonoscopy and sigmoidoscopy are both important tools in investigating patients presenting with perianal features. While both are sensitive in detecting pathology in the left side of colon our study concluded that although colonoscopy is the ideal procedure in detecting lesions in the whole colon (proximal & distal to splenic flexure), but limited colo-

noscopy up to splenic flexure can be safely carried out in patients less than 45 years old presented with perianal diseases without the fear of missing important proximal colonic lesions.

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Disclosure: Nothing to disclose.

P0561

EFFECT OF LONG-TERM TREATMENT WITH SOMATOSTATIN ANALOGUES IN PATIENTS WITH GASTROINTESTINAL ANGIODYSPLASIA: A SINGLE-CENTER EXPERIENCE

A. Jiménez-Masip¹, A. Palacios¹, L. Alcalá¹, C. Alonso-Cotoner^{1,2,3}
¹Vall d'Hebron University Hospital, Gastroenterology / Medicine, Universitat Autònoma de Barcelona, Barcelona, Spain, ²Instituto de Salud Carlos III, Centro de Investigación Biomédica en Red de Enfermedades Hepáticas y Digestivas (CIBERHED), Madrid, Spain, ³Digestive System Research Unit, Vall d'Hebron Institut de Recerca (VHIR), Laboratory of Neuro-Immuno-Gastroenterology, Barcelona, Spain

Contact E-Mail Address: 94jimenezalba@gmail.com

Introduction: Gastrointestinal bleeding due to angiodysplasia represents up to 10% of gastrointestinal bleeding cases and about 60% of small bowel bleeding. First-line treatment consists of endoscopic argon plasma coagulation, but rebleeding occurs in up to 60% of the patients in the following 2 years.

Somatostatin analogues (SA) have emerged as an attractive medical treatment for those patients with multiple or refractory lesions. However, evidence in literature regarding its effectiveness is scarce.

Aims & Methods: To describe clinical characteristics of patients with gastrointestinal angiodysplasia (GIAD), and to analyze the effect of SA in the course of bleeding GIAD a year after its initiation.

Patients from our center with a history of GIAD-related bleeding with transfusion requirements, who initiated or had initiated SA were included between September 2019 and September 2021.

Clinical data were collected and transfusion requirements (number of packed red blood cells, pRBC), number of hospitalizations and number of endoscopic procedures were recorded in the year after and the year before starting SA. Full responders were defined as those patients with a reduction in the number of pRBC $\geq 50\%$.

Results: A total of 53 patients were included (51% women, median age of 77 $\pm$ 9 years). Among them, 67.9% had cardiac valvular disease and 37.7% chronic kidney disease. Most of the patients were under anti-thrombotic treatment: 52.8% on oral anticoagulants and 41.5% on antiplatelets. GIAD was present in 86.8% of the patients (43% colon, 21% small bowel, 15% multiple locations, 8% stomach), while 13.2% had positive fecal occult blood test with no endoscopic findings.

Up to 50.9% of patients received octreotide and the rest of them, lanreotide. SA treatment was associated with a significant reduction in the number pRBC (9.0 $\pm$ 0.9 vs. 5.5 $\pm$ 1.0; $p=0.001$), number of hospitalizations (3.0 $\pm$ 0.27 vs. 2.0 $\pm$ 0.38; $p=0.002$) and endoscopic procedures (3.6 $\pm$ 0.28 vs. 1.13 $\pm$ 0.26; $p<0.001$) after one year of treatment. Full response was observed in 66% of the patients.

No differences were found regarding the type of SA ($p=0.387$), anticoagulant ($p=0.245$) and/or antiplatelet therapy ($p=0.777$) between full responders and non-responders.

Conclusion: In our cohort, long-term treatment with SA has a beneficial effect in GIAD-related bleeding, significantly decreasing red blood cell transfusion requirements, as well as hospitalization and endoscopic procedures. Further studies are required to properly evaluate the efficacy of SA in GIAD-related bleeding.

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Disclosure: Nothing to disclose.

P0562

CHARACTERISTIC OF THE PATIENTS AND LESIONS WITH DELAYED BLEEDING AFTER COLORECTAL ESD THAT DO NOT REQUIRE HEMOSTASIS

S. Takahashi¹, K. Okimoto¹, T. Matsumura¹, T. Kaneko¹, N. Akizue¹, Y. Ohta¹, T. Taida¹, K. Saito¹, J. Kato¹, N. Kato¹

¹Chiba University, Gastroenterology, Graduate School of Medicine, Chiba, Japan

Contact E-Mail Address: u.satsuki.s.u@gmail.com

Introduction: Delayed Bleeding (DB) with colorectal endoscopic submucosal dissection (ESD) is a relatively frequent complication, and while some patients require hemostasis, others can be followed up without hemostasis. It is important to appropriately determine which cases are amenable to follow-up to avoid unnecessary invasive procedures.

Aims & Methods: The aim of this study was to identify the characteristics of the patients and lesions with DB after colorectal ESD that did not require hemostasis.

Method: Of 603 colorectal ESD cases performed at Chiba university hospital between June 2009 and January 2022, 147 patients and 151 lesions with DB were included (DB group). DB was defined as gross hematochezia (including a small amount of hematochezia) or decreases of Hb 2g/dL or more the day after ESD. DB group was classified into two groups: hemostasis group (H-group; endoscopic hemostasis performed) and follow-up group (FU-group; no endoscopy performed, or endoscopy performed but no hemostasis performed).

The patient/lesion backgrounds, details of ESD and postoperative statuses were analyzed retrospectively.

Results: Of DB group (147 patients, 151 lesions), H-group (34 patients (23.1%), 35 lesions (23.2%)) and FU-group (113 patients (76.9%), 116 lesions (76.8%)).

In univariate analysis, the following factors contributed to follow-up without hemostasis: small amount of hematochezia (definition; recorded in the medical chart as "small quantities hematochezia" or the like), hematochezia once a day, no symptoms of dizziness, hypotension, or abdominal pain, and use of traction method had significantly higher Odds ratio (OR) (5.9/7.9/4.1/8.0) respectively.

The OR was significantly higher for patients with ulcerative colitis as a factor contributing to hemostasis (7.3). Neither age or antithrombotic drug use was not a factor contributing to hemostasis.

Thirty of 151 patients (19.9%) had a decrease in Hb of 2g/dL or more on the day after ESD, but none of them without clinical findings required hemostasis. On multivariate analysis, the small amount of hematochezia was the most important factor contributing to the possibility of follow-up (OR 8.1, 95%CI:2.9-22.7, $p<0.01$).

Conclusion: We should pay attention to the amount and frequency of hematochezia, and DB symptoms after ESD. The use of traction device may have contributed to the follow-up factors, since it improved the visibility

of bleeding and appropriate hemostasis was performed during ESD. In addition, cases with UC complications should be noted because hemostasis may be necessary if DB is detected.

Disclosure: Nothing to disclose.

P0563

THE FACTOR ANALYSIS INFLUENCING THE DIAGNOSTIC YIELDS OF CAPSULE ENDOSCOPY IN PATIENTS WITH OBSCURE GI BLEEDING

K. Hong¹, W.-C. Chung¹

¹The Catholic University of Korea, St. Vincents Hospital, Internal Medicine, Suwon, Korea (Republic of)

Contact E-Mail Address: kuwa001@naver.com

Introduction: Small bowel capsule endoscopy (SBCE) is widely used for diagnosing obscure gastrointestinal bleeding (OGIB). In general, SBCE was proven as a diagnostic yield of approximate 50% for OGIB. This study was to identify factors to increase the diagnostic yield of SBCE in OGIB.

Aims & Methods: The patients who complained of melena or hematochezia were admitted at St. Vincent Hospital, Catholic University of Korea. All of them had negative results of esophago-gastroduodenoscopy and colonoscopy. Immediately on the same day or the next day of endoscopic examinations, SBCE was performed. A consecutive series of the patients were enrolled from March 2019 to December 2021.

Patients were categorized into two subgroups: positive (n = 78), and negative results of SBCE (n = 67). We analyzed the factors affecting diagnostic yields of SBCE— clinical characteristics, underlying conditions, process, and preparation of the procedures.

Results: The rate of positive diagnostic yield of SBCE was 44.8% (78/ 174). There were no significant differences of sex, body mass index (kg/ m²), the presence of diabetes, intake of nonsteroidal anti-inflammatory drugs or anti-platelet drugs, initial lowest hemoglobin level, procedure interval time (from episode to procedure), observation of ampulla of Vater, and duration of oral-to duodenum. The degree of bowel preparation affects the diagnostic yield of SBCE (P=0.003), and small bowel transit time was the significantly longer than negative results group (P=0.027).

In positive results group, the mean age of the patients was the older than negative results group (P=0.01), and the positive result rate of patients under age 60 was statistically low compared with those equal or over 60 (P<0.01).

Conclusion: In the relatively young patients (age <60) with OGIB, we should consider the SBCE carefully due to relatively lower diagnostic yield. Bowel preparation should be good. Small bowel transit time would be an important factor affecting diagnostic yield of SBCE in patients with OGIB.

Disclosure: Nothing to disclose.

P0564

OUTCOMES OF TRANSCATHETER AORTIC VALVE IMPLANTATION IN GASTROINTESTINAL BLEEDING

I. Latras Cortés¹, S. Díez Ruiz¹, R. González Núñez¹, L. Alcoba Vega¹, D. López Cuesta¹, L. Vaquero Ayala¹, S. Vivas Alegre¹, F. Jorquera Plaza¹, A.B. Domínguez Carbajo¹

¹University Hospital of León, Department of Gastroenterology, León, Spain

Contact E-Mail Address: irenelatrascortes@gmail.com

Introduction: Heyde's syndrome is characterized by a triad of aortic stenosis, angiodysplasia with bleeding and acquired von Willebrand syndrome; it is an uncommon cause of gastrointestinal bleeding and iron deficiency anemia.

Hypothesis: transcatheter aortic valve implantation (TAVI) might reduce the presence of gastrointestinal angiodysplasia and their complications.

Aims & Methods: The aim was to compare the existence of anemia (hemoglobin levels), requirements for blood transfusion, hospitalizations for gastrointestinal bleeding and number of endoscopies performed in patients with aortic stenosis before and after TAVI, and describe the medical treatment offered in the Gastroenterology consultation.

Method: Quasi-experimental study with before-and-after design. Data of TAVI performed from January 2018 to December 2020 were collected, and subjects with prior diagnosis of angiodysplasia were selected (n=10) for further analysis.

Results: Ten of the 146 patients (6.85%) who had a TAVI performed had a prior diagnosis of angiodysplasia.

The mean age of the patients with angiodysplasia at time of the TAVI procedure was 83.27 years (SD 3.77); 60% were males.

Regarding medical treatment, 8 patients (80%) were followed in Gastroenterology Consultation. Apart from endoscopic therapy, iron infusion and blood transfusion, octreotide was administered in three of them (37.5%). The mean level of hemoglobin in the 12 months before TAVI was 10.79 g/dl vs 12.01 in the 12 months after TAVI; with statistically significant difference (p=0.0479). There were also statistically significant differences in the comparison of the mean of hospitalizations, endoscopies and blood transfusions before and after TAVI (Table 1).

	Before TAVI	After TAVI	p value
Hemoglobin (g/dl)	10.79 (SD 1.22)	12.01 (SD 1.15)	0.0479
Hospitalizations for gastrointestinal bleeding	1.40 (SD 2.41)	0 (SD 0)	0.0162
Endoscopies	3.30 (SD 3.30)	0.30 (SD 0.67)	0.0129
Blood transfusions	11.90 (SD 19.65)	2.20 (SD 2.62)	0.0244

Table 1. Comparison of levels of hemoglobin, hospitalizations for gastrointestinal bleeding, number of endoscopies and blood transfusion before and after TAVI (expressed as means, standard deviation and p value).

Conclusion: - TAVI reduces gastrointestinal bleeding and improves anemia, so it decreases blood transfusion requirements.

- Anemia, in selected cases, might constitute a criterion for aortic stenosis intervention in the future.

- A multidisciplinary follow-up in Gastroenterology consultation is necessary in order to prepare the patient to the TAVI procedure, by offering endoscopic and medical treatment with somatostatin analogs when iron infusion and blood transfusion are not enough.

Disclosure: Nothing to disclose.

P0565

INTRARECTAL FORMALIN TREATMENT FOR HAEMORRHAGIC RADIATION INDUCED PROCTOPATHY: EFFICACY AND SAFETY

D. Kohoutova¹, C. Gee¹, D. Cunningham¹, A. Wilson¹

¹Royal Marsden Hospital NHS Foundation Trust, London, United Kingdom

Contact E-Mail Address: darina.kohoutova@seznam.cz

Introduction: Radiotherapy is a curative treatment option for localized malignancies, nevertheless it is limited by the dose dependent toxicity to the surrounding organs. From the gastrointestinal tract, rectum is the most frequently affected organ due to:

1. Proximity to the irradiated pelvic organs;
2. Its fixed position within the field of radiation.

Total doses exceeding 60Gy are associated with a higher risk of rectal toxicity and bleeding. Patients with chronic radiation proctopathy (CHRP) have symptoms similar to acute proctitis, however full-thickness bowel ischaemia and fibrotic changes contribute to additional complications: severe rectal bleeding, fistulas, strictures, perforations. Neovascularization and formation of teleangiectasias are responsible for rectal bleeding. If bleeding is severe and/or causes iron-deficiency anaemia, treatment should be offered. Sucralfate enema (if applicable) is the first line treatment. If this fails, argon plasma coagulation (few bleeding teleangiectasias) can be used, or installation of intrarectal formalin (widespread teleangiectasias) is opted.

Aims & Methods: Aim of this retrospective study from a prospective database was to analyze efficacy and safety of intrarectal formalin treatment for haemorrhagic CHRP at the Royal Marsden Hospital. Adult patients were enrolled between March 2018 and October 2021. Contraindications were presence of ulcers, fistulas and strictures. Haemoglobin was evaluated before the first and after the last formalin treatment. Antiplatelet, anticoagulation treatment and administration of transfusion (indication: haemorrhagic CHRP) were recorded. Interval between the completion of radiotherapy and first intrarectal formalin treatment was assessed; dose of radiotherapy was evaluated.

Clinical assessment of frequency and amount of rectal bleeding (rectal bleeding score) was adapted from classification used by Takemoto et al. (Ref 1). Endoscopic classification followed classification used by Chi et al. (Ref 2).

Intrarectal formalin treatment was performed by one operator in an outpatient setting, usually after full bowel preparation and without sedation and/or analgesia. Individual treatment sessions were 6-8 weeks apart. Complications were recorded.

Results: Nineteen patients were enrolled: 13 males (68%) and 6 women. All males received radiotherapy for prostate cancer, two females for endometrial, two for anal, one for cervical and one for rectal cancers. Mean age was 75±9 years.

After exclusion of one outlier, median time between completion of radiotherapy and the first formalin treatment was 20 months, inter-quartile range (IQR): 15. Median dose of radiotherapy was 68 Grey, IQR: 14. Median volume of formalin for a single treatment was 35ml, IQR: 10ml. Median duration of a single formalin treatment was 180s, IQR: 150-180s; (min.: 60s, max.: 180s).

Thirty two procedures were performed (1.7 procedure per patient). In total, 9/19 (47%) patients were receiving anticoagulation and/or antiplatelet medication. Five patients (5/19, 26%) received transfusion. Mean value of haemoglobin before the first treatment was 110±18g/l, after the last treatment 123±16g/l; $p=0.022$. Median of rectal bleeding score before the first treatment was 6 (IQR: 0), after the last treatment 2 (IQR: 1-4); $p<0.001$. Median of endoscopy score on the day of the first treatment was 3 (IQR: 0); on the day of the last treatment 1 (IQR: 1-2); $p<0.001$. Three patients developed ulcers. One patient with a healed ulcer developed a recto-vaginal fistula subsequently.

Conclusion: Treatment with intrarectal formalin in haemorrhagic CHRP is effective and safe.

References:

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2. Chi KD et al. *J Clin Gastroenterol* 2005; 39(1): 42-6.

Disclosure: Nothing to disclose.

P0566

INTERNATIONAL ON-LINE QUESTIONNAIRE ABOUT SEVERE LOWER GASTROINTESTINAL BLEEDING MANAGEMENT. DO WE HAVE IT CLEAR?

M. Ayude Galego¹, N. Garcia Morales¹, M.M. Rodriguez Gonzalez¹, D. Nogueira Senties¹, A. Iglesias Doallo¹, N. Fernández Fernández¹, S. Alonso Lorenzo¹, A. Gómez Rodríguez¹, N.C. Quintáns Pinazas¹, B. Romero Mosquera¹, A. Germade Martinez¹, A.J. Rodríguez De Jesús¹, S. Vázquez Rodríguez¹, J.i. Rodriguez Prada¹

¹Álvaro Cunqueiro University Hospital, Gastroenterology, Vigo, Spain

Contact E-Mail Address: monica.ayude.galego@sergas.es

Introduction: The diagnostic and therapeutic strategy in severe lower gastrointestinal bleeding (LGIB) varies depending on the patient's clinical situation. Actual clinical practice guidelines propose different management strategies.

Aims & Methods: We aim to know the attitude of the gastroenterologists from different hospitalary centers in the management of this entity. For this, we have made a descriptive and observational study using an on-line questionnaire addressed to gastroenterologists in Spain and Latin America in December 2021.

Results: We included 281 anonymous questionnaires of gastroenterologists, 223 associate doctors (79.4%) and 58 medical residents (20.6%), from Spanish hospitalary centers (171, 60.9%) and from 15 Latin American countries (110, 39.1%). Diagnostic and therapeutic management of severe LGIB was heterogeneous among the participants.

Regarding to the first diagnostic modalities they showed variability between performing computed tomography angiography (CTA) (44.5%), gastroscopy (33.1%), colonoscopy (20.6%) and arteriography (1.1%). The therapeutic attitude after a positive CTA varied between performing arteriography (38.1%), colonoscopy (44.1%) or rectosigmoidoscopy if the bleeding location was in left colon (12.8%).

If negative CTA, in the majority of cases a gastroscopy was performed. If the patient needed intensive critical unit (ICU) care and to undergo colonoscopy, most participants performed an urgent colonoscopy (<24 hours) (31% always, 43.4% in most cases); while if the patient did not require ICU admission this percentage was lower (10% always, 33.8% in most cases). Most of the participants (234, 83.3%) gave previous bowel preparation to patients undergoing colonoscopy in the first 8-12 hours.

For bowel preparation, 149 (53%) used polyethylene glycol, 37 (13.2%) sodium picosulfate, 4 (1.4%) enema and 74 of them (26.3%) depending on the case. A total of 115 participants admitted having doubts about the management of this patients. The need for thase creation of an action protocol was considered from 276 of the participants (98.2%) and 170 of them (60.5%) answered that they did not have any available at their center.

Conclusion: There is a high interhospitalary variability on the management of severe lower gastrointestinal bleeding among gastroenterologists and most of them have doubts about its management. It is necessary to create and spread an action protocol for diagnosis and treatment of this pathology.

Disclosure: Nothing to disclose.

P0567

HYDRAULIC LOCAL INFUSION OF EPINEPHRINE-CONTAINING SALINE IS EFFECTIVE IN PREVENTING POSTOPERATIVE BLEEDING IN COLD SNARE POLYPECTOMY UNDER ANTICOAGULATION THERAPY

M. Yasuda^{1,2}, Y. Naito²

¹Uji-Tokushukai Medical Center, Dept. of Gastroenterology and Hepatology, Uji City, Japan, ²Kyoto Pref University of Medicine Gastroenterology, Dept. of Gastroenterology, Kyoto, Japan

Contact E-Mail Address: koutoku7@fa2.so-net.ne.jp

Introduction: Cold snare polypectomy has been reported to be useful in the treatment of colorectal polyps in recent years, and has become popular worldwide. For HSP (Hot Snare Polypectomy) using radiofrequency devices, CSP is recognized as having a low risk of post-polypectomy bleeding and a low risk of post-polypectomy bleeding complications, which is a post-polypectomy syndrome, because CSP does not coagulate with heat, although bleeding occurs immediately after polyp removal. In recent years, however, due to the development of anticoagulants, antithrombotic agents such as NOAC and aspirin have been administered to a large number of patients for the purpose of preventing cardiovascular diseases, and in the case of colorectal polypectomy, antithrombotic agents have been administered in an increasing number of patients.

Therefore, it is necessary to pay attention to the prevention of bleeding after CSP. In general, physiological saline infusion using the Water Jet mechanism is used to prevent bleeding after CSP. We examined whether adding a small amount of epinephrine to the saline helps prevent postoperative bleeding.

Aims & Methods: From January 2018 to March 2019, 200 patients who underwent CSP with antithrombotic agents in our hospital were prospectively enrolled and randomly assigned to receive hydraulic local infusion of either normal saline (NS group) or epinephrine saline (ES group). The concentration of epinephrine was 0.1%, 2 ml/1A dissolved in 200 ml of physiological saline as a 100-fold dilution. In the NS group, saline was hydraulically injected to the polypectomy wound after CSP, and in the ES group, epinephrine-added saline was hydraulically injected to the polypectomy wound after CSP. The procedure of CSP and equipment such as snare were all the same. The post-CSP fluid infusion was terminated in both groups when the ablated surface bulged, and hemostasis was achieved using Olympus OFP-2 as a Water Jet pump device.

Postoperative bleeding events were defined as the occurrence of anal bleeding from the day following polypectomy. In the CSP, all cases were examined with magnifying endoscopy, and only those diagnosed as adenoma by the diagnosis of JNET TYPE 2A by the magnifying observation of NBI or BLI were examined.

Results: There were no significant differences in age, sex, polyp size, polyp shape, location, mean number of resected polyps, or polyp histology between the NS and ES groups. There was no difference in antithrombotic therapy between the two groups. However, there was a difference in the frequency of postoperative bleeding between the two groups. Postoperative bleeding occurred in 2/100 of patients in the NS group.

Postoperative bleeding occurred in 0/100 patients in the ES group. There was a significant difference in the incidence of postoperative bleeding events between the NS and ES groups.

Conclusion: Hydraulic local infusion of epinephrine-containing saline is effective in preventing postoperative bleeding in cold snare polypectomy under anticoagulation therapy.

Disclosure: Nothing to disclose.

P0568

BARRIERS AND WILLINGNESS FOR COLORECTAL CANCER SCREENING IN A MUSLIM POPULATION OF SOUTH ASIAN COUNTRY: NATIONWIDE SURVEY (INTERIM ANALYSIS)

T. Shaikh¹, L. Kamani¹, K.A. Tareen², M.S. Yousaf³, T.K. Bhatti⁴, H. Bashir¹, J. Devi⁵, M. Akram⁶

¹Liaquat National Hospital Karachi, Gastroenterology and Hepatology, Karachi, Pakistan, ²Shaik Khalifa bin Al Nayan Hospital Quetta, Gastroenterology and Hepatology, Quetta, Pakistan, ³Prime Teaching Hospital Peshawar, Gastroenterology and Hepatology, Peshawar, Pakistan, ⁴SZABMU, Pims, Gastroenterology and Hepatology, Islamabad, Pakistan, ⁵Liaquat University of Medical and Health Sciences Jamshoro/Hyderabad, Gastroenterology and Hepatology, Hyderabad, Pakistan, ⁶Multan Medical and Dental College/Ibn-E-Sina Hospital and Research Institute, Gastroenterology and Hepatology, Multan, Pakistan

Contact E-Mail Address: tauqeershek@live.com

Introduction: Colorectal cancer (CRC) is the third most common cancer worldwide. CRC death is largely preventable if detected early. Barriers and willingness for CRC screening are not studied previously in Pakistan.

Aims & Methods: To evaluate barriers to CRC screening in the Pakistani population aged > 40 years.

A cross-sectional, questionnaire-based study was conducted among the general population from all provinces of Pakistan. Data were analyzed by using IBM SPSS Statistics v27.

Results: It is an ongoing study where 4877 participants were included with a mean age of 46.05 ± 14.65 years. Out of these, 3365 (69%) were males. The results showed that 3822 (78.4%) participants were unaware of CRC disease. Furthermore, 3518 (72.1%) participants had no intention to get screened in the future.

The main barriers were, lack of knowledge/awareness of CRC screening test 70.5% (p<0.0001), cost and lack of government-funded screening program 84.4% (p<0.0001), shame of getting screened and absence of preferred gender doctor for colonoscopy 59.9% (p<0.0001).

Ineffectiveness of screening tests and doubt about the safety of colonoscopy 50.4% (p<0.0001), fear of getting abnormal results 57.6% (p<0.0001), and lack of doctor's recommendation for CRC screening 75.1% (p<0.000) was also found to be a significant barrier.

Conclusion: In our ongoing survey, we found multiple colorectal cancer screening barriers among the general Pakistani population. A majority of participants were unaware of CRC disease. An extensive government-led awareness campaign must be launched and doctors should discuss CRC screening with their patients. Moreover, the availability of preferred gender endoscopists must be ensured to increase compliance.

Disclosure: Nothing to disclose.

P0569

SOCIOECONOMIC AND ETHNIC DISPARITIES IN COLORECTAL SCREENING BEFORE AND DURING THE COVID-19 PANDEMIC: A POPULATION-BASED STUDY IN ISRAEL

Z. Levi^{1,2}, N. Abu-Frecha^{3,4}, D. Comanesther⁵, T. Bacenstein⁵, S. Eizenstein¹, A.D. Cohen^{5,4}, O. Weinstein⁵

¹Tel Aviv University, Tel Aviv, Israel, ²Rabin Medical Center, Division of Gastroenterology, Petach Tikva, Israel, ³Soroka Medical Center, Beer Sheva, Israel, ⁴Ben-Gurion University, Beer Sheva, Israel, ⁵Clalit Health Services, Tel Aviv, Israel

Contact E-Mail Address: Zohar.levi.gastroenterology@gmail.com

Introduction: Subjects from the low socioeconomic state (SES) and racial or ethnic minorities have lower colorectal cancer (CRC) screening rates worldwide due to educational gaps and disparity in health care resources. **Aims & Methods:** We aimed to compare the rate and trend of being updated with screening and colonoscopy completion rate after a positive fecal occult blood test (FOBT) before and during the COVID-19 pandemic among subjects with low SES and minorities compared with others.

This is a retrospective analysis of all insured subjects aged 50-75 years within the Clalit health services in 2019-2021. Up to date with screening was defined as having a colonoscopy within ten years or an FOBT within one year; colonoscopy completion rate was defined as having a colonoscopy within six months of a positive FOBT.

Results: In 2019, out of 918,135 subjects, a total of 61.3% were up to date with screening; 65.9% for high-SES (referent), 60.1% for medium-SES [Odds Ratio (OR) 0.81, 95%CI 0.80-0.82] and 59.0% for low-SES (OR 0.75, 95%CI 0.74-0.75); 61.9% for Jews (referent), 59.7% for Arabs (OR 0.91, 95%CI 0.90-0.92), and 51.7% for Ultraorthodox Jews (OR 0.77, 95%CI 0.75-0.78). Out of 21,308 with a positive FOBT, the colonoscopy completion rate was 51.8%; 59.8% for high-SES (referent), 54.1% for medium-SES (OR 0.79, 95%CI, 0.73-0.86), and 45.5% for low-SES (OR 0.60, 95%CI 0.56-0.65); 54.7% for Jews (referent), 51.4% for Ultraorthodox Jews (OR 0.91, 95%CI 0.90-0.92) and 44.7% for Arabs (OR 0.77, 95%CI 0.75-0.78).

In 2020-2021 there was a slight drop in the rate of being up to date with screening (up to Δ -1.8%) and the colonoscopy completion rate (up to Δ -1.3%), while the of the discrepancies were kept or slightly increased with time (Δ SES 7.9% vs. 6.9% for being up to date with screening; 14.0% vs. 12.5% for colonoscopy completion rate; Jews-Ultraorthodox Jews: Δ 8.4% vs. 6.5% for being up to date with screening; Δ 7.6% vs. 3.3% for colonoscopy completion rate; Δ Jews-Arabs 4.2% vs. 2.2% for being up to date with screening; 10.9% vs. 10.0% for colonoscopy completion rate), P for interaction with time <0.001 for most measures.

Conclusion: In this population-based study, we report that in 2019, about 61% of the target population were up to date with screening, and the colonoscopy completion rate was 52%, with significant socioeconomic and ethnic disparities.

In 2020-2021 there was only a slight drop in both screening measures, while the disparities were kept or slightly increased. These findings should direct health policymakers to build specific programs to improve the screening measures for subjects from low SES and ethnic minorities.

Disclosure: Nothing to disclose.

P0570

IMPACT OF THE COVID-19 PANDEMIC ON THE COLORECTAL CANCER SCREENING PROCEDURES IN THE CZECH REPUBLIC

S. Suchanek^{1,2}, T. Grega^{1,2}, K. Hejzmanova^{3,4}, O. Ngo^{3,4}, O. Májek^{3,4}, M. Zavoral^{1,2}

¹Military University Hospital, Department of Medicine, Prague, Czech Republic, ²Military University Hospital, Department of Gastrointestinal Oncology, Prague, Czech Republic, ³Faculty of Medicine, Masaryk University, Institute of Biostatistics and Analyses, Brno, Czech Republic, ⁴Institute of Health Information and Statistics of the Czech Republic, Prague, Czech Republic

Contact E-Mail Address: stepan.suchanek@uvn.cz

Introduction: The organized, population-based National Colorectal Cancer (CRC) Screening Program in the Czech Republic is focused on asymptomatic individuals. Since age 50, the immunochemical fecal occult blood test (FIT) is offered annually at age 50 – 54 and biennially at age ≥ 55 , followed by FIT+ colonoscopy, if positive. As an alternative, there is a choice of screening colonoscopy from age 50, in 10 years interval.

Aims & Methods: Evaluation of FITs and screening colonoscopies performed in the years 2021 (data from January to September) and 2020 (all year), both compared to the same period in the year 2019. The analysis was performed using the database of the National Registry of Reimbursed Health Services in the Czech Republic.

Results: Comparing years 2020 and 2019, there was decrease of the FITs (-16.9 %) with maximum in April (-75.6 %) and screening colonoscopies (-12.0 %), maximum in April (-58.1 %). In comparison between the years 2021 and 2019, the numbers of FITs have dropped by 4.1 % (maximum in January, -20,6 %) and the number of screening colonoscopies has risen by 3.1%.

Despite the decrease of FITs and screening colonoscopies in the year 2020, the number of FIT-positive colonoscopies has risen (from 22.137 to 27.234 procedures), and 1.797 adenomas and 49 colorectal cancers were diagnosed more compared to the year 2019. This phenomenon was caused by the increase of the FIT positivity from 6.8% in the year 2019 to 10.1% in the year 2020.

Conclusion: Despite the reduction of FIT and screening colonoscopies during the COVID-19 pandemic up to now, the number of colorectal adenomas and cancers have risen in the year 2020 thank to the increase in FIT positivity and therefore the number of FIT-positive colonoscopies performed.

References: Supported by the Czech Ministry of Health grants NV18-08-00246 and NU22-08-00424 and projects MO1012 and Cooperatio.

Disclosure: Nothing to disclose.

P0571

SERINE, AN AMINO-ACID INVOLVED IN PRO-CARCINOGENIC EFFECTS OF COLIBACTIN-PRODUCING *ESCHERICHIA COLI* IN THE COLON

A. Devaux¹, R. Villéger¹, B. Diémé², M. Lagrée², M. Rodrigues¹, G. Roche¹, N. Barnich¹, C. Jousse², M. Bonnet¹

¹Université Clermont Auvergne, M2iSH Microbes, Intestin, Inflammation & Host Susceptibility, Clermont-Ferrand, France, ²Université Clermont Auvergne / INRAé, Plateforme d'Exploration du Métabolisme MetaboHUB, Clermont-Ferrand, France

Contact E-Mail Address: amandine.devaux@uca.fr

Introduction: The colonic tissues are abnormally colonized by colibactin-producing *Escherichia coli* (CoPEC) in colorectal cancer (CRC) patients. Colibactin is a genotoxin produced by enzymes encoded by the *pks* genomic island. The pro-carcinogenic effects of CoPEC and colibactin have

been demonstrated using various animal models. Metabolomic studies have shown that CoPEC infection results in reprogramming of intestinal epithelial cell metabolism, leading to a decrease of serine concentration (intracellular and extracellular levels).

The aim of this study is to investigate whether serine allows CoPEC to better persist in the gastrointestinal tract and/or exert their pro-carcinogenic functions.

Aims & Methods: Human colorectal carcinoma T84 cells were infected with a reference CoPEC strain (11G5) isolated from a human CRC sample, its colibactin-negative mutant (11G5- Δ pks) or a commensal strain of *Escherichia coli* (K12C600). Expression of genes coding for the serine utilization and biosynthesis operon was evaluated by RT-qPCR 3h following infection. The impact of a serine- and glycine- depleted diet (SD) on the persistence and genotoxic effects (γ H2Ax immunolabeling) of CoPEC was studied using wild-type animals and APC^{min/+} mouse model of CRC.

Results: Three hours post-infection, we have shown *in vitro* that the CoPEC 11G5 strain uses serine from the enterocyte, via activation of serine-utilization-genes, which provides to CoPEC a competitive growth advantage over a commensal strain or its mutant (11G5- Δ pks). To highlight the specific role of serine on CoPEC colonization and genotoxic effect, APC^{min/+} mice were fed with a SD diet.

As control, we measured a decrease of the serine level in the serum by liquid chromatography–mass spectrometry in SD diet mice compared to control diet mice. SD diet induced an early and transient decrease in CoPEC 11G5 bacterial colonization associated with a decrease of its genotoxic properties, and lower DNA damages induced by infection. Experiments are in progress with the 11G5- Δ tdcA mutant, unable to metabolize serine, to validate the impact of serine utilization on CoPEC virulence.

Conclusion: Altogether, the present study demonstrates that serine could be a metabolite of interest, used by CoPEC to colonize the digestive tract and to exert its genotoxic properties. This work allows us to elucidate the mechanisms of action of CoPEC in colonic carcinogenesis and could identify novel therapeutic targets.

Disclosure: Nothing to disclose.

P0572

SLC26A9 PROMOTES COLORECTAL TUMORIGENESIS VIA WNT/ β -CATENIN SIGNALING

M. Zhang¹, Z. Ma¹, B. Tuo¹, T. Li², X. Liu¹

¹Department of Gastroenterology, Affiliated Hospital of Zunyi Medical University, Zunyi, China, ²Department of General Surgery, Affiliated Hospital of Zunyi Medical University, Zunyi, China

Contact E-Mail Address: anhuimazhiyuan@163.com

Introduction: Colorectal cancer (CRC) is a common malignant tumor and a major health threat worldwide. SLC26A9 (solute carrier family 26 member 9) is a member of SLC26A family of multifunctional anion transporters, which functions as Cl⁻ channel.¹

Our previous study showed that SLC26A9 deficiency results in gastric tumorigenesis in mice, which demonstrated that its role in the carcinogenesis for the first time.² However, what's the role of SLC26A9 in the CRC onset is not clear and never reported.

Aims & Methods: We utilized a large patient cohort and mouse models of CRC as well as CRC cells to determine the role of SLC26A9 and associated mechanism in CRC.

Results: SLC26A9 was expressed low levels in the cytoplasm of normal colorectal epithelium, polyps and adenomas, but significantly increased in the colorectal adenocarcinoma and translocated to the nucleus. Moreover, increased levels of SLC26A9 associated with high-risk of the disease and poor prognosis.

Compared with normal colon cell line (NCM460), SLC26A9 was significantly upregulated in the all CRC cell lines, with highest expression in cell line COLO201, but the lowest expression in cell line SW48. The shRNA silencing of SLC26A9 expression in COLO201 induced cell cycle arrest and apoptosis, but inhibited cell proliferation and xenograft-tumor growth both *in vitro* and *in vivo*.

Mechanistic analysis revealed showed that SLC26A9 was co-localized with β -catenin in the nucleus of CRC, translocation of these two proteins from cytoplasm to the nucleus reflected the activation of WNT signaling, the key signaling pathway implicated in colorectal carcinogenesis, and promoted the transcription of downstream target proteins including C-myc/pC-myc, CyclinD1, snail, BCL2 and BAX expressions, but inhibited expression of cytochrome C (Cyt-C), Caspase9, Caspase3, apoptosis-inducing factor (AIF) and endonuclease G (Endo G), indicating that the suppression of caspase dependent and independent apoptosis.

Accompanying with alteration of epithelial mesenchymal transition (EMT) markers, including downregulation of E-cadherin, but increasement of N-cadherin, as well as EMT induced cancer stem cell (CSC) phenotypes including upregulation of CD44, CD133, Lgr5, OCT4 and Nanog.

Conclusion: Upregulation and translocation of SLC26A9 to the nucleus reflected the activation of WNT/ β -catenin signaling pathway, resulted in the development and progression of CRC. SLC26A9 might be a novel candidate oncogene of CRC.

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Disclosure: Nothing to disclose.

P0573

TRIGLYCERIDE GLUCOSE INDEX (TYG INDEX) AND RISK OF COLORECTAL ADENOMATOUS POLYPS

D.S. Kim¹, K.-C. Huh¹, H.S. Koo¹

¹Konyang University College of Medicine, Gastroenterology and Hepatology, Daejeon, Korea (Republic of)

Contact E-Mail Address: hornkim0404@gmail.com

Introduction: Insulin resistance is associated with the risk of colorectal adenomatous polyp. Insulin resistance has been constantly associated with high triglyceride. Triglyceride glucose index (TyG index) is a useful indicator of insulin resistance. We investigated the association of TyG index with the risk of colorectal adenomatous polyps.

Aims & Methods: This study was performed on 163 subjects who underwent colonoscopy at university hospital from March to December 2021. TyG index was calculated as formula: $\ln$ [fasting triglycerides (mg/dL) $\times$ fasting plasma glucose (mg/dL)/2]. Variables were investigated using chi-squared test, t-test and Mann-Whitney U test, as appropriate. Logistic regression model was used to investigate the relationship between the risk of colorectal adenomatous polyp and TyG index.

Results: The mean of fasting glucose, fasting triglyceride, and TyG index were all significantly higher in the group with colorectal adenomatous polyps ($p < 0.01$; $p = 0.012$; $p = 0.002$, respectively). Logistic regression analysis showed that fasting triglyceride (TG) [adjusted odds ratio (OR), 1.005; 95% Confidence interval (CI), 1.001–1.009; $p = 0.028$] and TyG index [adjusted odds ratio (OR), 2.049; 95% Confidence interval (CI), 1.121–3.745; $p = 0.020$] were positively associated with an adenomatous polyp detection. The subjects were divided into four groups according to the quartile of each parameter, and the adjusted odds ratios for the 4th quartile group of fasting TG and TyG index were statistically significant.

		Adjusted OR (95% CI)*	P
Fasting TG (mg/dl)	Q1 (38–70)	1	
	Q2 (71–103)	1.231 (0.415–3.654)	0.707
	Q3 (104–166)	1.358 (0.467–3.951)	0.575
	Q4 (167–548)	3.055 (1.064–8.771)	0.038
TyG index	Q1 (7.37–8.14)	1	
	Q2 (8.15–8.62)	1.810 (0.603–5.430)	0.290
	Q3 (8.63–9.08)	1.777 (0.590–5.358)	0.307
	Q4 (9.09–10.44)	3.465 (1.167–10.287)	0.025

* adjusted for age and sex

Table. The risk for colorectal adenoma by quartiles of parameters of insulin resistance

Conclusion: TyG index may predict the presence of colorectal adenomatous polyps, which is particularly pronounced in the group with a high TyG index. Therefore, screening colonoscopy should be recommended for people with a high TyG index. In addition, further studies are needed to establish an appropriate cut-off value.

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P0574

COLORECTAL CANCER IN PATIENTS WITH SERRATED POLYPOSIS SYNDROME: THE CONTRIBUTION OF THE ADENOMA CARCINOMA PATHWAY

J. Ijspeert¹, D. van Toledo¹, H. Boersma¹, A. Bleijenberg¹, A. Musler², E. Dekker¹, C. van Noesel²

¹Amsterdam University University Centers, Gastroenterology & Hepatology, Amsterdam, Netherlands, ²Amsterdam University University Centers, Pathology, Amsterdam, Netherlands

Contact E-Mail Address: j.e.ijspeert@amc.uva.nl

Introduction: Patients with serrated polyposis syndrome (SPS) have an increased risk to develop colorectal cancer (CRC). Because of the large numbers of serrated polyps (SPs) in these patients, CRC is assumed to arise mainly through the serrated neoplasia pathway rather than the adenoma-carcinoma pathway. SPS patients, however, also harbour significant num-

bers of adenomas, and about half of all CRCs occur in the distal colon, the preferential location of adenomas. This suggests that adenomas may also play a role in CRC development in these patients. We aimed to study the contribution of the adenoma-carcinoma pathway to CRC development in SPS patients.

Aims & Methods: We collected a cohort of SPS patients with CRCs at our expertise center. Data regarding polyps and CRCs were retrieved from endoscopy and pathology reports. All CRCs were immunohistochemically stained for expression of MLH1, BRAF^{V600E} and p53. CRCs were divided into ‘serrated-CRC’ and ‘adenoma-CRC’ based on the presence or absence of BRAF^{V600E} expression. CRC characteristics (location, MLH1 expression) were compared between serrated-CRCs and adenoma-CRCs. The proximal colon was defined as proximal from the descending colon.

Primary outcome measure was the proportion of serrated-CRC vs. adenoma-CRC. Statistical comparison between serrated-CRC and adenoma-CRC was performed with Chi-square statistics for categorical variables and Mann-Whitney U statistics for continuous variables.

Results: A total of 43 CRCs from 35 SPS patients were included in the study. Patients had a median age at time of diagnosis of 63 years (IQR, 59–69) and 68.6% (24/35) were female. Twenty-one (49%) CRCs were serrated-CRCs and 22 (51%) were adenoma-CRCs. Loss of MLH1 expression was observed in 10 (48%) serrated-CRCs and in none of adenoma-CRCs. In total, 17 (81%) serrated-CRCs and 5 (23%) adenoma-CRCs were located in the proximal colon (p<0.001).

	Total	Serrated-CRC	Adenoma-CRC	p-value
Total cohort size; n (%)	43 (100)	21 (49)	22 (51)	
CRC location; n (%)				<0.001
Proximal	22 (51)	17 (81)	5 (23)	
Distal	21 (49)	4 (19)	17 (77)	
Loss of MLH1 expression; n (%)	10 (23)	10 (48)	0	<0.001

Table 1: Colorectal cancer characteristics comparing serrated-CRCs and adenoma-CRCs.

Conclusion: Although SPS patients have an abundance of serrated polyps, still half of their CRCs evolve via the non-serrated pathway, i.e. from conventional adenomas. This finding is important in understanding carcinogenesis in SPS patients and underlines the clinical importance of conventional adenomas in these patients.

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All other authors: none.

P0575

CANCER-ASSOCIATED FIBROBLASTS ARE KEY DETERMINANTS OF TUMOUR PROGRESSION IN THE EARLIEST STAGE OF COLORECTAL CANCER

H. Dang¹, T.J. Harryvan¹, A. Liao², E.H.J. Danen², V.N.L.N. Spalburg¹, S.M. Kielbasa³, H. Mei³, J. Hardwick¹, J.J. Boonstra¹, N.F.C.C. de Miranda⁴, L. Hawinkels¹

¹Leiden University Medical Centre, Department of Gastroenterology and Hepatology, Leiden, Netherlands, ²Leiden Academic Centre of Drug Research, Leiden University, Division of Drug Discovery and Safety, Leiden, Netherlands, ³Leiden University Medical Centre, Department of Biomedical Data Sciences, Leiden, Netherlands, ⁴Leiden University Medical Centre, Department of Pathology, Leiden, Netherlands

Contact E-Mail Address: h.dang@lumc.nl

Introduction: Improving clinical management of early-stage colorectal cancers (T1CRCs) requires a better understanding of their underlying biology. Accumulating evidence shows that cancer-associated fibroblasts (CAFs) are important determinants of tumour biology in advanced colorectal cancer (CRC), but their role in early stages of CRC tumorigenesis is unknown.

Aims & Methods: The aim of our study was to characterize CAFs in T1CRCs (T1CAFs) and to investigate their role in early cancer progression. Primary T1CAFs and patient-matched normal fibroblasts (NFs) were isolated from endoscopic biopsies of histologically confirmed T1CRCs and normal mucosa, respectively. The impact of T1CAFs and NFs on tumour behaviour was studied using 3D co-culture systems with primary T1CRC organoids and extracellular matrix (ECM) remodelling assays. Whole transcriptome sequencing and gene silencing were used to pinpoint mediators of T1CAF functions.

Results: In 3D co-cultures, matrix invasion of T1CRC organoids was induced by T1CAFs, but not by NFs. T1CAFs also exhibited enhanced ECM remodelling capacity as compared to NFs. RNA sequencing of 10 NF-T1CAF pairs revealed 404 differentially expressed genes, with significant enrichment for ECM-related pathways in T1CAFs. Cathepsin H, a cysteine-type protease that was specifically upregulated in T1CAFs but not in tumour fibroblasts from pre-malignant or advanced CRC stages, was identified as a key factor driving matrix remodelling by T1CAFs. Finally, we validated the relative abundance of Cathepsin H-expressing T1CAFs on primary T1CRC tissue sections, highlighting the translational potential of our findings.

Conclusion: Already in early CRC stages, tumour progression is importantly determined by CAFs via direct interactions with tumour cells and stage-specific, Cathepsin H-dependent matrix remodelling.

Disclosure: Nothing to disclose.

P0576

ESTABLISHMENT OF CRISPR-CAS9 RIBONUCLEOPROTEINS AS A GENOME EDITING TOOL FOR ARRAYED PHENOTYPIC SCREENING IN COLORECTAL CANCER

C.P. Schilling¹, K.E. Boonekamp¹, F. Heigwer¹, M. Boutros¹

¹German Cancer Research Center, Division Signaling and Functional Genomics, Heidelberg, Germany

Contact E-Mail Address: cps@schilling-mueller.de

Introduction: Wnt signaling and the p53 signaling pathway play key roles in carcinogenesis of colorectal cancer (CRC). Truncations and inactivating mutations of the APC gene, a negative regulator of Wnt/ β -catenin signaling, as well as mutations in the tumor suppressor gene TP53 can be observed in the majority of CRCs. In CRC, p53 has been shown to induce Wnt3

transcription and thereby activate Wnt/ β -catenin signaling. Thus, we hypothesized that the p53 and the Wnt signaling pathways interact in CRC. To this end, we developed an innovative method to further investigate the crosstalk between these central pathways for cancer initiation, progression, and drug resistance.

Aims & Methods: To gain insight into CRC biology and facilitate further study of this cancer, we established a CRISPR-Cas9 ribonucleoprotein (RNP) based genome editing tool for arrayed phenotypic screening as well as a fluorophore-based reporter system to monitor transcriptional pathway activity.

Utilizing RNPs for genome editing and mutating specific target genes in an arrayed screening approach allows for faster and more precise editing when compared with traditional plasmid-based methods or lentiviral transduction. In addition, there are less off-target effects. We employed single guide RNA (sgRNA) generated by *in vitro* transcription. In our screening approach, we used two different sgRNAs for each target gene to achieve a high editing efficiency while also limiting cellular toxicity caused by DNA cleavage.

As a readout, we developed a fluorophore-based reporter system coupled to DNA transcription factor binding sites of p53 and Transcription Factor 7 Like 2 (TCF7L2), a downstream transcription factor in the Wnt/ β -catenin signaling pathway. Experiments were conducted in HCT116 cells. After cell fixation and staining of nucleus and cell body, we used fluorescence microscopy images for cell segmentation *in silico*. This allowed us to then analyze transcriptional activity in p53 and Wnt/ β -catenin signaling as well as cell morphology on a single cell basis.

Results: We succeeded in establishing an easy-to-scale 384-well CRISPR/Cas9 transfection platform to generate high-efficiency gene knockouts (KO). Depending on the individual sgRNA used, we were able to achieve a genome editing efficiency of 40-60% 48 hours after transfection without the need for cytostatic selection. This is a major advantage in comparison with established plasmid-based editing methods that require cytostatic selection.

As a proof of concept, we were able to show that our specifically designed reporter system has a high sensitivity for changes in transcriptional activity for both pathways using pharmacological treatments with Chiron, a GSK3 inhibitor that activates Wnt/ β -catenin signaling and Nutlin3a, a MDM2 inhibitor that increases p53 signaling. Combining this readout with our high-efficiency KOs, we demonstrated upregulation of Wnt signaling after KO of APC, as well as GSK3. We are currently extending this approach to CRC organoids.

Conclusion: Here we report an innovative arrayed CRISPR-Cas9 RNP screening method and its application in CRC that allows to investigate p53 and Wnt/ β -catenin signaling activity. This approach is easily scalable to any other cancer gene or signaling pathway of interest. Our method is particularly valuable for screening for pathway activation/deactivation after gene KO in CRC. Furthermore, it can be applied for genetic interaction screening and drug sensitivity screening.

Disclosure: Nothing to disclose.

P0577

INCREMENTAL YIELD OF ARTIFICIAL INTELLIGENCE IN A FECAL OCCULT BLOOD TEST BASED ORGANIZED SCREENING POPULATION PROGRAM

E.V. Pesatori^{1,2}, S.M. Milluzzo^{1,2}, P. Cesaro¹, S. Piccirelli^{1,2}, F. Catino¹, A. Quadarella^{1,2}, N. Olivari¹, L. Minelli Grazioli¹, M. Codazzi¹, A. Bizzotto¹, C. Hassan³, C. Spada^{1,2}

¹Fondazione Poliambulanza Istituto Ospedaliero, Brescia, Italy,

²Policlinico Universitario A.Gemelli IRCCS, Rome, Italy, ³IRCCS Humanitas Research Hospital, Rozzano, Italy

Contact E-Mail Address: eugenaviattori.pesatori01@universitadipavia.it

Introduction: Fecal Occult Blood Test (FOBT) is the first line test in organized Colorectal Cancer screening settings in several countries. Adenoma miss rate is still a concerning issue during colonoscopy, related to an increased risk of interval colorectal cancer. Artificial Intelligence (AI) is a technology potentially able to improve diagnostic performance of colonoscopy and to reduce inter- and intra-operator variability.

Aims & Methods: The aim of this study was to compare the diagnostic yield of AI-assisted colonoscopy with that of standard colonoscopy (SC). This is a single-center RCT evaluating consecutive patients undergoing colonoscopy in a FOBT based organized screening population program. Patients were randomly assigned to SC or AI. Subjects with < 6 score at Boston Bowel Preparation Scale were excluded from analysis.

Polyp Detection Rate (PDR), Adenoma Detection Rate (ADR), Serrated Detection Rate (SDR), patients with advanced adenomas (i.e. villous histology, high-grade dysplasia or low-grade dysplasia > 1cm) and patients with at least 3 precancerous lesions were compared between the groups using χ^2 -test. At two-tailed test, $P < 0.05$ was considered statistically significant.

Results: Data about 464 patients were collected, of whom 231 were assigned to AI, while 233 to SC arm. Due to inadequate bowel cleansing, 22 patients (10 AI and 12 SC group) were excluded. PDR and ADR were both significantly higher in the AI group compared to SC group (respectively 81.9% [181/221] vs 71.5% [158/221]; $p = 0.01$ and 69.2% [153/221] vs 60.2% [133/221]; $p = 0.04$).

Patients with advanced adenomas and with at least 3 precancerous lesions were increased in the AI group (respectively 25.3% [56/221] vs 24.4% [54/221]; $p = 0.82$ and 30.8% [68/221] vs 22.6% [50/221]; $p = 0.05$). SDR was slightly increased in the SC arm (14.9% [33/221] vs 16.2% [36/221]; $p = 0.69$).

	AI	SC	p-value
ADR	81.9% [181/221]	71.5% [158/221]	0.01
PDR	69.2% [153/221]	60.2% [133/221]	0.04
SDR	14.9% [33/221]	16.2% [36/221]	0.69
ADVANCED ADENOMAS	25.3% [56/221]	24.4% [54/221]	0.82
≥ 3 ADENOMAS	30.8% [68/221]	22.6% [50/221]	0.05

Conclusion: AI improves ADR and PDR in a screening FOBT based setting. The impact of a AI supported colonoscopy in surveillance intervals needs to be further evaluated.

Disclosure: Nothing to disclose.

P0578

PREDICTION OF LYMPH NODE METASTASIS IN T1 COLORECTAL CANCER BY ARTIFICIAL INTELLIGENCE USING HISTOLOGIC WHOLE-SLIDE IMAGES

Y. Takashina¹, S. Kudo¹, Y. Kouyama¹, H. Miyachi¹, K. Ichimasa^{2,1}, K. Mochizuki¹, Y. Ogawa¹, Y. Maeda¹, Y. Mori³, T. Kudo¹, Y. Takehara¹, S. Mukai¹, T. Hayashi¹, K. Wakamura¹, Y. Enami¹, N. Sawada¹, T. Nemoto¹, T. Baba¹, F. Ishida¹, M. Misawa¹

¹Showa University Northern Yokohama Hospital, Digestive Disease Center, Yokohama, Japan, ²National University Hospital, Department of Gastroenterology and Hepatology, Singapore, ³University of Oslo / Showa University, Clinical Effectiveness Research Group / Digestive Disease Center, Oslo, Norway

Contact E-Mail Address: y_takashina2011@yahoo.co.jp

Introduction: The risk of lymph node metastasis in T1 colorectal cancer is known to be about 10%, and preoperative prediction is essential for determining a treatment strategy. Several histopathological values and scoring systems for predicting lymph node metastasis have been reported. However, interobserver variability for histologic diagnosis remains a major problem. Therefore, we developed a novel artificial intelligence (AI) system using whole-slide images (WSI) to predict lymph node metastasis in T1 colorectal cancer.

Aims & Methods: A retrospective single-center study was conducted analyzing 714 colorectal lesions resected from April 2001 to August 2021. Hematoxylin and eosin stained, formalin fixed, all slide images scanned by NanoZoomer (Hamamatsu Photonics, Japan) were collected for analysis. 614 of these slides were used for training the AI system and 100 (T1 cancer) for validation, which were consecutive cases from January 2019. A deep convolutional neural network was used, and in addition to the slide images, the gender and age of the patient and the tumor location were added as factors. Surgical specimens were used as the gold standard for the presence of lymph node metastases, and the area under the receiver operating characteristic curve (AUC) was calculated for the AI system's performance in identifying patients with lymph node metastases.

Results: A total of 714 colorectal lesions (adenoma: 150 lesions, lymph node positive T1: 60 lesions, lymph node negative T1: 124 lesions, lymph node positive T2: 140 lesions, lymph node negative T2: 140 lesions) were included for study. Of the lesions excluding adenomas, 242 were male and 48 had lesions located in the rectum. The median age was 65.4±11.6 years, and the median number of lymph nodes removed was 18.7±12.5. A total of 100 T1 colorectal cancers were used for validation, and the percentage of lymph node metastases was 15%. The AUCs for the AI system and guidelines in the test cases were 0.68 (95% confidence interval, 0.53-0.88) and 0.52 (95% confidence interval, 0.50 - 0.55), respectively. With a sensitivity of 100%, the specificity was 21.2%.

Conclusion: It is suggested that a lymph node metastasis prediction system based on AI analysis using WSI may contribute to the decision for additional surgical resection after endoscopic treatment of T1 colorectal cancer.

Disclosure: Nothing to disclose.

P0579

DETECTING COLORECTAL ADENOMAS AND CANCER VIA VOLATILE ORGANIC COMPOUNDS IN EXHALED BREATH, A PROOF OF PRINCIPLE STUDY TO IMPROVE SCREENING

H.R. Cheng^{1,2,3}, R.W.R. van Vorstenbosch^{4,5}, D.M. Pachén^{4,5}, L.W.T. Meulen^{1,3}, J.W.A. Straathof^{1,2}, J.W. Dallinga^{4,5}, D.M.A.E. Jonkers^{1,5}, A.A. Masclee^{1,5}, F. van Schooten^{4,5}, Z. Mujagic^{1,5}, A. Smolińska^{4,5}

¹Maastricht University Medical Center+, Division of Gastroenterology-Hepatology, Department of Internal Medicine, Maastricht, Netherlands, ²Máxima Medical Center, Department of Gastroenterology and Hepatology, Veldhoven, Netherlands, ³Maastricht University, GROW, School for Oncology and Reproduction, Maastricht, Netherlands, ⁴Maastricht University, Department of Pharmacology and Toxicology, Faculty of Health, Medicine and Life Sciences, Maastricht, Netherlands, ⁵Maastricht University, NUTRIM, School of Nutrition & Translational Research in Metabolism, Maastricht, Netherlands

Contact E-Mail Address: haorancheng@gmail.com

Introduction: Colorectal cancer (CRC) is the third most common cancer worldwide and poses an important healthcare issue with significant morbidity, mortality, and economic impact.¹

CRC can be prevented if precursor lesions are identified and removed endoscopically.² National bowel cancer screening programs have been implemented which significantly reduced CRC related morbidity and mortality.³

These programs often use the fecal immunochemical test (FIT) and when tested positive subsequent colonoscopy. However, FIT suffers from a high number of false positives resulting in many unnecessary colonoscopies (*i.e.* no colorectal neoplasia detected) and is insensitive for detecting clinically relevant advanced adenomas (AA).⁴

Therefore, more accurate, non-invasive screening tools are needed.

Aims & Methods: In this multicenter prospective study, the utility of analyzing volatile organic compounds (VOC) in exhaled breath in a FIT positive population to detect the presence of colorectal neoplasia was studied. Breath samples were collected from FIT positive patients with subsequent colonoscopy participating in the national Dutch bowel screening program. Breath sampling was performed prior to colonoscopy.

One room was assigned for breath collection in each study center. Subjects were asked to inflate a 3 L Tedlar bag and its contents were transferred onto carbon-filled stainless-steel desorption tubes. Exhaled VOCs were analyzed using Thermal Desorption - Gas Chromatography - Mass Spectrometry (TD-GC-MS) and the data was pre-processed and analyzed using machine-learning techniques. Three predictive models were created: CRC vs. controls, AA vs. controls, and non-AA vs. AA vs. controls.

Results: 382 FIT positive subjects (n=84 negative controls, n=130 non-AA, n=138 AA, and n=30 CRC) with breath, colonoscopy, and histopathology data were included between July 2016 and January 2018. Using ten discriminatory VOCs AA could be distinguished from negative controls with a sensitivity and specificity of 79% and 70%, respectively.

The discrimination of CRC from negative controls yielded a sensitivity and specificity of 67% and 70%, respectively. CRC sample size was insufficient for biomarker selection. Using the five most important VOCs from the AA vs. controls model, CRC and CRC/AA combined could be discriminated from controls with sensitivities of 80% and 70%, respectively, and a specificity of 70% (see Table 1). Lastly, the feasibility to discriminate non-AA from controls as well as AA was assessed (data not shown).

Group	Sensitivity	Specificity	AUC	Biomarkers
CRC vs. controls	67%	70%	0.73	N/A
AA vs. controls	79%	70%	0.79	10 VOCs
- CRC vs. controls	80%	70%	0.76	5 VOCs*
- CRC and AA vs. controls	77%	70%	0.75	5 VOCs*

* Five most important VOCs from AA vs. controls model.

Table 1: sensitivity, specificity, and AUC ROC of analyzed groups.

CRC: colorectal cancer, AA: advanced adenoma, AUC: area under the curve, VOC: volatile organic compound

Conclusion: In this proof of principle study, VOCs in exhaled breath can detect the presence of CRC and AA in a CRC screening population. Breath based analysis could be used in combination with FIT or as a standalone screening test and may improve CRC screening in the future.

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Disclosure: Agnieszka Smolińska is assistant professor at Maastricht University and is an advisor at Owlstone Medical (Cambridge, UK), a breath-based medical company aiming for the non-invasive detection of diseases. The remaining authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

P0580

LOWER HEALTHCARE COSTS ASSOCIATED WITH COLORECTAL CANCER TREATMENT FOLLOWING SCREEN DETECTION

J. Dressler¹, L. Sopina², M. Rasmussen¹, L. Nannestad Jørgensen¹

¹Bispebjerg Hospital, Digestive Disease Center, København NV, Denmark, ²University of Southern Denmark, Danish Center for Health Economics, Odense, Denmark

Contact E-Mail Address: jannie.dressler@regionh.dk

Introduction: Colorectal cancer (CRC) is the 3rd most common type of malignancy. With an approximate 1 million deaths in 2020, CRC is a major burden for public health care systems.⁽¹⁾ In 2014 a national colorectal cancer screening (CRCS) program was implemented in Denmark. Although the implementation and operation of a CRCS program is costly, little is known about its potential financial benefits.

Aims & Methods: This retrospective cohort study based on national databases aimed to evaluate the differences in total healthcare costs between patients with screen-detected colorectal cancer (SD-CRC) and non-screen-detected colorectal cancer (NSD-CRC). The SD-CRC group was defined as patients receiving a CRC diagnosis within 6 months of participating in

CRCS from 2014 to 2018. The NSD-CRC group included patients receiving a CRC diagnosis after non-participation in the CRCS or not attending the follow-up colonoscopy after a positive screening test. All patients with post-colonoscopy- and interval cancers were excluded to avoid length bias. For each group mean quarterly costs were calculated from two years before until two years after the date of diagnosis. Hereafter, we estimated the differences in healthcare costs, using a quasi-experimental difference-in-difference analysis.

Results: Healthcare costs were primarily driven by hospital costs. During the two years before receiving their diagnosis, the mean healthcare costs for the SD-CRC and the NSD-CRC groups were not statistically different. In the two years following the CRC diagnosis, the mean healthcare costs in each quarter were significantly higher in the NSD-CRC group.

Conclusion: This study suggests that NSD-CRC is more costly to treat and surveille than SD-CRC. Funds should be redirected to improve recruitment to CRCS – thus enhancing treatment and prognosis for patients with CRC.

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P0581

QUALITY OF ENDOSCOPIC SCREENING FOR COLORECTAL CANCER IN ITALY: A NATIONAL SURVEY

M.F. Maida¹, B. Annibale², A. Benedetti³, P. Burra⁴, L. Frulloni⁵, G. Ianaro^{6,7}, F. Luzzza⁸, A. Repici⁹, E. Savarino¹⁰, E. Sinagra¹¹, M. Vecchi¹², L. Ricciardiello¹³, Italian Society of Gastroenterology (SIGE)

¹S. Elia-Raimondi Hospital, Caltanissetta, Gastroenterology and Endoscopy Unit, Caltanissetta, Italy, ²Digestive Disease Unit, Sant'Andrea University Hospital, ENETS Center of Excellence, Roma, Italy, ³Università Politecnica delle Marche, Department of Gastroenterology and Hepatology, Ancona, Italy, ⁴Multivisceral Transplant Unit, Department of Surgery, Oncology and Gastroenterology, Padova, Italy, ⁵University of Verona, Department of Medicine, Gastroenterology Unit, Pancreas Center, Verona, Italy, ⁶Fondazione Policlinico Universitario Agostino Gemelli IRCCS, Digestive Disease Center, Roma, Italy, ⁷Università Cattolica del Sacro Cuore, Department of Translational Medicine and Surgery, Roma, Italy, ⁸University Magna Graecia, Department of Health Sciences, Catanzaro, Italy, ⁹Humanitas Research Hospital, Humanitas University, Digestive Endoscopy Unit, Division of Gastroenterology, Rozzano, Italy, ¹⁰University of Padua, Department of Surgery, Oncology and Gastroenterology - DiSCOG, Padova, Italy, ¹¹Fondazione Istituto San Raffaele Giglio, Gastroenterology and Endoscopy Unit, Cefalù, Italy, ¹²Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico, Department of Internal Medicine Gastroenterology and Endoscopy Unit, Milano, Italy, ¹³S. Orsola-Malpighi Hospital, Gastroenterology Unit, Department of Medical and Surgical Sciences, Bologna, Italy

Contact E-Mail Address: marcello.maida@hotmail.it

Introduction: Colorectal cancer (CRC) is a major healthcare problem all over the world and screening is effective in reducing mortality and increasing survival.

Since colonoscopy has a central role in faecal immunochemical test (FIT)-based CRC screening and surveillance, consistent quality measures are es-

sential to ensure quality and outcomes. Nevertheless, screening modalities in clinical practice may differ according to the centers experience and the local availability of instrumentation and devices.

Aims & Methods: To assess the quality of endoscopic screening for CRC and adherence to international guidelines across Gastroenterology Departments in Italy.

All members of the Italian Society of Gastroenterology (SIGE) were invited to answer a web-based survey.

Results: Data from 64 hospitals from 17 Italian regions were analyzed. Overall, 32/64 (50.0%) were from northern, 12/64 (18.75%) from central and 20/64 (31.25%) from southern Italy. Half of the centers (57.8%) were non-academic public hospitals, while the others were academic (29.7%) or private hospitals (12.5%).

Surveyed centers perform a median of 4600 (IQR 2500-7750) endoscopic examinations per year and a median of 600 (IQR 300-1000) screening colonoscopies per year.

Each center is equipped with a median of 5.0 (IQR 3.5-7.0) endoscopists involved in CRC screening, 71.4% of which are gastroenterologists.

After a positive FIT, most centers (93.8%) schedule a colonoscopy within 3 months. High-definition video endoscopy is routinely performed in 68.8% and chromoendoscopy in 53.1% of centers. Withdrawal time is ≥ 6 minutes in 79.9% and cecal intubation rate is $\geq 90\%$ in 94.4% of departments.

Moreover, in 92.7% of centers adenoma detection rate (ADR) overcome the minimum standard of 25%. Analyzing the data by regional areas, a significant higher number of median endoscopic examinations/year (6500 vs 4000 and 3000 respectively, $p=0.024$) and of endoscopists per center (6.5 vs 5.0 and 3.5 respectively, $p<0.001$) has been registered in the northern compared to central-southern centers.

Finally, in most of the surveyed centers (62.5%), a program aimed at training young endoscopists to perform quality screening for CRC is absent.

Conclusion: Data from this survey show adequacy and good quality of endoscopic screening for CRC in Italy, highlighting, at the same time, relevant deficiencies and a discrepancy in procedural attitudes between the different centers.

These findings call for urgent action to overcome the shortcomings, refine and homogenize the behaviour of all screening centers in the national territory and improve the outcomes.

Disclosure: Nothing to disclose.

P0582

CHANGE IN COLONOSCOPY RECEIVING RATE FOR POSITIVE FECAL IMMUNOCHEMICAL TEST AND A DELAY OF COLORECTAL CANCER DETECTION UNDER THE COVID-19 PANDEMIC

F. Ishibashi¹, S. Suzuki¹, D. Shida², M. Nagai¹, K. Mochida¹, T. Morishita¹

¹International University of Health and Welfare Ichikawa Hospital, Department of Gastroenterology, Chiba, Japan, ²Institute of Medical Science, University of Tokyo, Division of Frontier Surgery, Tokyo, Japan

Contact E-Mail Address: f.jazzmaster@gmail.com

Introduction: There is concern that the COVID-19 pandemic may cause people to refrain from undergoing examination resulting in delayed detection of colorectal cancer (CRC).

Aims & Methods: The purpose of this study was to investigate whether there was a delay in CRC detection due to withholding of screening. As a longitudinal cohort study, we selected cases who underwent fecal immunochemical test (FIT) (twofold method) as a cancer screening program supported by Tama District administration in Japan every year from 2019 to 2021.

Among recipients of initial screening by FIT, changes over time in the receiving rate of colonoscopy under scrutiny for positive FIT recipients and the detection rate of CRC. Furthermore, the stages of CRC cases detected as a result of positive FIT in each year were compared.

Results: A total of 30,172 patients were initially screened by FIT over a 3-year period. The number (rate) of FIT positives was 420 (4.6%) in 2019, 453 (4.9%) in 2020, and 504 (4.3%) in 2021, with no difference, but the number (rate) of colonoscopy secondary scrutiny visits was 160 (38.1%) in 2019, 117 (25.8%) in 2020, and 286 (56.7%) in 2021 with a decrease in 2020 and an increase in 2021. The number (rate) of CRC detected among colonoscopy recipients was 7 (4.4%) in 2019, 6 (5.1%) in 2020, and 23 (8.0%) in 2021. The advanced adenoma detection rate increased from 11.1% in 2020 to 15.7% in 2021. Stage 1 or higher accounted for 42.9% (3/7) of CRCs detected in 2019, 50.0% (3/6) in 2020, and 69.6% (16/23) in 2021. Among the CRC cases detected each year, 1 (14.3%), 1 (16.7%), and 10 (43.5%) did not undergo colonoscopy despite positive FIT results in the previous year.

Year	2019	2020	2021
Patients who received FITs	9,156	9,255	11,760
Patients with positive FITs (%)	420 (4.6%)	453 (4.9%)	504 (4.3%)
Patients who underwent colonoscopy (%)	160 (38.1%)	117 (25.8%)	286 (56.7%)
Colorectal cancers detected (%)	7 (4.4%)	6 (5.1%)	23 (8.0%)
Stage 0	4	3	7
Stage 1,2	2	2	10
Stage 3,4	1	1	6
Advanced adenomas detected (%)	21 (13.1%)	13 (11.1%)	45 (15.7%)

Conclusion: In 2020 under COVID-19 pandemic, the colonoscopy receiving rate for FIT-positive recipients decreased, but in 2021, the colonoscopy receiving rate and the number of CRC found increased perhaps with the lifting of behavioral restrictions by COVID-19 pandemic. Many of the CRC cases detected in 2021 were stage 1 or higher, suggesting a delay in diagnosis due to the previous year's refraining from examinations. One of the challenges of FIT-based CRC screening is that under conditions such as the COVID-19 pandemic, behavioral changes in recipients are likely to result in changes in the inspection rate, even if the receiving rate of primary screening by FIT remains unchanged. As a result, the accuracy of the cancer screening may decline.

Disclosure: Nothing to disclose.

P0583

ROUTINE IMMUNOHISTOCHEMICAL ANALYSIS OF MISMATCH REPAIR PROTEINS IN COLORECTAL CANCER - A PROSPECTIVE ANALYSIS

J. Lemos Garcia¹, I. Rosa², S. Saraiva¹, I. Marques¹, R. Fonseca³, P. Lage², I. Claro²

¹Instituto Português de Oncologia de Lisboa Francisco Gentil, Gastroenterology, Lisboa, Portugal, ²Instituto Português de Oncologia de Lisboa Francisco Gentil, Gastroenterology, Familiar Cancer Clinic, Lisboa, Portugal, ³Instituto Português de Oncologia de Lisboa Francisco Gentil, Pathology, Lisbon, Portugal

Contact E-Mail Address: joanalemosgarcia@gmail.com

Introduction: Colorectal cancer (CRC) is the third most common cancer type. Recognition of an hereditary CRC syndrome is of paramount importance and Lynch Syndrome (LS) is the most frequent. The diagnosis can be suspected by using the Amsterdam criteria (AC) and the revised Bethesda guidelines (BC), but both lack sensitivity and specificity. International guidelines recommend universal tumour screening for mismatch repair proteins (MMR) deficiency.

Aims & Methods: The goal of this study was to confirm the importance of routine immunohistochemistry (IHC) screening in CRC patients.

An unicentric cohort study was conducted in a central Oncological Hospital, which integrates a Familiar Risk Clinic. All patients under 70 years-old admitted due to CRC during 07/2017-06/2019 were included.

Data collected included demographic information, tumour characteristics, relevant family history, MMR protein status, genetic diagnosis when available and outcome.

Results: 292 patients were included; 56.0% males; median age 61.0 (IQR 54.0-65.0); stage IV CRC 5.8%; located in the right colon 21.8%, left 28.0% and rectum 50.2% (synchronous CRC in 5 patients). Histological analysis revealed high grade (G3) adenocarcinoma in n=23 (8.4%); mucinous and/or signet ring differentiation n=31 (11.3%); lymphocyte infiltrate n=82 (29.8%). AC and BC were fulfilled in n=11 and n=74 patients, respectively (simultaneously in 6). IHC revealed loss of expression of MMR in n=24 (8.7%) – MLH1 and PMS2 n=15; PMS2 n=4; MSH2 and MSH6 n=1; MSH2 n=1; MSH6 n=2; MLH1, PMS2 and MSH6 n=1. Among these, 0 patients fulfilled AC and 13 fulfilled BC. BRAF mutation was found in n=3 and MLH1 promoter hypermethylation in n=3.

Overall, genetic diagnosis was performed in 51 patients, LS was diagnosed in 3, in whom only BC were present in n=2, which means that one patient would not have been investigated without routine IHC screening. 2 patients had MSH2 and MSH6 mutations with uncertain pathogenicity. 2 patients have their genetic study results pending.

Conclusion: These results strengthen the important role of universal IHC screening for MMR proteins loss of expression in CRC.

Disclosure: Nothing to disclose

P0584

FIRST CLINICAL EXPERIENCES OF THE NON-COMMERCIAL, PUBLICLY AVAILABLE POLYP DETECTION SYSTEM ENDOMIND

T. Lux¹, M. Banck^{1,2}, Z. Saßmannshausen¹, J. Troya¹, A. Krenzer^{2,1}, D. Fitting¹, B. Sudarevic¹, W. Zoller³, F. Puppe², A. Meining¹, A. Hann¹

¹University Hospital Wuerzburg, Internal Medicine II, Interventional and Experimental Endoscopy (InExEn), Wuerzburg, Germany,

²Julius-Maximilians-Universität Wuerzburg, Institute for Computer Science, Artificial Intelligence and Knowledge Systems, Würzburg, Germany, ³Katharinenhospital, Department of Internal Medicine and Gastroenterology, Stuttgart, Germany

Contact E-Mail Address: a.hann@posteo.de

Introduction: The ability of artificial intelligence to recognize specific pattern lead to a wide area of applications in the medical field. In colonoscopy, it is used to detect polyps. Resection of adenomatous polyps correlates with the decrease of colorectal cancer risk.

In various randomized controlled studies, computer-aided polyp detection systems (CADE) increased the adenoma detection rate. Anyhow, most studies are limited by being monocentric and the systems work solely on one processor type. Furthermore, most systems are purely focused on detection.

Aims & Methods: We developed the for research purpose publicly available CADE system EndoMind. Besides its ability of real time polyp detection, it offers the opportunity of end-to-end data acquisition. We aim to evaluate the practical value of EndoMind in a prospective multicenter study in three outpatient practices and one community based hospital in Germany.

To specify the performance of EndoMind, colonoscopies were analyzed regarding diagnosed polyps, adenoma detection rate (ADR) and time to first detection of a polyp.

A questionnaire containing the System Usability Scale was used to examine the usability of EndoMind.

Results: Overall 41 colonoscopies were performed in 4 study centers with 4 different endoscopy processor types. EndoMind detected 66 of 66 polyps and 29 of 29 adenomas with a median time to first detection of 130 ms (95%-CI, 80 – 200 ms). EndoMind maintained a median false positive rate of 2.2 % (95%-CI, 1.7 - 2.8 %), while the ADR for these examinations was 41.5%. EndoMind reached a median System Usability Score of 96.3 (95%-CI, 70 - 100), which ranges above average.

Conclusion: EndoMind proved its practical value in clinical practice and for research with its high usability, sensitive real time predictions and ability of data acquisition. A prospective randomized multicenter study has to determine the clinical benefit of EndoMind regarding ADR.

Disclosure: The authors declare no conflicts of interest.

P0585

DIFFERENCES IN ERYTHROCYTE AND SERUM MEMBRANE FATTY ACID LEVELS IN PATIENTS WITH COLORECTAL CANCER OF DIFFERENT LOCATIONS, WITH A FOCUS ON EARLY CANCER

M.V. Kruchinina^{1,2}, A.A. Gromov¹, M.V. Shashkov³, A.S. Sokolova⁴, I.N. Yakovina⁵, A.A. Shestov⁶

¹Research Institute of Internal and Preventive Medicine - Branch of the Institute of Cytology&Genetics, Siberian Branch of the Russian Academy of Sciences, Novosibirsk, Russian Federation,

²Novosibirsk State Medical University, Novosibirsk, Russian Federation, ³Boriskov Institute of Catalysis, Siberian Branch of the Russian Academy of Sciences, Novosibirsk, Russian Federation,

⁴Vorozhtsov Institute of Organic Chemistry, Siberian Branch of the Russian Academy of Sciences, Novosibirsk, Russian Federation,

⁵Novosibirsk State Technical University, Novosibirsk, Russian Federation,

⁶University of Pennsylvania, Perelman School of Medicine, Philadelphia, United States

Contact E-Mail Address: kruchmargo@yandex.ru

Introduction: Colorectal cancer (CRC) is a very heterogeneous disease, with special features due to the different location of the tumour. It has been suggested that the risk of colorectal cancer differs for tumours located in the proximal and distal segments, due to the different influence of environmental and genetic factors [1].

There is conflicting information about the effect of fatty acids (FAs) on the risk of developing CRC in different locations, and about FAs' levels associated with tumour localisation in different segments of the colon [2-4].

Aims & Methods: The purpose of the research: To study the characteristics of erythrocyte membrane FAs' composition in patients with different tumour localisation in CRC, including the early stages of the disease.

Materials and methods: Using a gas chromatography-mass spectrometric system (GC/MS) based on three Agilent 7000B quadrupoles (USA), the composition of the FAs' membranes of erythrocytes (Er) of 129 patients with CRC has been studied: (average age 63.2±9.4 years, 68 of them men and 61 women; 25 – with proximal, 98 – with distal localisation of the tumour) and 35 people of the comparison group.

According to the TNM classification, 65 patients have been diagnosed with stages I-II of the disease, 64 have been found to have advanced stages of colorectal cancer - III-IV.

Results: There was a greater degree of reduction in levels of saturated, monounsaturated fatty acids (SFAs, MUFAs) ($p=0.015-0.0001$), and, in contrast, an increase in polyunsaturated fatty acid (PUFAs) levels ($p=0.002-0.00001$) in patients with distal tumour localisation compared to healthy controls than the same ratio in the proximal CRC tumour – healthy controls pair ($p=0.034-0.002$).

There was a greater degree of increase in omega-3 PUFAs than omega-6, which was reflected in the n-6/n-3 ratio, which was significantly lower in cancer patients, more so in distal tumour localisation ($OR=0.589$, $p=0.004$). The most relevant for distinguishing between tumours localised in different parts of the colon were as follows: saturated fatty acids - myristic C14:0 ($p<0.001$) and pentadecanoic C15:0 ($p=0.012$), α -linolenic acid n-3 (C18:3 n-3) ($p=0.02$), whose levels were significantly higher and, in contrast, most omega-6 PUFAs (C18:2 n-6, C20:3 n-6, C20:4 n-6) and one omega-3 PUFA, C22:6 n-3 ($p<0.05$), whose levels were significantly lower in the proximal than in the distal tumour.

A study of the associations between FAs' levels and tumour localisation in early-stage CRC identified the biomarkers most relevant for distinguishing between proximal and distal tumours (Volcano plot method): serum FAs - C18:3 n-3 (FC 0.659, $\log_2$ (FC) -0.602, $p=0.02$), C22:6 n-3 (FC 0.749, $\log_2$ (FC) -0.46, $p=0.03$), erythrocyte membrane FAs - C18:3 n-3 (FC 0.36, $\log_2$ (FC) -1.44, $p=0.00007$), C15:0 (FC 0.64, $\log_2$ (FC) -0.64, $p=0.02$), C14:0 (FC 0.71, $\log_2$ (FC) -0.48, $p=0.05$), C20:2 n-6 (FC 0.76, $\log_2$ (FC) -0.39, $p=0.05$).

Conclusion: The results obtained indicate the importance of taking into account the localization of the tumor in patients with CRC when conducting studies of metabolic profiles. The revealed differences in FAs' levels in the early stages of CRC of different localisations may be useful for the development of new diagnostic markers of this disease.

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Disclosure: Nothing to disclose.

P0586

A PROSPECTIVE STUDY OF REAL-TIME USE OF COMPUTER-AIDED CHARACTERIZATION FOR COLORECTAL LESIONS

M. Misawa¹, S. Kudo¹, Y. Miyata¹, Y. Minegishi¹, Y. Mori^{2,1}, Y. Maeda¹, H. Nakamura¹, T. Kudo¹, T. Hisayuki¹, T. Hayashi¹, K. Wakamura¹, H. Miyachi¹, T. Baba¹, F. Ishida¹

¹Showa University Northern Yokohama Hospital, Digestive Disease Center, Yokohama, Japan, ²University of Oslo / Showa University, Clinical Effectiveness Research Group / Digestive Disease Center, Oslo, Norway

Contact E-Mail Address: misawaanny@gmail.com

Introduction: Computer-aided characterization (CADx) may be used to implement optical biopsy strategies into colonoscopy practice; however, the impact of CADx on endoscopic diagnosis remains unknown.

Aims & Methods: We aimed to evaluate the comprehensive performance of endoscopists using CADx for the assessment of colorectal polyps. This was a single-center, prospective study conducted between July 2021 and September 2021. We developed CADx for narrow-band imaging colonoscopy (NBI-CAD) with three potential pathological predictions: adenoma, sessile serrated lesion (SSL), and hyperplastic polyp.

We enrolled patients who underwent colonoscopy using real-time NBI-CAD, and participating endoscopists then predicted the pathology of the polyps considering the NBI-CAD output.

The primary outcome was the diagnostic sensitivity for diminutive (≤ 5 mm) neoplasms with high confidence predictions, based on pathology as the gold standard.

In this study, SSLs were treated as neoplasms and the latest WHO criteria was used for pathological diagnosis. The surveillance interval agreement between the endoscopist's diagnosis and pathology-based interval and the negative predictive value (NPV) for rectosigmoid neoplasms were also calculated.

Results: A total of 397 patients were enrolled and 395 diminutive polyps from 181 eligible patients were analyzed, including 259 adenomas (65.6%) and 25 SSLs (6.3%). The high-confidence diagnosis rate was 92.7% (366/395). The sensitivity for diminutive neoplasms diagnosed with high confidence was 95.8% (95% confidence interval [CI]: 92.7%–97.9%). The surveillance interval agreement with American guidelines was 90.1% (84.7%–94.0%) and the NPV for rectosigmoid neoplasms diagnosed with high confidence was 94.1% (83.8%–98.8%).

Conclusion: In conclusion, we developed a CADx for colorectal polyps and prospectively evaluated its performance in a real-world setting. The developed CADx showed diagnostic competence that allowed the implementation of optical biopsy strategies into clinical practice.

Disclosure: Shin-ei Kudo, Masashi Misawa, and Yuichi Mori received speaking honoraria from Olympus Corporation and have an ownership interest in the products of Cybernet Systems.

P0587

APPLICATION OF MODULAR MULTI-SENSOR VOC ANALYSER FOR NON-INVASIVE DETECTION OF COLORECTAL CANCER

L. Anarkulova^{1,2,3}, I. Polaka¹, J. Gloeckler⁴, L. Mezmale^{1,5,6}, A.M. Lescinska^{1,5,6}, A. Pcolkins^{1,5,6}, B. Mizaikoff⁷, J. Mitrovics⁷, G. Shani⁸, H. Haick⁸, M. Leja^{1,5,6,9}

¹Institute of Clinical and Preventive Medicine, University of Latvia, Riga, Latvia, ²Liepaja Regional Hospital, Liepaja, Latvia, ³Faculty of Residency, Riga Stradins University, Riga, Latvia, ⁴Institute of Analytical and Bioanalytical Chemistry, University of Ulm, Ulm, Germany, ⁵Riga East University Hospital, Riga, Latvia, ⁶Faculty of Medicine, University of Latvia, Riga, Latvia, ⁷JLM Innovation GmbH, Tuebingen, Germany, ⁸Technion - Israel Institute of Technology, Haifa, Israel, ⁹Digestive Diseases Center GASTRO, Riga, Latvia

Contact E-Mail Address: linda.anarkulova@gmail.com

Introduction: The incidence of colorectal cancer (CRC) is increasing worldwide and is one of the main causes of cancer-related deaths. The mortality rate of CRC is high when it is detected in advanced stages, which requires effective screening methods to detect it early. Although there are screening modalities for CRC, there is still room for improvement. The analysis of exhaled breath by sensors that detect volatile organic compounds (VOCs) is a unique and progressive method of detecting CRC and could become a promising screening method.

Aims & Methods: The aim of the study was to evaluate the ability of a modular multi-sensor VOC analyser to distinguish between the breaths of CRC patients and healthy individuals' breaths.

Altogether 53 patients were enrolled in the study: 23 patients with CRC (histologically confirmed CRC) and 30 healthy individuals (histologically without CRC). Their breath was measured with a modular multi-sensor VOC analyser. The device included 48 repeated gold nanoparticle sensors (GNP) for improved robustness (6 sets of 8 different sensors), 11 analogue metal oxide sensors (MOX), and 12 digital MOX sensors. The signal of

each sensor was normalized against sensors response to ambient air and smoothed to remove noise using moving median approach. The sensor responses were analysed using the mean signal at the end of the measurement after the sensor readings were stabilized. These values were used to build a decision tree classifier, evaluation was carried out using leave-one-out approach.

Results: The classification model that was built on sensor data showed 79.25% overall accuracy. The sensitivity (correctly recognized cancer cases) was 69.6% and specificity (correctly recognized control cases) was 86.7%.

Conclusion: The results demonstrate that the proposed approach (device and machine learning model) is promising and could effectively distinguish CRC specific breath from controls. The study will be continued to build and evaluate more specific detection models in larger patient groups.

Disclosure: Nothing to disclose.

P0588

BOWEL LAVAGE FLUID: CHARACTERIZATION AND MRNA ARRAY OF EXTRACELLULAR VESICLES IN COLORECTAL CANCER PATIENTS

M. Alorda-Clara¹, M.G. Trelles-Guzman², J. Sastre-Serra^{1,3}, J. Oliver^{1,3}, D.G. Pons¹, P. Roca^{1,3}, J. Reyes^{1,2}

¹Grupo Multidisciplinar de Oncología traslacional, Institut Universitari d'Investigació en Ciències de la Salut (IUNICS), Universitat de les Illes Balears, Instituto de Investigación Sanitaria de les Illes Balears (IdISBa), Palma, Spain, ²Servicio Aparato Digestivo. Hospital Comarcal de Inca. Islas Baleares, Inca, Spain, ³CIBER Fisiopatología Obesidad y Nutrición (CB06/03), Instituto de Salud Carlos III, Madrid, Spain

Contact E-Mail Address: marina.alorda@uib.es

Introduction: Colorectal cancer is the third most common cancer worldwide and the second cancer death cause. Nowadays, extracellular vesicles have become an important diagnostic strategy. These extracellular vesicles have a different cargo according to the cell of origin and participate in a varied kind of functions, such as cellular communication, proliferation, and migration, among others. The different omics techniques, as mRNA array, allow to generate a huge amount of data that can be used as screening to find new biomarkers.

Aims & Methods: Our aim was to characterize the extracellular vesicles obtained of the bowel lavage fluid of colorectal cancer patients and realize a mRNA array to achieve the differential gene expression in the different type of patients.

Bowel lavage fluid samples were collected during colonoscopy, stored at -80°C, and divided according to pathology: without pathology, with polyps (divided into low- and high-risk of suffering from neoproliferative processes according to their number and size) and with neoproliferative processes. Subsequently, extracellular vesicles were extracted from the intestinal lumen aspirate by the differential ultracentrifugation method.

For the characterization of the extracellular vesicles, these were observed in the atomic force microscope on a mica surface and dried with nitrogen. RNA from these extracellular vesicles was extracted with TRI Reagent LS® and divided into 3 pools of 6 samples each without pathology, 3 pools of 5 low-risk samples each, 3 pools of 6 high-risk samples each, and 3 pools of 3 cancer samples each to be analyzed in a Clariom S Human mRNA array. The array results were studied by gene set enrichment and the gene differentially expressed by the package limma, Bioconductor.

Results: The atomic force microscope revealed that the extracellular vesicles diameter in all samples was between 40-100 nm. The analysis of the mRNA array demonstrated the presence of some mRNAs differentially

expressed between samples (34 mRNA differentially expressed between control and low-risk, of these, only 2 mRNA were differentially expressed between control and high-risk and, of these, only 1 mRNA was differentially expressed between control and cancer) and the altered biological functions, some of them belonging to mitochondria.

Conclusion: The analysis of the extracellular vesicles obtained from the bowel lavage fluid could increase the knowledge of colorectal cancer and could be an improvement in the diagnostic of the disease because of the possible biomarkers that extracellular vesicles could carry on inside.

Disclosure: Nothing to disclose.

P0589

CLINICOPATHOLOGICAL FEATURE OF DEPRESSED-TYPE COLORECTAL NEOPLASM

S. Kudo¹, S. Semba¹, Y. Kouyama¹, Y. Ogawa¹, K. Ichimasa¹, S. Matsudaira¹, H. Nakamura¹, M. Misawa¹, Y. Mori¹, T. Kudo¹, N. Ogata¹, T. Hisayuki¹, T. Hayashi¹, K. Wakamura¹, H. Miyachi¹, T. Nemoto², T. Baba¹, F. Ishida¹

¹Showa University Northern Yokohama Hospital, Digestive Disease Center, Yokohama, Japan, ²Showa University Northern Yokohama Hospital, Department of Clinical Pathology, Yokohama, Japan

Contact E-Mail Address: kudos@med.showa-u.ac.jp

Introduction: Several development concepts have been proposed for colorectal neoplasms in the carcinogenesis of colorectal cancer. One is “adenoma-carcinoma sequence”. In this concept, polypoid adenoma develops into early polypoid cancer and finally develops to advanced cancer. One is “serrated-pathway”. In this concept, serrated lesion develops into early cancer.

The other is “de novo” pathway. In this concept, early cancers develop without preexisting adenoma. We investigated clinicopathological characteristics of depressed-type colorectal carcinomas considered as “de novo” pathway.

Aims & Methods: A total of 43679 colorectal neoplasms excluding advanced cancers were resected endoscopically or surgically in our center from April 2001 to February 2022 at our center. Of these, 1384 lesions were T1 cancers. According to the developmental morphology classification, they were divided into 3 types: 303 lesions (21.9%) were depressed-type, 497 lesions (35.9%) were flat-type and 584 lesions (42.2%) were protruded-type. We analyzed the pathological difference of these types.

Results: The average tumor size were 15mm, 30mm, and 19mm in depressed-type, flat-type and protruded-type lesions, respectively. The rates of vessel invasion were 48%, 23% and 22%, that of poorly differentiated or mucinous adenocarcinoma were 17%, 11% and 15% in depressed-type, flat-type and protruded-type lesions, respectively.

The rates of these pathological factors were significantly higher in depressed-type lesions than other types. On the other hand, the rates of adenomatous component were 6%, 56% and 53%, and the rates of polypoid growth were 15%, 56% and 97%, respectively.

These rates were significantly lower in depressed-type lesions than other types, suggesting that they emerge directly from normal epithelium without going through the adenomatous stage. The rate of distant metastasis or recurrence was observed in 0.9% (13/1384). Among these 13 cases, 7 cases were depressed-type lesions among which one showed a para-aortic lymph node metastasis and five showed a lung metastasis.

Conclusion: Depressed-type colorectal carcinomas had significantly lower adenomatous components and smaller size than flat-types or protruded-types, and they also contained worth pathological features than other types. So, depressed colorectal carcinoma can be the important lesions for clinical diagnosis.

Therefore, during routine colonoscopy, we should give a greater attention to the morphological features of the depressed-type colorectal carcinomas.

Disclosure: Nothing to disclose.

P0590

WHICH IS THE BETTER PREDICTOR OF LYMPH NODE METASTASIS IN T1 COLORECTAL CANCER, LEAST OR PREDOMINANT DIFFERENTIATION? A SINGLE-CENTER STUDY OF 853 LESIONS

O. Shiina¹, S. Kudo¹, K. Ichimasa^{1,2}, Y. Kouyama¹, K. Mochizuki¹, Y. Takashina¹, Y. Morita¹, T. Kuroki¹, S. Kato¹, Y. Mori^{1,3}, M. Misawa¹, T. Kudo¹, K. Wakamura¹, T. Hayashi¹, N. Sawada¹, T. Nemoto⁴, T. Baba¹, F. Ishida¹, H. Miyachi¹

¹Showa University Northern Yokohama Hospital, Digestive Disease Center, Yokohama, Japan, ²National University Hospital, Department of Gastroenterology and Hepatology, Lower Kent Ridge Road, Singapore, ³University of Oslo, Clinical Effectiveness Research Group, Oslo, Norway, ⁴Showa University Northern Yokohama Hospital, Department of Diagnostic Pathology, Yokohama, Japan

Contact E-Mail Address: showa-417036@med.showa-u.ac.jp

Introduction: Several guidelines such as US, European and Japanese include “tumor differentiation” as a risk factor for lymph node metastasis in T1 colorectal cancer. Surgical resection with lymph node dissection is recommended as an additional treatment, if poorly differentiated adenocarcinoma, signet-ring cell carcinoma or mucinous carcinoma are observed during histological findings of the endoscopically resected specimens. However, the way to diagnose the tumor differentiation is different among these guidelines (least differentiation in US guidelines, predominant differentiation in Japanese guidelines).

Aims & Methods: The aim is to determine which is more reliable method in risk stratification of lymph node metastasis, least or predominant differentiation analysis. We initially evaluated the consecutive 853 patients with T1 colorectal cancer who underwent initial or additional surgical resection with lymph node dissection from 2001 to 2019 at our institution, for inclusion in this retrospective study. We then excluded those who had (a) metachronous or synchronous advanced cancer, (b) invasion to the muscularis propria or deeper in surgical specimens, (c) Lynch syndrome, familial adenomatous polyposis or ulcerative colitis, (d) preoperative chemotherapy or radiotherapy, or (e) missing data.

Finally, we enrolled 805 patients in this study. We evaluated tumor differentiation in two methods (least or predominant) and divided into low-risk (well or moderately differentiated adenocarcinoma, or papillary adenocarcinoma) and high-risk (poorly differentiated adenocarcinoma, signet-ring cell carcinoma or mucinous carcinoma) in each method. The correlation between two patterns of differentiation analysis (least or predominant) and the rate of lymph node metastasis was investigated. Operative specimens were used as the gold standard for the presence of lymph node metastasis.

Results: Lymph node metastasis was found in 9.7% (78/805). Mean number of dissected lymph nodes were 15±10. Rates of high-risk cases in least and predominant analysis were 16.3% (131/805) and 0.7% (6/805), respectively. Sensitivity, specificity, and area under the receiver operating characteristics curve for lymph node metastasis in least and predominant analysis were 28.2%, 85.0%, 0.56 and 2.6%, 99.4%, 0.50, respectively.

Conclusion: Least differentiation analysis would be more effective in predicting the risk of lymph node metastasis in T1 colorectal cancer than predominant differentiation analysis.

Disclosure: Nothing to disclose.

P0591

IS A NEGATIVE FIT FALSELY REASSURING?: A RETROSPECTIVE EVALUATION

S. Manning¹, D. Maxfield¹, R. Bragg¹, H. Gillott¹, M. Clarkson-Cox¹, I. Malik¹, C.J. Rees², L.J. Neilson³

¹South Tyneside District Hospital, South Tyneside, United Kingdom, ²South Tyneside General Hospital South Tyneside NHS Trust, Dept. of Gastroenterology, South Tyneside, United Kingdom, ³South Tyneside and Sunderland NHS Foundation Trust, Gastroenterology, South Shields, United Kingdom

Contact E-Mail Address: s.h.manning@outlook.com

Introduction: FIT (faecal immunochemical test) is recommended by NICE in the assessment of symptomatic patients who do not meet criteria for an urgent suspected cancer referral. It can be a useful tool, in patients where there is a lower suspicion of cancer and may avoid unnecessary colonoscopies in select cases. However, previous studies have reported a cancer miss rate of 7-13% [1,2]. The aim of this audit was to identify the number of FIT-negative new colorectal cancer (CRC) cases in a single centre.

Aims & Methods: This was a single centre, retrospective audit. New CRC cases between June and December 2021 were identified. UK Bowel Cancer Screening Programme (BCSP) patients were excluded, as all of these patients, by default, have a positive FIT. Where histology was available, adenocarcinomas and polyps with high grade dysplasia were included. If only a radiological diagnosis was available, patients were included if the diagnosis was presumed to be CRC. Neuroendocrine tumours, cancers of non-colorectal primary, lymphomas and anal squamous cell carcinomas were excluded. Data was collected on symptoms, tumour location, histology, metastases and FIT level. A FIT cut off of <10ug/g was used as recommended by NICE.

Results: 122 patients were identified and included in the audit. 67 of these patients had FIT tests prior to their diagnosis, of which 5 were negative (7.5%). Of the FIT negative cases, patient age ranged from 56-82 years and cancer location varied (rectum, splenic flexure, hepatic flexure, ascending colon and caecum). Two of these patients had presented with iron deficiency anaemia, one with rectal bleeding, one with weight loss and diarrhoea and a further patient with weight loss alone.

Conclusion: 7.5% of CRC cases had a negative FIT, which is a false negative rate consistent with previous literature. This adds to the existing body of evidence that a negative FIT does not rule out CRC in symptomatic patients and urgent referral should be offered if red flag features are present. In our series, one patient did not meet NICE criteria for suspected CRC and therefore referral would not have been indicated based on FIT alone. Clinicians must consequently bear this in mind, thoroughly assess risk factors and use clinical judgement on an individual patient basis when considering whether to refer for investigation.

This was a small, single centre audit and further studies and therefore, larger data sets would be recommended and required to accurately assess FIT's sensitivity and specificity, on a larger scale.

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COLONIC POLYPS: SMALL IN SIZE, BIG IN IMPACT?

C. Chia¹, S. Tsao², S. Thrumurthy²

¹Tan Tock Seng Hospital, Gastroenterology & Hepatology, Novena, Singapore, ²Tan Tock Seng Hospital, Gastroenterology & Hepatology, Singapore, Singapore

Contact E-Mail Address: tzechris@gmail.com

Introduction: Removal of colonic adenomas is proven to reduce incidence of colorectal cancer (CRC) and mortality. The current practice of routinely resecting all diminutive (1-5mm) and small (6-9mm) colonic polyps and submitting them for histopathologic assessment has several disadvantages in terms of cost-effectiveness and risks from repeated colonoscopies. The resect-and-discard (RD) strategy has been proposed to reduce retrieval of diminutive polyps (1-5mm) for histology which has been deemed not to have advanced histologic features. RD strategy for small polyps (6-9mm) are still controversial. The prevalence of advanced histologic features in the diminutive and small polyp category remains small but not clearly defined.

Aims & Methods: In this cross-sectional study, we aim to find the prevalence of small & diminutive polyps resected that shows advanced histologic features such as high grade dysplasia(HGD) or villous histologic features to determine if RD policy is feasible in the local Asian tertiary setting. Data was retrieved over 2 years with assistance from the Pathology Department to identify all submitted colonic polyp specimens. Each patient also had their colonoscopy report and detailed histology report reviewed by 2 separate colleagues within the team to ensure data consistency. The variables captured include age, gender, ethnicity, total polyp number, polyp distribution in the colon, histology, polyp size and respective number in each histology subtype and concurrent CRC. Data was analysed using SPSS v.20.

Results: There were a total 1482 colonic polyps retrieved for histology from 871 patients. 88% of the cases with colonic polyps were ≥50 years with male gender making up 60% of total cases and the major ethnic group being Chinese, comprising 88%. The colonic distribution of the polyps was 45.4% right-sided and 54.6% left-sided, including 8.5% rectal. There were 844 diminutive polyps (1-5mm), 447 small polyps(6-9mm) and 191 large polyps(≥10mm).

The proportion of HGD seen in each of these groups were 18.7%, 37.6% and 56.5% respectively (p<0.001). This was relatively high and significant compared to figures in published literature. The proportion of polyps containing villous histology was 3.0% for diminutive polyps and 12.5% for small polyps(p=0.041). There were no concurrent malignancy seen in all the polyps.

Polyp size	Diminutive (1-5mm)	Small (6-9mm)	Large (≥10mm)
Total number (1482)	844 (57.0%)	447 (30.1%)	191(12.9%)
Proportion with HGD	18.7%	37.6%	56.5%
Proportion with villous histology	3.0%	12.5%	37.1%
O'Brien et al. Gastroenterology 1990	1.0%	5.0%	21.0 %

Table.

Conclusion: These findings showed that a significant proportion of diminutive polyps(18.7%) and small polyps(37.6%) harboured features of HGD, which is significantly higher than previous findings of 1% for diminutive polyps and 5% for small polyps in some literature.

Based on size alone without the aid of narrow band imaging (NBI) or other forms of image enhanced endoscopy(IEE), we find that RD strategy for diminutive or small polyps may miss a significant group of patients with advanced neoplastic histology who needs earlier colonoscopic surveillance.

There may be merits in the RD approach but this would require incorporation of other real-time endoscopic modalities such as IEE and more robust evaluation.

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Disclosure: Nothing to disclose.

P0593

IMMUNOREACT 0: BIOPSY-BASED IMMUNE BIOMARKERS AS PREDICTORS OF RESPONSE TO NEOADJUVANT THERAPY FOR RECTAL CANCER: A SYSTEMATIC REVIEW AND META-ANALYSIS

A. Stepanyan¹, M. Scarpa², F. Scognamiglio¹, G. Spolverato¹, I. Angriman¹, S. Pucciarelli¹, I. Castagliuolo³, M. Scarpa¹

¹Azienda Ospedaliera Universitaria di Padova, General Surgery 3 Unit, Padova, Italy, ²Veneto Institute of Oncology IOV-IRCCS, Lab. of Advanced Translational Research, Padova, Italy, ³Azienda Ospedale Università di Padova, Microbiology Unit, Padova, Italy

Contact E-Mail Address: astghik.stepanyan@aopd.veneto.it

Introduction: The standard therapy for rectal cancer patients is neoadjuvant therapy (NT), including chemotherapy and radiotherapy followed by surgery. Immune biomarkers are potential predictors of the response to NT, however, none of them have achieved an application in clinical practice.

Aims & Methods: The aim of this study is to evaluate predictive role of biopsy-based biomarkers including tumor-infiltrating lymphocytes (TILs) and immune checkpoints in rectal cancer patients.

To identify relevant studies, the search was conducted in PubMed, Ovid MEDLINE and EMBASE databases. Two independent researchers selected studies followed by data extraction, quality assessment and data analysis.

Results: From the total of 321 studies identified between May 1979 and October 2021, 36 were included in qualitative synthesis, while 17 were eligible for meta-analysis.

The final results have shown that high levels of total CD8+ TILs (OR 2.25, 95% CI 1.64 to 3.08; participants = 690; $P < 0.00001$) as well as its stromal (OR 1.52, 95% CI 1.05 to 2.18; participants = 542, $P = 0.03$) and intraepithelial (OR 3.43, 95% CI 2.56 to 4.62; participants = 961, $P < 0.00001$) compartments individually, CD4+ TILs (OR 2.26, 95% CI 1.30 to 3.94; participants = 239, $P = 0.004$), CD3+ TILs (OR 1.78, 95% CI 1.08 to 2.95; participants = 267, $P = 0.02$) and high levels of tumoral and immune cell expression of PD-L1 (OR 2.21, 95% CI 1.17 to 4.16; patients = 182; $P = 0.01$ significantly predict good pathological response to NT.

On the contrary, high levels of intraepithelial CD4+ TILs (OR 0.35, 95% CI 0.15 to 0.84; participants = 275, $P = 0.02$) were correlated with poor pathological response. Furthermore, FoxP3 TILs, tumoral PD-L1, CTLA-4 were not predictive biomarkers for the treatment response.

Conclusion: Collectively, our meta-analysis demonstrated that high density tumor inflammatory infiltrate is associated to improved pathological response in patients that underwent NT for the rectal cancer and could assist to predict the good response. To further verify the predictive role of PD-L1 and the possibility of distinct role of CD4+ TILs depending on the site of infiltration, more studies with fractionated CD4+ TILs levels and fractionated tumoral and TILs expression of PD-L1 are required.

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P0594

A SIMPLE SCORING MODEL BASED ON ENDOSCOPIC FEATURES FOR SELECTION OF COLORECTAL CANCER AMENABLE TO ENDOSCOPIC RESECTION

S.J. Han¹, Y. Jung², J. Yu³, J.-H. Kim⁴, Y.-H. Youn⁵, H.P. Hyojin Park⁴, J.J. Park⁴

¹Severance Hospital, Yonsei University College of Medicine, Seoul, Korea (Republic of), ²Soonchunhyang University Cheonan Hospital, Cheonan, Korea (Republic of), ³Severance Hospital, Yonsei University College of Medicine, Internal Medicine, Seoul, Korea (Republic of), ⁴Gangnam Severance Hospital, Yonsei University College of Medicine, Seoul, Korea (Republic of), ⁵Gangnam Severance Hospital, Internal Medicine, Seoul, Korea (Republic of)

Contact E-Mail Address: HAN_SO@yuhs.ac

Introduction: There was limited data regarding endoscopic features for predicting invasion depth of colorectal cancer. We aimed to develop simple scoring model for selection of colorectal cancer amenable to endoscopic resection.

Aims & Methods: From March, 2009 to September, 2019, a total of 854 patients who underwent colonoscopy and diagnosed with colorectal cancer invaded mucosa (Tis), submucosa (T1), and muscularis propria (T2) were enrolled at two tertiary medical center. All the cases are biopsy confirmed by endoscopic resection or surgery.

Development model was designed with significant endoscopic features that were selected through chi-square analysis and multiple regression model. Thereafter, this scoring model was examined with validation model to evaluate its power to predict invasion depth.

Results: Then we randomly selected two-thirds of cases (n=570) to establish development model. Six meaningful endoscopic morphological features were selected by Chi-square tests, multiple logistic regression model and simplified risk predicting model was designed in consideration of odds ratios.

The numerical formula is as below; size (0: under 20mm; 1: over 20mm) x1 + fold convergence (0: no fold convergence; 1: fold convergence)x1 + crumple (0: no crumple; 1: crumple)x1 + demarcated depression (0: no demarcated depression; 1: demarcated depression)x1 + nonstructural pit pattern (0: regular pit pattern; 1: pit pattern with VI, VN)x2 + surface ulceration (0: no ulceration; 1: ulceration)x3.

Validation model with remained 284 cases were tested to evaluate efficacy of this simple model. Area under curve (AUC) for development model was 0.763 (0.724-0.801) and 0.819 (0.768-0.870) for validation model, respectively.

Conclusion: A simple predicting model composed of six endoscopic morphological features might guide to differentiate early colorectal cancer that is amenable to endoscopic resection.

Disclosure: none.

P0595

RISK OF ADVANCED LESIONS AT SURVEILLANCE COLONOSCOPY COMPARING PATIENTS WITH SERRATED LESIONS AND HIGH-GRADE DYSPLASTIC ADENOMAS

E. Medawar¹, R. Djinbachian¹, M. Taghiakbari¹, T. Khoury¹,

A. Zoughlami², M. Zarandi-Nowroozi¹, D. von Renteln¹

¹University of Montreal, Montreal, Canada, ²McGill University, Montreal, Canada

Contact E-Mail Address: edgard.medawar@mail.mcgill.ca

Introduction: Patients with serrated lesions (SL = sessile serrated lesions (SSL) and traditional serrated adenomas (TSA)) or high-grade dysplastic adenomas (HGD) are at risk to develop advanced colorectal adenomas (AA) or colorectal cancer (CRC).

However, studies evaluating the risk of developing total metachronous advanced neoplasia (TMAN) for patients diagnosed with HGD or SL, and comparing this risk, are lacking.

Aims & Methods: Study aim was to compare the incidence of TMAN in surveillance colonoscopies of patients diagnosed with SL <10 mm, SL ≥10 mm or HGD at index colonoscopy. A cohort study was conducted. Through pathology database search, we identified 1529 patients with HGD and 2428 patients with SL diagnosed between 2010 and 2019 at the University of Montreal Hospital Center.

We excluded patients under 45 or over 75 years of age, with inflammatory bowel disease, hereditary CRC syndromes, previous or synchronous CRC, first surveillance <12 months after complete index, or concomitant SL and HGD at index. Patient files were reviewed for demographic data and findings at index and follow-up colonoscopies. Follow-up was continued until the outcome of interest or the last colonoscopy within 10 years.

The primary outcome was TMAN (=either advanced neoplasia (AN), which combines AA and CRC, or advanced serrated lesion (ASL), defined as SSL ≥10 mm or with dysplasia, TSA or hyperplastic polyp (HP) ≥10 mm). The secondary outcomes were AN, ASL, [TMAN or ≥5 SSLs or ≥5 adenomas] and [TMAN or ≥3 SSLs or ≥3 adenomas].

Continuous and categorical variables were compared between the three groups using 1-way ANOVA and the Pearson chi-squared test, respectively, followed by post-hoc tests. For the outcomes, we performed univariate and multivariate Cox regressions and present hazard rate ratios (HR) with their 95% confidence intervals.

Results: A total of 585 patients were eligible (55% male; mean age 63 years). The mean duration of follow-up was 3.67 years (range 0.94 – 9.88 years). There were 226 patients in the SL <10 mm group (216 SSL and 10 TSA), 204 patients in the SL ≥10 mm group (198 SSL and 6 TSA) and 155 patients in the HGD group.

Compared to SL <10 mm (reference group), SL ≥10 mm resulted in a higher rate of TMAN (HR=2.08 (1.38-3.15)), a similar rate of AN (HR=1.45 (0.81-2.77)), and a higher rate of ASL (HR=2.53 (1.50-4.25)), [TMAN or ≥5 SSLs or ≥5 adenomas] (HR=1.87 (1.25-2.78)) and [TMAN or ≥3 SSLs or ≥3 adenomas] (HR=1.64 (1.14-2.37)), after adjusting for age, sex, family history of CRC, proximal location of HGD or SL, tubulovillous or villous adenomas (TVA/VA), adenomas ≥10 mm and ≥3 adenomas.

Compared to SL <10 mm, HGD resulted in a similar rate of TMAN (HR=0.87 (0.62-1.20)) and AN (HR=1.08 (0.74-1.57)), a lower rate of ASL (HR=0.40 (0.19-0.85)), and a similar rate of [TMAN or ≥5 SSLs or ≥5 adenomas] (HR=0.84 (0.62 – 1.16)) and [TMAN or ≥3 SSLs or ≥3 adenomas] (HR=0.87 (0.65-1.17)), after adjusting for the same covariates.

A significant univariate effect of HGD was observed on TMAN and AN, but adjusting for either adenomas ≥10 mm, TVA, VA or ≥3 adenomas was sufficient to lose this effect. Compared to all SLs, HGD had a similar rate of TMAN and AN, and a lower rate of ASL.

Conclusion: Patients with a SL ≥10 mm at index colonoscopy have the highest risk of developing TMAN compared to patients with HGD and to patients with SL <10 mm. HGD does not increase the risk of TMAN compared to SL <10 mm.

The apparently increased risk of TMAN in the HGD group compared to SL <10 mm was explained by the multiple synchronous high-risk adenomas found with HGD or that HGD was in, and not by HGD itself.

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THE EFFECT OF EDIBLE SEAWEED CONSUMPTION ON RISK OF COLORECTAL CANCER: A SYSTEMATIC REVIEW

M.L. Adnan¹, R. Rahmawati²

¹Universitas Islam Indonesia, Sleman, Indonesia, ²Universitas Islam Indonesia, Pharmacology, Sleman, Indonesia

Contact E-Mail Address: luthfiadnan35@yahoo.co.id

Introduction: Colorectal cancer is one of the most common malignancies in the world after lung and breast cancer. Diet is known to affect the risk of colorectal cancer incidence. Consumption of seaweed is common to use in Asian culinary. However, the relationship between seaweed consumption and the risk of colorectal cancer is still unclear because there is limited evidence. The aim of this study is to discuss the relation of seaweed consumption to the risk of colorectal cancer incidence.

Aims & Methods: The aim of this study is to discuss the relation of seaweed consumption to the risk of colorectal cancer incidence. The preparation of this systematic review was conducted according to PRISMA guidelines. Literature searches were conducted from February-May 2021 with the search engines PubMed, Google Scholar, and ScienceDirect with limited publication between 1990-2021. The keywords used were "colorectal cancer", "seaweed", "incidence", "risk factor", and "diet". The inclusion criteria used were nonrandomized controlled trials (RCTs) such

as observational studies, case-control, and cohort studies with full text in English. The exclusion criteria used were a review, systematic review, or meta-analysis, studies that were not conducted in humans.

Results: Six studies, 4 case-control and 2 cohort studies meet the criteria. Based on the comparison of case and control groups, seaweed consumption is significantly associated with a lower risk of colorectal cancer. A recent cohort study from Minami *et al*(2020) showed there is frequent seaweed intake was inversely associated with the risk of all-cause death among patients with colon cancer (Ptrend = 0.03).

Rectal cancer patients who had frequently consumed seaweed tended to have a lower risk of rectal cancer death (Ptrend = 0.02). Some confounding can affect are age, sex, family history, nutritional status, comorbidities, occupation, and history of treatment.

Conclusion: Seaweed consumption has been associated with a lower incidence and mortality of colorectal cancer.

Disclosure: There is no conflict of interest between the author.

Author (years)	Title	Country	Type of study	Population (N, Men/Women)		Intake of seaweed consumption	Data collection	Statistical analyzes were performed	Results	Pvalue	Confounding (If reported)
				Control	Incidence/sample size						
Kato <i>et al</i> (1990)	A comparative case-control study of colorectal cancer and adenoma [5]	Japan	Case-control	578 (377 M/201 W)	221 (138 M/83 W) with 132 (79 M/53 W) colon cancer and 91 (60 M/31 W) rectal cancer	Daily intake compare to less than daily intake	June 1986-March 1990	Relative Risk (RR) (95% CI)	1.02 (0.65-1.59) in colon cancer and 0.42 (0.22-0.82) in rectal cancer	NA	Sex, age, residence
Hoshiyama <i>et al</i> (1993)	A Case-Control Study of Colorectal Cancer and Its Relation to Diet, Cigarettes, and Alcohol Consumption in Saitama Prefecture, Japan [6]	Japan	Case-control	653 (343 M/310 W)	181 (79 Colon cancer (37 M/42 W) and 102 Rectal Cancer (61 M/41 W))	Low (≤ 4 times/week) Moderate (5-7 times/week) High (≥ 8 times/week)	August 1984-July 1990	Relative Risk (RR) (95% CI)	0.5 (0.3-0.8) and 0.2 (0.0-0.9) from intermediate to high intake group in colon cancer and 0.5 (0.3-0.9) and 0.4 (0.1-1.1) from intermediate to high intake group in rectal cancer	<0.01	Sex and age
Ping <i>et al</i> (1998)	Lifestyle and colorectal cancer: A case-control study.[7]	Japan	Case-control	265 (NA)	100 (77 M/23 W)	50.6% control group and 45% colorectal group usually consumed seaweed	1 April 1986-31 March 1994	Odd ratio (OR) (95% CI)	0.80 (0.5-1.27) in the group that usually consumed seaweed	0.03	Not reported
Khan <i>et al</i> (2004)	Dietary habits and cancer mortality among middle aged and older Japanese living in Hokkaido, Japan by cancer site and sex. [8]	Japan	Cohort study	NA	29 (15 M/14 W)	Reference group (never, several times per year, and several times per month) and comparison group (several times per week and every day)	1984-1985 until 2002	Relative Risk (RR) (95% CI)	1.2 (0.4-3.7) in men and 0.8 (0.2-2.5) in women between reference group and comparison group	NA	Not reported
Kim <i>et al</i> (2019)	Associations among dietary seaweed intake, c-MYC rs6983267 polymorphism, and risk of colorectal cancer in a Korean population: a case-control study.[9]	South Korea	Case-control	1846 (1250 M/596 W)	923 (625 M/298 W)	2.22 $\pm$ 2.18 gram/day in control group and 1.72 $\pm$ 1.32 gram/day in incidence group	2010-2013	Odds ratio (OR) (95% CI)	1.05 (0.82-1.34) in group with seaweed 1.09- $<$ 2.27 gram/day and 0.65 (0.50-0.85) in group with seaweed intake $\geq$ 2.27 gram/day	0.011	Age, sex, BMI, education level, occupation, income, alcohol consumption, physical activity, first degree family history of CRC, and total caloric intake.
Minami <i>et al</i> (2020)	Associations of Japanese food intake with survival of stomach and colorectal cancer: A prospective patient cohort study.[10]	Japan	Cohort study	NA	793 (428 M/365 W) colon cancer patient and 510 (320 M/190 W)	Never or 1-2 times per month, 1-2 times per week, 3-4 times per week, everyday	1997-2013	Hazard ratio of all cause death (HR) (95% CI)	1.05 (0.70-1.58) and 1.01 (0.61-1.69) in colon and rectal cancer group with frequent seaweed consumption 1-2 times per week, 0.98 (0.64-1.51) and 0.78 (0.46-1.33) in colon and rectal cancer group with frequent seaweed consumption 3-4 times per week, and 0.65 (0.41-1.03) and 0.70 (0.37-1.34) in colon and rectal cancer group with frequent seaweed consumption everyday	0.03 for colon cancer and 0.10 for rectal cancer	Age, sex, year of diagnosis, referral status (from screening, other), stage (0-I, II, III, IV), histological type (adenocarcinoma, other), occupation (professional or office work, other), comorbidities (no, yes), pretreatment body mass index (BMI), curative resection (no, yes), chemotherapy (no, yes) and energy intake

P0596 Table.

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MODIFIED UNDERWATER ENDOSCOPIC MUCOSAL RESECTION FOR INTERMEDIATE-SIZE SESSILE COLORECTAL POLYPS

D.H. Kim¹, H. Kim², S.-Y. Park¹, H.S. You¹, S.Y. Cho¹

¹Chonnam National University Hospital and Medical School, Division of Gastroenterology, Department of Internal Medicine, Gwangju, Korea (Republic of), ²Chonnam National University Hospital, Gastroenterology, Gwangju, Korea (Republic of)

Contact E-Mail Address: bono343@naver.com

Introduction: The European Society of Gastrointestinal Endoscopy (ESGE) guideline recommends cold snare polypectomy (CSP) for 6–9 mm sized sessile polyps. Hot snare polypectomy (with or without submucosal injection) is suggested for the removal of sessile polyps 10–19 mm in size.[1] According to a recent paper, the rate of complete resection was higher with underwater endoscopic mucosal resection (UEMR) than with conventional endoscopic mucosal resection (CEMR) for the polyps 10–20 mm in size.[2]

In general, UEMR is performed after infusing about 200–1000 mL of water. [2–4] However, some intestinal lumens cannot be easily filled with water. Therefore, sometimes, an excessive amount of water fills the lumen,; the procedure takes a long time, causing abdominal discomfort; and there is a concern of hypernatremia or hyponatremia depending on the nature of the water.[5] Moreover, when performing UEMR, the lumen decreases after filling with water, making visualization difficult.

Hence, the authors devised a modified version of UEMR that compensates for the shortcomings of conventional UEMR. We aimed to elucidate the effectiveness and safety of this modified UEMR method.

Aims & Methods: This prospective, observational, single-center study included consecutive patients with intermediate-sized (10–20 mm) sessile colorectal polyps. The modified UEMR method was used to initially snare the lesion without injection or water infusion.

Thereafter, water was infused until the lesion was submerged, then it was resected using electrocautery. We also evaluated the rates of complete resection and procedure-related complications.

Results: Forty-two patients with 47 polyps were enrolled in the study. The median procedure time and fluid infusions were 71 s (42–607) and 50 mL (30–130), respectively. The rates of R0 resection and *en bloc* resection were 80.9% and 97.9%, respectively, with 100% technical success. R0 resection was observed in 42.9% of polyps sized ≥15 mm and 87.5% sized <15 mm (*p* <0.01). Muscle entrapment was found in 71.4% of patients with polyps sized ≥15 mm and 10% <15 mm (*p* <0.01).

	Total (n=47)	Polyp size ≥15 mm (n = 7)	Polyp size <15 mm (n = 40)	p value
Ro resection rate, n(%)	38 (80.9)	3 (42.9)	35 (87.5)	<0.01
Muscle entrapment, n(%)	9 (19.1)	5 (71.4)	4 (10.0)	<0.01
<i>En bloc</i> resection rate, n (%)	46 (97.9)	6 (85.7)	40 (100)	0.15
Piecemeal resection rate, n (%)	1 (2.1)	1 (14.3)	0	
Technical success, n (%)	47 (100)	7 (100)	40 (100)	
Median procedure time, seconds (range)	71 (42–607)	110 (69–379)	68 (42–607)	0.16
Fluid infusion (mL), median (range)	50 (30–130)	70 (40–130)	50 (30–120)	<0.01
Snare tip ablation, n (%)	13 (27.7)	3 (42.9)	10 (25.0)	0.38
Coagrasper use, n (%)	3 (6.4)	2 (28.6)	1 (2.5)	0.054

Table 1. Procedure-related Outcomes

Immediate bleeding occurred in 12.8% of cases and was controlled using a snare tip or coagrasper. Snare-tip ablation and coagrasper ablation were performed in 27.7% and 6.4% of patients, respectively. No delayed bleeding, perforation, or any other complications were reported.

Conclusion: Modified UEMR can be used in cases in which securing visibility or performing the existing UEMR is challenging. Careful treatment is required when removing polyps >15 mm in size.

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Disclosure: Nothing to disclose.

P0598

COMPOUND SCREENING IN A 3D SPHEROID MODEL IDENTIFIES CURCUMIN ANALOG AS A COLORECTAL CANCER STEM CELL INHIBITOR

V. Marques¹, M.B. Afonso¹, M. Clariano¹, N. Aniceto¹, A. Trindade², J. C David¹, M.J. Perry¹, R. C Guedes¹, A. Duarte², C. MP Rodrigues¹

¹Research Institute for Medicines (iMed.Ulisboa), Faculty of Pharmacy, Universidade de Lisboa, Lisbon, Portugal, ²Centre for Interdisciplinary Research in Animal Health (CIISA), Faculty of Veterinary Medicine, Universidade de Lisboa, Lisbon, Portugal

Contact E-Mail Address: mbafonso@ff.ul.pt

Introduction: The importance of cancer stem cells (CSCs) on tumor formation, invasion, and resistance to therapy in colorectal cancer (CRC) is currently widely accepted.

Aims & Methods: Here, we explored the anti-CSC potential of a novel curcumin analog – MVC12 – identified in a compound screening campaign based on a tumorsphere forming assay.

Human CRC cell lines HT29, HCT116, and SW620, and AML12 immortalized murine hepatocytes were incubated with MVC12 under tumorsphere forming (3D) and adherent (2D) conditions, and dose-response curves were built. The impact of MVC12 on tumorsphere formation and stemness regulation was assessed by qRT-PCR and immunoblotting.

Flow cytometry analysis of cell death markers, caspase-3/7 activity assays, and Hoechst staining were used to evaluate apoptotic cell death. MVC12 anti-tumor effectiveness was evaluated *in vivo* using xenografted HT29 subcutaneous tumors in Foxn1^{nu/nu} athymic mice treated with 10 mg/kg intraperitoneal administrations every two days. Potential molecular targets were evaluated *in silico*, *in vitro*, and *in vivo*.

Results: MVC12 presented equal or better efficacy than salinomycin (CSC-targeting agent) and 5-fluorouracil (5-Fu, traditional chemotherapy agent) in reducing cell viability in 3D and 2D cell cultures and was up to four times less toxic in AML12 cells. MVC12 decreased tumorsphere size and number. Further, MVC12 decreased stemness markers and increased differentia-

tion markers as well as apoptosis in both 3D and 2D cell cultures. MVC12 significantly reduced tumor burden *in vivo*, accompanied by increased differentiation and apoptosis in tumors. *In silico* screening and molecular docking analysis revealed NF- κ B and STAT3 as putative molecular targets of MVC12. Experimental validation confirmed reduced NF- κ B and STAT3 activity after MVC12 treatment *in vitro* and *in vivo*.

Conclusion: In conclusion, we describe a novel curcumin analog that targets colorectal CSCs and efficiently reduces tumor burden *in vivo* by inducing apoptosis and modulating stemness. Functional assays will further validate MVC12 putative targets and mechanisms of action in future studies.

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Disclosure: Nothing to disclose.

P0599

RATES OF SYNCHRONOUS ADVANCED NEOPLASIA AND COLORECTAL CANCER IN PATIENTS WITH COLONIC SERRATED LESIONS

R. Djinbachian¹, M.-L. Lafontaine¹, T. Dufault¹, M. Boivin¹, M. Bouin¹, D. von Renteln¹

¹Centre Hospitalier de l'Université de Montreal (CHUM), Montreal, Canada

Contact E-Mail Address: rdjinbachian@gmail.com

Introduction: Serrated lesions (SL) have been associated with significant risks of developing colorectal cancer (CRC). There is little data on synchronous findings after detection of SLs during colonoscopy.

Aims & Methods: Our study aim was to evaluate the rate of synchronous advanced neoplasia (S-AN) and synchronous CRC (S-CRC) in colonoscopies where SLs were detected. We conducted a retrospective study of screening aged patients 45-74y with a colorectal SL (sessile serrated polyp [SSP] or traditional serrated adenoma [TSA]) detected during a screening, surveillance, or diagnostic colonoscopy. Exclusion criteria were: inflammatory bowel disease; hereditary CRC syndromes; personal history of CRC; serrated polyposis syndrome; patients referred for CRC or resection of large adenomas.

Primary outcome was risk of S-AN in patients with SL. Secondary outcomes included risk of S-AN or S-CRC stratified by SL characteristics. Multivariate logistic regression was performed and adjusted for colonoscopy indication; sex; bowel preparation quality.

Results: The study included 1262 patients with 1649 SLs (1214 with SSPs and 48 with TSAs). 47.2% were female and 22.9% of exams were screening colonoscopies, 48.2% surveillance, 28.9% diagnostic. The overall rates of S-AN and S-CRC were 15.1% and 1.7% respectively. Presence of SSPs ≥ 10 mm was associated with higher rates of S-AN, (18.1 vs 12.2%, Odds Ratio [OR]=1.61 [95% Confidence Interval [CI]1.17-2.23], $p=0.004$). SSP dysplasia was predictive of both S-AN, (30.3 vs 14.1%, OR=2.68 [95%CI 1.24-5.78], $p=0.012$) and S-CRC, (12.1 vs 1.3%, OR=9.79 [95%CI 3.03-31.62], $p<0.001$). SSP number (≥ 3) was not a predictor of S-AN, (17.8 vs 14.4%, OR=1.13 [95%CI 0.67-2.15]) or S-CRC, (2.4 vs 1.5%, OR=1.60 [95%CI 0.36-7.08]). SSP location (proximal) was not a predictor of S-AN, (14.5 vs 16.5%, OR=0.85 [95%CI 0.50-1.46]) or S-CRC, (1.2 vs 3.7%, OR=0.37 [95%CI 0.12-1.12]).

Conclusion: Patients with SLs are at significant risk of S-AN and S-CRC. Findings of SSPs ≥ 10 mm are associated with significant risk of S-AN, and SSP dysplasia is associated with significant risks of both S-AN and S-CRC. Endoscopists should exercise heightened vigilance for synchronous findings when SLs are detected, especially SSPs ≥ 10 mm or when bowel preparation is suboptimal. Expedited repeat colonoscopy is warranted after detection of SSPs with dysplasia to rule out advanced lesions and CRC.

Disclosure: Roupen Djinbachian was supported by a resident clinical research award from the American College of Gastroenterology for the conduction of this study.

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P0600

MANAGEMENT OF COLORECTAL HIGH-GRADE DYSPLASIA OR CANCER RESECTED BY COLD SNARE POLYPECTOMY: A MULTICENTRE EXPLORATORY STUDY

I. Hisada¹, K. Inoki², H. Takamaru¹, H. Furuhashi³, Y. Kishida⁴, Y. Shimodate⁵, Y. Sumida⁶, K. Hosotani⁷, H. Ueyama⁸, Y. Furumoto⁹, S. Hashimoto¹⁰, Y. Takeuchi¹¹, R. Ichijima¹², Y. Yoshizawa¹³, T. Suzuki¹⁴, Y. Minoda¹⁵, K. Mizukami¹⁶, T. Matsumura¹⁷, T. Kasai¹⁸, T. Yamamura¹⁹, K. Ohnita²⁰, K. Hara²¹, M. Esaki^{22,15}, A. Katagiri²³, H. Ishikawa²⁴, T. Gotoda¹²

¹National Cancer Center Hospital Endoscopy Division, Tokyo, Japan, ²Showa University School of Medicine, Division of Gastroenterology, Medicine, Tokyo, Japan, ³The Jikei University School of Medicine, Endoscopy, Kanagawa, Japan, ⁴Shizuoka Cancer Center, Division of Endoscopy, Shizuoka, Japan, ⁵Kurashiki Central Hospital, Gastroenterology and Hepatology, Kurashiki, Japan, ⁶National Hospital Organization Kyushu Medical Center Clinical Research Institute, Gastroenterology, Hukuoka, Japan, ⁷Kobe City Medical Center General Hospital, Gastroenterology, Kobe, Japan, ⁸Juntendo University School of Medicine, Gastroenterology, Tokyo, Japan, ⁹Tokyo Metropolitan Bokutoh Hospital, Gastroenterology, Tokyo, Japan, ¹⁰Yamaguchi University Graduate School of Medicine, Gastroenterology and Hepatology, Yamaguchi, Japan, ¹¹Osaka International Cancer Institute, Gastrointestinal Oncology, Osaka, Japan, ¹²Nihon University School of Medicine, Medicine, Division of Gastroenterology and Hepatology, Tokyo, Japan, ¹³Seirei Hamamatsu General Hospital, Gastroenterology, Hamamatsu, Japan, ¹⁴Chiba Cancer Center, Endoscopy, Chiba, Japan, ¹⁵Graduate School of Medical Sciences, Kyushu University, Medicine and Bioregulatory Science, Fukuoka, Japan, ¹⁶Oita University, Gastroenterology, Oita, Japan, ¹⁷Chiba University Hospital, Gastroenterology, Chiba, Japan, ¹⁸Fukaya Red Cross Hospital, Gastroenterology, Saitama, Japan, ¹⁹Nagoya University, Gastroenterology and Hepatology, Nagoya, Japan, ²⁰Shunkaikai Inoue Hospital, Gastroenterology and Hepatology, Nagasaki, Japan, ²¹Hyogo College of Medicine, Division of Gastroenterology, Nishinomiya, Japan, ²²Kitakyushu Municipal Medical Center, Gastroenterology, Hukuoka, Japan, ²³National Cancer Center Hospital, Tokyo, Japan, ²⁴Kyoto Prefectural University of Medicine, Osaka, Japan

Contact E-Mail Address: izumi.t.0819@gmail.com

Introduction: In cases of positive or indefinite margin status after cold snare polypectomy (CSP) for high-grade dysplasia (HGD) or cancers, the risk of post-colonoscopy colorectal cancer should be considered and managed appropriately. Nonetheless, the management after CSP for HGD or cancers has not been fully investigated, and varies depending on the institution's policy.

The limited number of these cases contaminates the data on the recurrence pattern of HGDs or cancers after CSP, and the lack of evidence makes it difficult to decide on the appropriate management strategy.

Aims & Methods: The present study aimed to investigate the recurrence pattern of colorectal HGDs or cancers after CSP and the appropriate management strategy. This nationwide multicentre retrospective exploratory cohort study was conducted at 22 secondary or tertiary care centres in Japan. The study was approved by the institutional review board of each participating centre and registered with the University Hospital Medical Information Network (UMIN) Clinical Trials Registry as UMIN000043670. The data of patients over 20 years of age who underwent CSP for colorectal HGD or cancer between January 2014 and December 2020 and had undergone one or more follow-up colonoscopies at the participating 22 centres were retrospectively analysed.

We divided the curability of CSP into three categories: curative, borderline, or non-curative resection. The pathological diagnosis was based on the Japanese classification of colorectal, appendiceal, and anal carcinomas, to which we included the presence of intramucosal carcinoma. In the present study, intramucosal carcinomas were classified as having HGD. The lesion where the tumour invaded the submucosa was classified as cancerous. We investigated the detection rate of CSP scars, local recurrence rate (LRR), risk factors for local recurrence, and the follow-up strategy.

Results: The study included 155 patients with 156 lesions. The median tumour size was 6 mm (range: 2–18 mm), and the most frequent macroscopic type was protruded (70.5%). CSP scars were identified in 22 (31.4%), 41 (54.7%), and 10 (90.9%) patients with curative, borderline, and non-curative resection, respectively. Of them, the residual tumours were observed in one (4.5%), six (14.6%), and three (30.0%) cases, respectively.

The total LRR was 13.7% (95% confidence interval, 6.8–23.8). R1 resection cases (either horizontal or vertical margins positive for tumour) were associated with local recurrence ($p = 0.031$). Salvage endoscopic resection or surgery was performed on 21 and 10 patients, respectively. Of them, the proportion of endoscopically suspected residual tumours was significantly higher ($p < 0.001$) in the residual tumour positive (100%) than in the negative group (28.6%).

All residual tumours were diagnosed at first surveillance colonoscopy. The median observation period after CSP was 12.7 months (range: 0.6–77.1). The median number of times of colonoscopic surveillance was two (range: 1–7). Although three patients died due to duodenal cancer, cerebral infarction, and an unknown cause, none of them died due to colorectal cancer.

Conclusion: Identification of CSP scars is sometimes difficult; the LRR after CSP for HGDs or cancers is 13.7% based on scar-identified cases. Salvage endoscopic or surgical resection should be performed according to the curability of the lesions and the endoscopic findings during surveillance endoscopy. Further long-term follow-up studies including cases with unidentified CSP scars are necessary.

Disclosure: Nothing to disclose.

P0601

A PILOT CONSEQUENCES OF COLORECTAL CANCER VIRTUAL CLINIC IN LINCOLNSHIRE DURING THE COVID-19 PANDEMIC

D. Fernandes¹, J. Andreyev^{1,2}

¹Lincoln County Hospital, Gastroenterology, Lincoln, United Kingdom, ²University of Nottingham, The Biomedical Research Centre, Nottingham Digestive Diseases Centre, School of Medicine, Nottingham, United Kingdom

Contact E-Mail Address: dcrfernandes@gmail.com

Introduction: Recent reductions in cancer mortality rates are the result of better screening and the use of improved treatments. Whilst there has been a longstanding awareness of the psychological and social impact of cancer therapy, there has been little emphasis on dealing with the physical symptoms that are a frequent complication of treatment. This can include living with chronic and debilitating bowel symptoms as well as problems with sexual and urinary function.

At the United Lincolnshire Hospitals Trust, over 400 patients are diagnosed and treated for colorectal cancer annually. We therefore sought to develop a unique virtual service to help patients who have developed gastrointestinal symptoms following treatment.

Aims & Methods: A virtual telephone clinic was set up during the COVID-19 pandemic. Patients in need of specialist gastroenterology input were identified by colorectal cancer nurse specialists, colorectal surgeons or oncology specialists in their follow up clinics. Patients were then reviewed by a gastroenterology research fellow via a telephone consultation. Investigations requested included blood tests, faecal elastase, faecal calprotectin, SeHCAT scan, abdominal x-ray and breath test.

Results: 38 patients (18 male, 20 female) were reviewed between October 2020 to October 2021. The median age was 71 (range 44 to 86) and the average duration of symptoms was 38 months (range 8 to 86). All had been diagnosed with colorectal cancer and received treatment that included surgery, chemotherapy, radiotherapy either alone or in combination with one another. Symptoms included loose stool, bloating, increased frequency and incontinence with diagnoses made shown in Table 1.

Constipation	8
Bile Acid Malabsorption	6
Pancreatic Insufficiency	5
Small Intestinal Bacterial Overgrowth	4
Radiation Proctopathy	2
Reoccurrence	2
Excessive Alcohol Intake	2
Fistula	2
Excess Fibre	2
Possible Colitis	1

Table 1

Patients' symptoms pre-referral and post treatment were assessed objectively using the gastrointestinal symptoms rating scale (GSRs), with an average GSRs on referral of 29.5, improving to 16.2 following investigation and treatment.

Conclusion: In most patients referred to our specialist clinic, we have been able to identify one or more cause for their problems. Treatment, that may include laxatives, bile acid sequestrants, antibiotics and dietary changes may lead to a dramatic improvement in symptoms. Future recommendations include earlier recognition of patients in need of specialist referral

through the use of symptom questionnaires, improved funding for this neglected field in post cancer treatment and the development of similar consequences of cancer clinics in trusts nationwide.

Disclosure: No conflict of interest.

P0602 WITHDRAWN

P0603

EVALUATION OF SHORT-TERM OUTCOMES FOR UNDERWATER ENDOSCOPIC MUCOSAL RESECTION AND ENDOSCOPIC SUBMUCOSAL DISSECTION FOR COLORECTAL POLYP 21-30 MM: A PROSPECTIVERANDOMIZED CONTROLLED PHASE 2 TRIAL

K. Okimoto¹, T. Matsumura¹, N. Akizue¹, T. Ishikawa¹, D. Maruoka¹, T. Kaneko¹, Y. Ohta¹, T. Taida¹, K. Saito¹, S. Ogasawara¹, Y. Inaba², K. Matsusaka³, J. Kato¹, J.-i. Ikeda³, N. Kato¹

¹Chiba University Hospital, Department of Gastroenterology, Graduate School of Medicine, Chiba, Japan, ²Chiba University Hospital Clinical Research Center, Biostatistics Section, Chiba, Japan, ³Graduate School of Medicine, Chiba University,, Department of Molecular Pathology, Chiba, Japan

Contact E-Mail Address: kenrunaway@yahoo.co.jp

Introduction: Both underwater endoscopic mucosal resection (UEMR) and endoscopic submucosal resection (ESD) are effective procedures for removing colorectal polyps. Currently, there are no prospective studies evaluating the short-term outcomes of UEMR and ESD for relatively large colorectal polyps. Thus, the aim of this phase 2 randomized controlled trial was to evaluate the short-term outcomes of UEMR and ESD for colonic polyps (21–30 mm).

Aims & Methods: We conducted a single center randomized controlled trial at Chiba University Hospital, Japan. This study was performed in accordance with the Declaration of Helsinki. The study protocol was reviewed and approved by the Chiba University Graduate School of Medicine Ethics Review Committee (registration no. G2020032) on January 21, 2021. The study protocol was not changed after trial commencement. All patients provided written informed consent. The study was registered in the Japan Registry of Clinical Trial as jRCT1030210015.

Patients diagnosed with suspected colorectal intramucosal carcinoma (diameter from 21–30 mm and adaptable for both UEMR and ESD) were randomly assigned in a 1:1 ratio to UEMR and ESD group. Only one polyp per one patient was enrolled. In total, 11 polyps in the UEMR group and 11 polyps in the ESD group were analyzed.

The primary endpoint was whether the lower limit of 95% confidence interval (CI) for the R0 resection rate (The polyp in the resected specimen is negative for horizontal and vertical margin) exceeds the set threshold. For UEMR, the threshold for R0 resection rate was set at 30%, and for ESD, the threshold for R0 resection rate was set at 40%.

Results: The R0 resection rate (%) (95% CI) was 36 (11-69)/ 100 (72-100) for UEMR and ESD respectively with significant difference (p=0.002, Welch Two Sample t-test). The lower limit of 95% CI for ESD exceeded the threshold of 40%, while the lower limit of 95% CI for UEMR did not exceed the threshold of 30%. En bloc resection rates (%) were 82 (48-97)/ 100 (72-100), respectively, and were not significantly different (p=0.167, Welch Two Sample t-test). There were no intraoperative/ delayed perforation nor delayed bleeding in both groups. Treatment time (min) mean ± standard deviation was 8 ± 6/ 48 ± 29, which was significantly shorter for UEMR (p=0.001, Welch Two Sample t-test). UEMR was performed in all cases as an outpatient and ESD was performed in all cases as an inpatient.

Conclusion: The R0 resection rate of UEMR did not exceed the set threshold, while that of ESD was preferable and superior. On the other hand, the en bloc resection rate was comparable between UEMR and ESD. UEMR may be beneficial with less burden on the patient in that it requires shorter procedure time compared to ESD, and can be performed on a outpatient basis.

Disclosure: There are no Conflict of Interest.

P0604

IMPACT OF FECAL IMMUNOCHEMICAL TEST SCREENING ON COLORECTAL CANCER INCIDENCE AND MORTALITY

P.H.A. Wisse¹, F.E.R. Vuik¹, W. de Klaver², S.A.V. Nieuwenburg¹, N. Erler³, I. Lansdorp-Vogelaar⁴, E. Dekker⁵, M.C.W. Spaander¹
¹Erasmus University Medical Center, Gastroenterology and Hepatology, Rotterdam, Netherlands, ²Amsterdam University Medical Center, Amsterdam, Netherlands, ³Erasmus University Medical Center, Biostatistics and Epidemiology, Rotterdam, Netherlands, ⁴Erasmus University Medical Center, Public Health, Rotterdam, Netherlands, ⁵Amsterdam University Medical Center, Gastroenterology & Hepatology, Amsterdam, Netherlands

Contact E-Mail Address: p.wisse@erasmusmc.nl

Introduction: Many countries have implemented fecal immunochemical test (FIT) -based colorectal cancer (CRC) screening programs. However, little is known about the effectiveness of FIT-based screening on CRC incidence and mortality.

The aim of this study was to evaluate this impact.

Aims & Methods: Before implementing a national screening program, a population-based cohort study was performed in The Netherlands. The screened individuals, aged 50-75 years, participated in a biennial FIT screening program between 2006-2014, with a follow-up until December 31st 2018. All Dutch inhabitants aged 50-75 years on January 1st 2006 - same time period as the screening cohort started - were used as reference cohort.

Since an organized nationwide CRC screening program was gradually implemented from 2014 onwards, persons in the reference cohort needed to be censored when they were eligible to participate in the national CRC screening program, resulting in a shorter follow-up time.

To enable analyses with a longer time horizon, we additionally included all Dutch inhabitants aged 50-75 years at January 1st 2001. They were eligible to participate in the nationwide CRC screening after at least 13-years and could therefore be followed until December 31st 2013. The Kaplan Meier method and Cox regression analysis were performed to evaluate the association between FIT screening and CRC incidence or mortality.

Results: In total, 15,397 individuals (mean age: 59.0 years; 52.6% female) participated at least once in the screening program ("screenees") and were compared to the cohort of non-screened individuals starting in 2001 (n=4,292,731) and the cohort starting in 2006 (n=4,682,982). The proportional hazards assumption of the Cox regression models was violated for age and year.

Therefore, analyses were performed by stratifying the follow-up time. Over 13-years of follow-up, screenees had a significantly lower CRC incidence (hazard ratio (HR) 0.78; 95%CI 0.68-0.90; p=0.001) compared to the non-screened individuals. In the first five years of screening an initial increase in cumulative CRC risk was found, followed by a subsequently decrease after seven years.

Screenees had a significantly lower CRC-related mortality (HR 0.39; 95%CI 0.29-0.53; p<0.001) compared to the non-screened individuals. Female gender was associated with a lower CRC-related mortality (HR 0.65; 95%

CI: 0.64-0.66, $p < 0.001$). Age was associated with an increased CRC-related mortality (HR 1.11 per year increase in the first two years of follow-up, which slightly decreased over time (HR 1.07 after 6 years).

Conclusion: Biennial FIT-based CRC screening is associated with lower CRC incidence and CRC-related mortality. However, healthy screenee bias cannot be ruled out. These results further encourage the implementation of FIT-based CRC screening programs.

Disclosure: Nothing to disclose.

P0605

ENDOSCOPIC SUBMUCOSAL DISSECTION OR PIECEMEAL ENDOSCOPIC MUCOSAL RESECTION FOR LARGE SUPERFICIAL COLORECTAL LESIONS: COST-EFFECTIVENESS IN THE ERA OF SYSTEMATIC COUNTERTRACTION

T. Wallenhorst¹, S. Scheer², J. Albouys³, R. Olivier⁴, M. Dahan⁵,
E. Pauliat^{6,7}, Q. Denost⁸, N. Christou⁹, S. Brischoux¹⁰, H. Lepetit¹¹,
G. Gschwind¹², R. Legros¹³, M. Pioche¹⁴, S. Geyl¹⁵, J. Jacques¹⁶

¹CHU Pontchaillou, Endoscopy Unit, Rennes, France,

²University Hospital of Poitiers, Gastroenterology Department,

Poitiers, France, ³CHU Limoges / University of Limoges,

Department of Gastroenterology, Limoges, France, ⁴CHU

de Poitiers, Vienne, Poitiers, France, ⁵CHU Limoges, Gastro-

enterology, Limoges, France, ⁶University Hospital of Vaudois,

Lausanne, Switzerland, ⁷University Hospital of Vaudois,

Pharm D, Lausanne, Switzerland, ⁸CHU de Bordeaux, Centre

Medico-chirurgical Magellan, Department of Colorectal

Surgery, Pessac, France, ⁹Limoges University Hospital,

Digestive Surgery, Limoges, France, ¹⁰University Hospital

of Limoges, Pharm D, Limoges, France, ¹¹CHU Limoges,

Gastroenterology Unit, Limoges, France, ¹²University Hospital

of Limoges, Public health care department, Limoges, France,

¹³Chu Limoges, Limoges, France, ¹⁴Hospices Civils de Lyon,

Gastroenterology and Endoscopy, Lyon, France, ¹⁵CHU Limoges,

Hepato-Gastro-Enterology, Limoges, France, ¹⁶CHU Limoges -

Hepato-Gastro-Enterology, Hepato-Gastro-Enterology, Limoges,
France

Contact E-Mail Address: timotheewallenhorst@gmail.com

Introduction: Endoscopic management is preferred to surgical management for large superficial colorectal lesions. However, the optimal endoscopic resection strategy (piecemeal endoscopic mucosal resection [pEMR] or endoscopic submucosal dissection [ESD]) is still debated from an economical point of view. To date, in France and other European countries, there is no Health Insurance reimbursement rate for either the procedure or the hospital stays related to ESD.

We searched to estimate the global cost of colorectal ESD and to define the most cost-effectiveness endoscopic strategy according to the resection strategy used and the results of optical diagnosis.

Aims & Methods: Since 1 January 2017, all superficial colorectal lesions larger than 20 mm have been removed by ESD with double clip traction (DCT-ESD) in our two centers. We searched to know what would have been the medical and economic outcomes if all those same lesions had been treated by a selective ESD or an exclusive pEMR strategies.

A model was created to compare the cost-effectiveness of ESD and pEMR according to optical diagnosis results using several classifications (Japan NBI Expert Team [JNET], laterally spreading tumour [LST], CONECCT) in real time before the procedure. We distinguished three groups from the same multicentre colorectal ESD cohort and compared the medical and economic outcomes. We also compared our real-life DCT-ESD data to modelled selective ESD and exclusive pEMR strategies.

We distinguished and analysed three groups from the same cohort.

1. Universal ESD strategy (U-ESD): actual strategy applied to the French multicentre cohort. All lesions were removed by DCT-ESD.
2. Selective ESD strategy (S-ESD): DCT-ESD was reserved for lesions considered at risk of submucosal cancer according to endoscopic classification (JNET IIb or CONECCT IIc or LST G with macronodule > 1cm or LST NG)
3. Universal pEMR strategy (U-EMR): removal of all lesions by pEMR.

Results: The en-bloc, R0, and curative resection rates were 97.5%, 86.5%, and 82.6%, respectively in the real life French ESD cohort of 833 colorectal lesions.

U-ESD was the least-expensive strategy, with a global cost of 2,858,048.17 €, i.e. 3,431.03 €/patient and was also the most effective strategy because it avoided 774 surgeries, which was more than any other strategy. It outperformed S-ESD CONECCT (global cost = 2,951,411.44 €, and 3,543.11 €/patient, 765 surgeries avoided, S-ESD LST (global cost = 3,055,951.53 €, and 3,668.61 €/patient, 749 surgeries avoided), and S-ESD JNET (global cost = 3,547,426.97 € and 4,258.62 €/patient, 704 surgeries avoided) and U-EMR (global cost = 4,060,547.62 € and 4,874.61 €/patient, 620 surgeries avoided). Even though a model which optimized pEMR results (0% technical failure, 0% primary surgery), U-EMR strategy remained the most expansive strategy and the one that avoided the least surgeries. Only the CONECCT classification referred to ESD whole submucosal cancer, contrary to LST and JNET classifications that missed 24% and 27% of those lesions by orienting them to pEMR.

Conclusion: In the era of clip-and-rubber-band countertraction, ESD for all large LSTs is more cost-effective than pEMR, and can be superior to a S-ESD depending on the reimbursement scheme.

The CONECCT classification, which combines overt and covert signs of carcinoma, is preferable to select lesions that will most benefit from an ESD. Data from the randomised French trial, RESECT-COLON (NCT03962868) are coming and may improve the management of patients with large colorectal LSTs.

Disclosure: Nothing to disclose.

P0606

A SECOND FIT AFTER A FIRST WEAK POSITIVE ONE AS A USEFUL STRATEGY TO REDUCE COLONOSCOPY LOAD IN CRC SCREENING

C. Borao¹, N. Saura Blasco², G. Hijos Mallada³,
R. Velamazán Sandalinas¹, A. Lanas⁴, C. Sostres Homedes⁵

¹Hospital Clínico Universitario Lozano Blesa, Zaragoza,

Spain, ²Hospital Clínico Universitario Lozano Blesa, Digestive

Diseases Service, Zaragoza, Spain, ³Hospital Clínico

Universitario Lozano Blesa, Gastroenterology, Zaragoza, Spain,

⁴University of Zaragoza University Hospital, Medicine and

Gastroenterology, Zaragoza, Spain, ⁵MYLAN, Gastroenterology,

Madrid, Spain

Contact E-Mail Address: crisboraolaguna@gmail.com

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: 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. We analyzed positive and negative predictive values (PPV and NPV), sensitivity (Se) and specificity (Sp).

The aim is to explore whether in those patients with a first FIT with a low positive determination ($\leq 35 \mu\text{gHb/g}$), a negative second FIT ($\leq 20 \mu\text{gHb/g}$) is associated with a low probability of CRC or those lesions that require endoscopic follow-up, according to ESGE 2020.

Results: 508 patients were included. In 220 (43.3%), the colonoscopy was normal. 20 cases of CRC (3.9%) and 133 (26.2%) of adenomas that require follow-up were diagnosed. In 347 (68.3%), the second FIT were negative. Considering patients with a low positive first FIT (132), the second was negative in 105 (79.5%). Diagnostic accuracy for all patients and for patients with a first low positive FIT is summarized in Table 1.

With a low positive first FIT ($\leq 35 \mu\text{gHb/g}$) and a negative second test, the probability of significant pathology (adjusted by sex and age) was 80% lower than in the other possible results in first FIT (high positive result, $> 35 \mu\text{gHb/g}$) and second FIT (positive result) (OR 0.2, 95% CI, 0.1-0.4). Nevertheless, with a positive first and second FIT, the probability of significant pathology is 4 times higher than in the other possible results (OR 4.8, 95% CI, 3.1-7.4).

		Se	Sp	PPV	NPV
All patients included (n= 508)	CRC (n=20)	75%	70.08%	9.32%	98.56%
	CRC + sessions that require follow-up (n= 153)	56.86%	79.15%	54.04%	80.98%
Patients with a first FIT $\leq 35 \mu\text{gHb/g}$ (n= 132)	CRC (n=3)	100%	81.4%	11.11%	100%
	CRC + sessions that require follow-up (n= 23)	52.17%	86.24%	44.44%	89.92%

Table 1.

Conclusion: In our CRC screening cohort, nearly 80% with a low positive ($\leq 35 \mu\text{gHb/g}$) first FIT had a negative second FIT, with a 90% NPV for CRC and lesions that require follow-up.

This strategy allows to reduce more than 20% of normal colonoscopies.

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P0607

3D COMPUTED TOMOGRAPHY IN PREOPERATIVE ANALYSIS OF VASCULAR ANATOMY OF PATIENTS WITH RIGHT SIDED COLON CANCER

A. Bedeniuk¹, I. Dzyubanovsky¹, S. Grytsenko¹, I. Hrytsenko²

¹Ternopil National Medical University, Department of Surgery with Urology №1 by L.Ya. Kovalchuk, Ternopil, Ukraine, ²Medical center "Omega", Kyiv, Ukraine

Contact E-Mail Address: stepan_grytsenko@ukr.net

Introduction: In modern science it is difficult, if not impossible, to say anything new in surgical vascular anatomy, but with widely used in clinical practice contrast-enhanced computed tomography (CT) has made it possible to reach a qualitatively new level in preoperative diagnosis and determination of treatment tactics for patients with colorectal cancer (CRC).

Aims & Methods: The aim of this study is to analyze the clinical and radiological aspects that usually need to be discussed before surgery by a multidisciplinary team in patients with right-sided colon cancer. Carry out a comparative analysis of 3DCT angiography data with intraoperative data. 103 patients with CRC who underwent preoperative 3D CT at Ternopil Regional Hospital between 2016 and 2021. We set the following objectives: determine the type of superior mesenteric artery (SMA); determine the distance from the root of the SMA to the root of the middle colic artery (MCA); the distance from the root of the MCA to the root of the ileocolic artery (ICA); variant structure of the right colic artery (RCA); the relationship between MCA and gastroduodenal trunk of Henle (TH); explore different variants of TH confluence.

Results: All patients underwent radical right hemicolectomy with complete mesocolic excision with central vascular ligation; the median quantity of removal lymph nodes were $24,71 \pm 10,04$ (range 13-58). Positive lymph nodes were revealed in 38,7 % cases. The incidence of metastatic lymph nodes in D1 zone was 38.7%, D2 zone - 3,2% and the zone D3 - 9,7%. Mean operative time was 82 minutes (range 63 -130 min).

Postoperative complications were developed in 7 patients. Anastomotic leakage was diagnosed in 1 patient. We have identified 8 types of SMA that are most common in practice: type A - MCA, RCA and ICA deviate classically independently of each other from the main SMA trunk; type B - RCA is absent; type C - RCA deviate from ICA; type D - RCA deviate from the right branch of the MCA or the main trunk of the MCA; type E - classical type A + the presence of additional MCA (AMCA); type F - right and left MCA branches deviate separately from the main SMA trunk; type G - MCA and ICA have a common trunk and RCA is absent; type H - RCA deviate from ICA + AMCA.

Our analysis showed that type A was detected in 27 (25.9%) patients, type B in 22 (21.4%) patients, type C in 20 (19.2%) patients, type D in 12 (11.6%) patients, type E in 9 (8.7%) patients, type F in 9 (8.7%) patients, type G in 3 (2.9%) patients and type H in 1 (0.9%) patients. In 64 (62,1 %) the ileocolic artery (ICA) crossed the superior mesenteric vein on the anterior surface and in 39 (37,9 %) on the posterior surface. In 58 (56.3%) patients RCA was either absent or was a non-independent branch of SMA. The distance from the root of the SMA to the root of the middle colic artery (MCA) was 37.8 ± 12.8 mm; from the root of the MCA to the root of the ICA was 29.5 ± 15.7 mm. In 66 (64.1%) patients trunk of Henle (TH) was above the root of the MCA, in 16 (15.5%) TH was at the same level with the MCA and in 18 (17.5%) TH was below the MCA.

Conclusion: Preoperative 3D-CT angiography is a key pattern in assessment of vascular anatomy and can potentially reduce intraoperative time for identifying key landmarks and reduce the risk of anastomotic leakage.

Disclosure: Nothing to disclose

P0608

COMPARISON OF TREATMENT OUTCOMES BETWEEN HOT SNARE POLYPECTOMY AND ENDOSCOPIC MUCOSAL RESECTION WITH BIPOLAR SNARE FOR 10-15 MM COLORECTAL LESIONS

N. Minakata¹, T. Murano¹, M. Wakabayashi², H. Sunakawa¹, K. Nakajo¹, T. Kadota¹, K. Shinmura¹, H. Ikematsu¹, T. Yano¹

¹National Cancer Center Hospital East, Department of Gastroenterology and Endoscopy, Kashiwa-shi, Japan, ²National Cancer Center, Biostatistics Division, Center for Research Administration and Support, Kashiwa-shi, Japan

Contact E-Mail Address: nminakat@east.ncc.go.jp

Introduction: Various methods have been developed to decrease complications associated with endoscopic resection (ER) for colorectal lesions. ER with bipolar snare, in which the electric current only passes through the tissue between the two electrodes of the device, is the one of prominent methods to potentially prevent perforation due to electricity.

In addition to the effect of reducing electronic damage to tissues, ER with bipolar snare has advantages over conventional monopolar snare in terms of safety and convenience, as it has less risk of burns even if any metal such as a pacemaker is present inside patients' body and doesn't require the attachment of a counter electrode.¹ In ex vivo porcine model, we recently reported that hot snare polypectomy (HSP) with bipolar snare for 10-15 mm lesions didn't cause thermal damage to the muscularis propria, whereas perforation was seen in HSP with monopolar snare.²

Furthermore, we found that such the thermal damage was not seen in bipolar HSP regardless of whether submucosal injection prior to resection is performed.

Therefore, ER with bipolar snare for 10-15 mm colorectal lesions is expected to have good treatment outcomes with high safety even without submucosal injection, but there are no reports comparing treatment outcomes with and without submucosal injection in clinical.

Aims & Methods: The aim of this study is to compare the outcomes of ER with bipolar snare for 10-15 mm colorectal lesions between HSP, which is the bipolar resection without submucosal injection, and endoscopic mucosal resection (EMR), which is the bipolar resection with submucosal injection.

We retrospectively enrolled all non-pedunculated colorectal lesions sized 10-15 mm which were diagnosed as JNET Type 2A by magnifying endoscopy and subsequently resected by either HSP or EMR at the National Cancer Center Hospital East between January 2018 and June 2021. We divided all polyps into two groups based on the treatment method, HSP and EMR group, respectively, and performed propensity score matching using age, gender, antithrombotic medication, lesion size, localization, morphology, and endoscopist experience as covariates.

And we compared en bloc resection rate, R0 resection rate, and the adverse events including delayed bleeding and perforation between HSP and EMR in the score matched cohort.

Results: Of the enrolled 565 polyps in 463 patients, 440 polyps in 346 patients were resected by HSP and 125 polyps in 117 patients were resected by EMR. After propensity score matching, 117 polyps in HSP group and 117 polyps in EMR group were finally selected, and almost all baseline characteristics became balanced (standardized differences < 0.1 between HSP and EMR). In the matched cohort, the en bloc resection rate was comparable in HSP group and EMR group (93.2% [109/117] vs 92.3% [108/117], chi-square test P=0.80).

There was no significant difference between HSP group and EMR group in the R0 resection rate (77.8% [91/117] vs 80.3% [94/117], P=0.63). The incidence of delayed bleeding was similar in the both groups, at 1.7% [2/117]. Perforation did not appear in the HSP group, but appeared in the EMR at 0.9% [1/117] (P=0.32).

Conclusion: There was no difference in treatment outcome between bipolar HSP and EMR. With bipolar snares, an effective and safe endoscopic resection may be achieved without submucosal injection for colorectal lesions sized 10-15 mm.

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P0609

DISCOVERY OF NOVEL COLON CANCER STEM CELL INHIBITORS BY INDUCING MULTIPLE REGULATED CELL DEATH PATHWAYS

M.B. Afonso¹, V. Marques¹, D.M. Pereira¹, J.C. David¹, A. Trindade², N. Aniceto¹, R. Capela¹, F. Lopes¹, A.S. Ressurreição¹, R. Pereira¹, A. Paulo¹, C.P. Frizzo³, M.M. Marques⁴, T.M. Pinho e Melo⁵, M. Salmain⁶, G. Jaouen^{6,7}, P. Pigeon^{6,7}, C. Alves⁸, H. Gaspar⁸, R. Pedrosa⁸, M.J.U. Ferreira¹, A. Duarte², R. Guedes¹, R. Moreira¹, C.A. Afonso¹, C.M. Rodrigues¹

¹Research Institute for Medicines (iMed.Ulisboa), Faculty of Pharmacy, Universidade de Lisboa, Biochemistry and Human Biology, Lisbon, Portugal, ²CIISA - Centro de Investigação Interdisciplinar em Sanidade Animal, Faculdade de Medicina Veterinária, Universidade de Lisboa, Lisbon, Portugal, ³Núcleo de Química de Heterociclos, Universidade Federal de Santa Maria, Santa Maria, Brazil, ⁴LAQV@REQUIMTE, Departamento de Química, Faculdade de Ciências e Tecnologia, Universidade Nova de Lisboa, Campus de Caparica, Caparica, Portugal, ⁵CQC and Department of Chemistry, University of Coimbra, Coimbra, Portugal, ⁶Sorbonne Université, CNRS, Institut Parisien de Chimie Moléculaire, Paris, France, ⁷Chimie ParisTech, PSL University, Paris, France, Paris, France, ⁸MARE-Marine and Environmental Sciences Centre, Instituto Politécnico de Leiria, Peniche, Portugal

Contact E-Mail Address: mbafonso@ff.ul.pt

Introduction: Cancer stem cells (CSCs) are implied in tumour formation, metastasis and recurrence. Here, we aimed to optimize and apply a phenotypic high-throughput screening (HTS) platform to identify novel molecules from diverse compound libraries that specifically impact on colorectal CSC phenotype.

Aims & Methods: Cell viability of HT-29, SW-620 and HCT116 cell lines plated at low density, in undifferentiated medium, in ultra-low attachment conditions for sphere formation was assessed upon incubation with compounds from in-house and external libraries for 7 days. Hit efficacy was validated *in vivo* in a HT-29 xenograft model at 10 mg/kg i.p., 3 days/week. The *in vivo* extreme limiting dilution assay was further used to determine the impact of the lead in colorectal CSCs. Target deconvolution was performed by machine learning, and molecular docking further applied to specific targets. The viability of CSC-enriched tumorspheres treated with the hit in the presence or absence of chemical inhibitors of distinct cell death modalities was assessed.

Results: The primary screening tested ~1500 compounds at 1 µM in HT-29-derived tumorspheres, leading to a 10% hit rate for the full library. Dose-response curves were built, and 69 compounds showed a half-maximal inhibitory concentration (IC₅₀) ≤ 2 µM. Twenty-four compounds were further selected based on their structural diversity and predicted drug-like properties and 17 compounds displayed an IC₅₀ ≤ 2 µM in HCT116 and SW-620 spheroids. From those, 7 compounds at the IC₅₀ dose robustly decreased the number and/or area of spheres *in vitro*.

Finally, 5 compounds were well tolerated in mice and prevented tumour growth in subcutaneous xenografts, accompanied by a reduction of stemness and increased differentiation markers. From those, 2 hits were tested *in vivo* extreme limiting dilution assay, showing the ability to reduce the colorectal cancer-initiating cell frequency.

Computational tools identified Bcl-2 as the putative target more prevalent in actives, while differentiation, iron homeostasis and ferroptosis are signalling pathways commonly modulated. The docking score and ligand efficiency, two readouts produced by molecular docking, further validated Bcl-2 as a potential target of a novel chemical scaffold. Curiously, although Bcl-2 is low expressed in HT-29 cells, the hit induced apoptosis, necroptosis and ferroptosis in both HT-29- and HCT116-derived CSC-enriched tu-

morspheres, concomitant with an increased extracellular release of ATP, a well-established damage associated molecular pattern. Future work will further validate the induction of immunogenic cell death by the hit, and dissect the contribution of Bcl-2 for its effect.

Conclusion: In conclusion, an HTS platform to test a wide range of candidate compounds targeting CSCs was developed, allowing the identification of novel colon cancer stem cell inhibitors that may grasp the tumor biological space and this therapeutic arena. In particular, a novel chemical scaffold was identified as an inhibitor of both bulk colon tumor cells and CSCs by triggering multiple types of regulated cell death with potential immunogenicity.

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P0610

SHORT-TERM OUTCOMES OF STAGE II/III NON-RIGHT-SIDED OBSTRUCTIVE COLON CANCER WITH SELF-EXPANDING METALLIC STENT OR TRANS-ANAL COLORECTAL TUBE PLACEMENT

K. Uno^{1,2}, T. Shimura¹, Y. Okuda¹, T. Yamada², T. Nukui³, T. Mizushima³, Y. Takenaka⁴, K. Ito⁴, Y. Inagaki⁵, T. Iwai⁵, K. Nagao⁶, M. Ebi⁶, E. Uchida⁷, S. Nomura⁷, Y. Nojiri⁸, S. Togawa⁸, H. Kataoka¹
¹Nagoya City University Graduate School of Medical Sciences, Department of Gastroenterology and Metabolism, Nagoya, Japan, ²Japanese Red Cross Aichi Medical Center Nagoya Daini Hospital, Department of Gastroenterology, Nagoya, Japan, ³Gifu Prefectural Tajimi Hospital, Department of Gastroenterology, Tajimi, Japan, ⁴Nagoya City University East Medical Center, Department of Gastroenterology, Nagoya, Japan, ⁵Toyokawa City Hospital, Department of Gastroenterology, Toyokawa, Japan, ⁶Aichi Medical University, Department of Gastroenterology, Nagakute, Japan, ⁷Nagoya City University West Medical Center, Department of Gastroenterology, Nagoya, Japan, ⁸Nagoya Memorial Hospital, Department of Gastroenterology, Nagoya, Japan

Contact E-Mail Address: k_uno510@yahoo.co.jp

Introduction: Non-right-sided obstructive colon cancer (NROCC) is an emergency situation causing high morbidity and mortality in the short term. Although emergency surgery is regarded as standard therapy for NROCC, one-stage surgery without colostomy is occasionally difficult in this emergency setting. Trans-anal colorectal tube (TCT) and self-expanding metallic stent (SEMS) are alternatives to conventional surgery for NROCC, enabling one-stage surgery without colostomy. We have previously shown that TCT can achieve safe one-stage surgery with laparoscopy-assisted colectomy¹ and equivalent long-term outcomes to emergency surgery for stage II/III NROCC².

SEMS is another alternative treatment for NROCC used worldwide; however, it remains controversial which one can achieve better short-term outcomes. Hence, we conducted a multicenter retrospective case-control study to analyze TCT and SEMS for NROCC, focusing on short-term outcomes.

Aims & Methods: Data from consecutive stage II/III NROCC patients who underwent surgery between January 2010 and December 2019 were retrospectively reviewed using the computerized databases at eight Japanese affiliate hospitals with the mutual exchange of endoscopists. NROCC was defined as obstructive colon cancer located in the transverse to the sigmoid colon. Propensity score (PS) matching was used to adjust baseline characteristics between the TCT and the SEMS groups.

Results: Among the 239 patients with stage II/III NROCC (TCT group 163 cases, SEMS group 76 cases), the PS matching identified 115 cases in the TCT group and 65 cases in the SEMS group. Baseline characteristics were well balanced between the two groups.

No significant differences were found in the technical success rate (TCT vs. SEMS, 98.3% vs. 98.5%, $p > 0.999$), clinical success rate (TCT vs. SEMS, 89.6% vs. 95.4%, $p = 0.175$), decompression-related perforation (TCT vs. SEMS, 7.0% vs. 4.6%, $p = 0.748$), and postoperative complications ($\geq$ grade 3) (TCT vs. SEMS, 10.4% vs. 7.7%, $p = 0.546$) between the TCT and SEMS groups. There were no deaths within 30 days of decompression in both the TCT and SEMS groups.

The primary resection/anastomosis rate in the SEMS group was significantly higher than in the TCT group (TCT vs. SEMS, 77.4% vs. 90.8%, $p < 0.001$), and overall stoma rates were significantly lower in the SEMS group than in the TCT group (TCT vs. SEMS, 22.6% vs. 9.2%, $p < 0.001$). The SEMS group achieved a significantly higher laparoscopic surgery rate than the TCT group (TCT vs. SEMS, 43.5% vs. 64.6%, $p < 0.001$).

Furthermore, the technical decompression time was significantly shorter in the SEMS group than in the TCT group (TCT vs. SEMS, 26 minutes vs. 21 minutes, $p = 0.046$).

Conclusion: Although both SEMS and TCT achieved similar technical and clinical success rates, SEMS placement enabled more primary resection/anastomosis and laparoscopic surgery than TCT for stage II/III NROCC patients, with shorter decompression times.

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P0611

MALIGNANT COLORECTAL POLYPS - ARE WE GETTING SUFFICIENT INFORMATION TO GUIDE MANAGEMENT?

C. Rodrigues¹, P. Sousa¹, A.C. Carvalho¹, S. Ventura¹, Â. Domingues¹, F.J. Sanches Pires¹, D. Martins¹, J. Pinho¹, R. Cardoso¹, R. Araújo¹, E. Cancela¹, P. Ministro¹, A. Castanheira¹, A. Silva¹

¹Centro Hospitalar Tondela-Viseu, Department of Gastroenterology, Viseu, Portugal

Contact E-Mail Address: claudiomelordrigues@gmail.com

Introduction: Malignant colorectal polyps (MPs) are polyps in which histology confirms the presence of carcinoma invading into the submucosa. A dilemma is evident after diagnosis of a MP: is surgery necessary to warrant complete clearance of disease or is polypectomy enough? The risks of major resectional surgery when no remaining disease is present versus recurrent/residual disease not properly treated are clear.

Aims & Methods: This was a single center, retrospective study, involving a cohort of patients referred to a multidisciplinary team (MDT) after endoscopic resection of MP between 2015-2021.

The primary aim was to assess the overall management of MPs in our center, the level of histological reporting of MPs and oncologic outcomes. Clinical, endoscopic and histopathological features were collected. High risk malignant polyp was considered if at least 1 high risk feature (HRF) was present; piecemeal resection; invasion depth > 1 mm (Haggitt 4: pedunculated tumours; Kikuchi 2/3: non pedunculated tumours); lymphovascular invasion; tumour budding; poor differentiation; positive resection margins/cannot be assessed.

Results: 72 patients were included, with 65% ($n=47$) being males and a median age of 69 (34-90) years. The median size of lesions was 20 mm (8-60) and most were located at sigmoid colon 61,1% ($n=44$). A polypoid morphology was present in 84,7%.

Piecemeal resection was performed in 27,8% (n=20); invasion depth > 1 mm in 30,6% (n=22) and not quantified in 58,3% (n=42); positive, indeterminate, or < 1 mm vertical margin in 62,5% (n=45); lymphatic invasion in 6,9% (n=5) and not reported in 16,7% (n=12); vascular invasion in 2,8 % (n=2) and not reported in 12,5% (n=9); poor differentiation in 2,8% (n=2) and degree not differentiated in 11,1% (n=8); tumour budding was present in 23,6% (n=37) and not reported in 66,7% (n=48); Haggitt 4 in none and Kikuchi 2/3 in 9,7% (n=7).

Overall, 75% (n=54) of patients had at least one HRF. The median follow-up was approximately 26 months (6-52).

Surgery with lymph node dissection was proposed to 38 patients, but 3 patients refused. Laparoscopic surgery was the preferred approach (n = 26). Two anastomotic colorectal leakages occurred after sigmoidectomy, one case after open surgery and the other after laparoscopic approach.

One patient had prohibitive factors for surgery and was proposed for chemoradiotherapy and posterior 'watchful waiting' approach and is doing well.

A total of 36 (50%) patients were managed with surveillance.

Residual lesion in lymph nodes was found in 3 (8,6%) patients submitted to surgery (n=35), and no residual disease was found in bowel wall. Distant metastasis at follow-up were found in 2 patients in surveillance: one had recurrent cancer (rectum, piecemeal resection) with hepatic and pulmonary metastases and another patient died from hepatic metastases (rectum, piecemeal resection).

4 patients died of other causes, without evidence of local or metastatic disease at last follow-up.

Conclusion: Metastatic lymph nodes were identified in 8,6%, a value in accordance with the literature (7,0-13,0%) (1,2). Those managed with bowel resection had no residual invasive disease in the resection specimen, meaning many patients undergoing bowel resection gained no additional benefit from major surgery with its associated risks.

Our findings point out that variables such as tumour budding and depth of submucosal invasion are between the less reported in real-world clinical practice. Hence, we highlight the importance of achieving complete histological reports to better refine risk stratification.

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Disclosure: Nothing to disclose.

P0612

QUALITY OF LIFE AND FUNCTIONAL OUTCOMES AFTER ILEORECTAL OR ILEOSIGMOIDAL ANASTOMOSIS VERSUS ILEAL POUCH-ANAL ANASTOMOSIS IN PATIENTS WITH FAMILIAL ADENOMATOUS POLYPOSIS

A.S. Aelvoet¹, T.N. Miedema¹, B.A.J. Bastiaansen¹, W.A. Bemelman², R. Hompes², E. Dekker¹

¹Amsterdam UMC Location University of Amsterdam, Cancer Center, Amsterdam Gastroenterology Endocrinology Metabolism, Gastroenterology and Hepatology, Amsterdam, Netherlands,

²Amsterdam UMC Location University of Amsterdam, Cancer Center, Surgery, Amsterdam, Netherlands

Contact E-Mail Address: a.s.aelvoet@amsterdamumc.nl

Introduction: To prevent colorectal cancer, patients with familial adenomatous polyposis (FAP) undergo colectomy at a young age. In most patients an ileorectal/ileosigmoidal anastomosis (IRA/ISA) or ileal pouch-

anal anastomosis (IPAA) is created. We aimed to compare the quality of life and functional outcomes after IRA/ISA versus IPAA and after open versus laparoscopic surgery.

Aims & Methods: We performed a cross-sectional questionnaire study including FAP patients with IRA/ISA and IPAA. Quality of life was assessed using the Short Form-36 (SF-36) health survey. Functional outcomes included bowel function, urological function and sexual function and those were assessed using the Vaizey score (including stool frequency), International Prostate Symptom Score (IPSS) for both men and women, International Index of Erectile Dysfunction (IIEF) and the Female Sexual Function Index (FSFI).

The primary aim was to compare IRA/ISA to IPAA and in sub-analysis we compared open versus laparoscopic surgery, primary versus secondary IPAA (after previous IRA/ISA), handsewn versus stapled IPAA and IRA versus ISA. Moreover, we studied the relation between bowel function and quality of life.

Results: Questionnaires were sent to 115 patients and returned by 92: 25 IRA/ISA patients, 67 IPAA patients (response rate 80%). We only included patients who filled in the questionnaires over 50%. No difference in quality of life, urological function or sexual function were observed between the groups. Although the stool frequency was significantly higher in the IPAA group (7.3 ± 3.8 versus 4.8 ± 2.3 , $p = 0.002$), no difference in incontinence was observed.

Sexual function was significantly better in patients who underwent laparoscopic IPAA vs open IPAA and a non-significant trend towards a better bowel and urological function after laparoscopic IPAA was observed. These differences were not seen when comparing open to laparoscopic IRA/ISA. Patients with primary IPAA had a significantly better urological function compared to patients with secondary IPAA ($p=0.011$) and almost significantly better incontinence score ($p=0.065$).

Comparing patients with IRA vs ISA and handsewn vs stapled IPAA did not show any differences. Patients with a stool frequency of 8 or higher and patients with higher fecal incontinence score (Vaizey score >12) had a significantly lower quality of life.

Conclusion: FAP patients with IRA/ISA and IPAA reported equal outcomes on quality of life, urological and sexual function. Bowel function was worse after IPAA and since bowel function was related to quality of life, IRA/ISA seems the preferred type of operation, if safe in terms of rectal polyp burden.

For IPAA, laparoscopic surgery results in better functional outcomes, and IPAA after previous IRA/ISA has worse functional outcomes compared to primary IPAA. These findings inform surgical counseling. However, larger studies are needed to confirm our findings.

Disclosure: Nothing to disclose.

P0613

THE NECESSARY PROPRIETY OF ADDITIONAL SURGERY FOR ELDERLY PATIENTS WITH T1 COLORECTAL CANCERS TREATED BY ENDOSCOPIC RESECTION

H. Miyachi¹, S. Kudo¹, K. Ichimasa^{2,1}, Y. Kouyama¹, K. Mochizuki¹, Y. Takashina¹, Y. Miyata¹, Y. Ogawa¹, Y. Maeda¹, H. Nakamura¹, S. Matsudaira¹, Y. Mori^{3,1}, M. Misawa¹, N. Ogata¹, T. Hisayuki¹, T. Kudo¹, T. Hayashi¹, K. Wakamura¹, N. Sawada¹, T. Baba¹, T. Nemoto⁴, F. Ishida¹

¹Showa University Northern Yokohama Hospital, Digestive Disease Center, Yokohama, Japan, ²National University Hospital, Department of Gastroenterology and Hepatology, Singapore, ³Institute of Health and Society, University of Oslo, Clinical Effectiveness Research Group, Oslo, Norway, ⁴Showa University Northern Yokohama Hospital, Department of Diagnostic Pathology, Yokohama, Japan

Contact E-Mail Address: miyachi@med.showa-u.ac.jp

Introduction: In the current guidelines around the world, the indication of surgical resection (SR) with lymph node dissection for T1 colorectal cancers (CRCs) is based merely on the risk of simultaneous lymph node metastasis, with no consideration of metachronous recurrence or overall survival (OS). It is also unclear whether SR can prolong OS by reducing recurrence. Moreover, there is no clear guidances on whether the indication criteria for additional SR in elderly patients should be the same as in non-elderly ones.

Aims & Methods: The aim of this study is to reconsider the indication for additional SR after ER for T1 CRC patients, taking into account recurrence and age. Of the 1359 patients with T1 CRCs endoscopically or surgically resected at our center from April 2001 to March 2019, 1271 patients (excluding complications of advanced cancer or hereditary colorectal cancer and so on) were retrospectively reviewed.

The 1271 subjects were divided into endoscopic treatment alone (ER) and surgical resection (SR) groups, and the effects of SR on distant recurrence and overall survival (OS) were examined. The OS was also compared focusing on the target population of 80 years of age and older.

Results: The mean observation period was 73.5 months. No recurrence was observed in the 287 patients who had no factors for additional SR according to the JSCCR guidelines. Among the 984 patients for whom additional SR should be recommended, 6 (3.33%) of the 180 patients in the ER alone group recurred and 4 (2.22%) died, while 9 (1.12%) of the 804 patients in the SR group recurred and 4 (0.50%) died.

Among the overall 1271 patients, the OS was significantly shorter in the ER alone group than in the SR group ($p=0.0017$). In those ≤ 80 years old, that was also shorter in the ER alone group ($p=0.047$), while in those >80 years, no significant difference was found in the OS ($p=0.49$) after propensity-score matching analysis.

Conclusion: For the overall T1 CRC patients, SR with lymph node dissection would reduce recurrence and prolong their OS, however, the effect on OS might disappear for the patients >80 years of age.

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P0614

IMPACT OF PRE-TREATMENT SARCOPENIA IN PATIENTS WITH COLORECTAL CANCER

Y. Ben Hamadi¹, M. Ayari¹, W. Khemiri¹, M. Mtir¹, A. Chehaider¹, I. Abdelaali¹, T. Jomni¹, M.H. Douggu¹

¹Internal Security Forces Hospital La Marsa, Gastroenterology Department, Tunis, Tunisia

Contact E-Mail Address: ayari.myriam@hotmail.fr

Introduction: Colorectal Cancer (CRC) is the third most common cancer diagnosed worldwide with an increasing incidence. In addition to traditional prognostic factors (high histologic grade, lymph node status, involved margins, tumor size) the identification of new clinical markers is the goal of ongoing research to improve the therapeutic management. In this context, there is growing awareness of the relationship between sarcopenia and outcomes in cancer including CRC, as sarcopenia patients may present impaired nutritional and immunological factors suggesting lower response to consecutive anti-tumor treatments.

Aims & Methods: The aim of our study was to determine the prevalence and to assess the impact of sarcopenia in CRC patients. we conducted a retrospective single-center study including patients diagnosed with CRC in between 2014 and 2021.

We collected anthropometric measurements, clinical, biological, histological data and outcomes. Total psoas muscle area (TPA) was determined by analyzing the tomographic total cross-sectional area of left and right psoas muscle at the level of lumbar 3rd vertebra at initial staging computed tomography. Then, the total psoas area index (TPAI) was calculated using the equation: $TPAI = TPA (mm^2) / height (m^2)$. The TPAI cut-offs used to define sarcopenia were $385 mm^2/m^2$ for female patients and $545 mm^2/m^2$ for male patients. We investigated the associated factors to sarcopenia. The Kaplan Meier method was used to analyse the influence of sarcopenia on overall survival (OS).

Results: Sixty-one patients were included. The mean age was 60.69 years (extremes: 32-88 years) and sex-ratio M/F of 2.05. The tumor was located in the right colon in 21 patients (34%), in the left colon in 22 patients (36%) and in the rectum in 18 patients (30%). Lieberkuhnien adenocarcinoma was the most frequent histological type (78.3%).

According to TNM classification, patients were mainly classified in stage II and stage III. Regarding treatment, 17 patients received neoadjuvant chemotherapy (27.9%), 10 patients received neoadjuvant radiotherapy (6.1%) and 51 patients underwent surgery (83.6%) divided between primary curative surgery (72%), urgent surgery (23%) and palliative surgery (5%). Adjuvant chemotherapy was indicated in 30 patients (62.5%).

The mean TPA was $555.95 \pm 222.12 mm^2$ (range 187.24-1718.24 mm^2). The overall incidence of sarcopenia was 42% (N=21) according to sex-adjusted cutoff. The mean survival was 27.35 months. The overall survival at 1 year and 3 years was of 76% and 67% respectively.

On univariate analysis, sarcopenia was significantly associated with elder age ≥ 65 years ($p=0.015$), male gender ($p=0.007$), bowel obstruction revealing CRC ($p=0.041$), lymphopenia ($p=0.015$), right-sided cancer ($p=0.036$), vascular emboli and perineural invasion ($p=0.03$). In terms of survival, sarcopenia was predictive of lower survival with statistically significant difference between the two Kaplan-Meier curves of sarcopenic versus non-sarcopenic patients (log rank test $p=0.008$).

Conclusion: In our study, pre-treatment sarcopenia negatively impacts the overall survival. Total psoas area index is valuable to assess sarcopenia which should be routinely screened in every patients with CRC at first presentation and considered in therapeutic management.

Disclosure: Nothing to disclose.

P0615

ENDOSCOPIC SUBMUCOSAL DISSECTION IS SAFE AND EFFECTIVE FOR LESIONS LOCATED AT THE ANO-RECTAL JUNCTION: ANALYSIS FROM TWO REFERRAL EUROPEAN CENTRES

M. Figueiredo Ferreira¹, J. Santos-Antunes², M. Marques², R. Morais², A. Lemmers¹, G. Macedo²

¹Erasmus University Hospital, Gastroenterology, Brussels, Belgium,

²Centro Hospitalar São João, Gastroenterology Department, Porto, Portugal

Contact E-Mail Address: mariana.fig.ferreira@gmail.com

Introduction: Endoscopic submucosal dissection (ESD) is well-established resection technique for colorectal superficial tumours. However, evidence of its efficacy in anorectal junctions is still scarce. We aimed to evaluate the feasibility, safety and efficacy of ESD for anorectal junction lesions (<20 mm from the dentate line) in comparison to more proximal rectal lesions.

Aims & Methods: Retrospective analysis of prospectively collected registries from two European referral centers, from 2015 to 2021.

Results: Two hundred and fifty-two lesions were included. From them, 60 (24%) were located in the anorectal junction, and the remaining 192 were located elsewhere in the rectum. Technical success was achieved in 248 procedures (98%), and it was similar in both locations ($p=0.246$). Most of them had high-grade dysplasia/ Tis adenocarcinoma (54%); 36 (15%) had submucosal adenocarcinoma, being 16 deeply invasive (>SM1 T1 cancers).

We found no differences between anorectal junction and rectal lesions regarding en bloc resection (100%vs96%, $p=0.204$), R0 resection (76%vs75%, $p=0.531$), curative resection (70%vs70%, $p=0.920$), duration of ESD (median 120min vs 90min, $p=0.072$), ESD velocity (14vs12 mm²/min, $p=0.415$) or histopathology result ($p=0.053$), as well as the need of surgery due to a non-curative ESD (5%vs3%, $p=0.739$).

Also, delayed bleeding (7%vs8%, $p=0.709$), perforation (0%vs5%, $p=0.075$) and the need of late admission due to adverse events (2% vs 2%, $p=0.939$) was similar. Ano-rectal stenosis ($p=0.003$) and anorectal pain ($p=0.002$) were more frequent in anorectal junction lesions.

Conclusion: ESD is a safe and efficient resection technique for the treatment of rectal lesions located in the anorectal junction.

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Disclosure: Nothing to disclose.

P0616

CLINICAL AUDIT OF ENBLOC RESECTION FOR LARGE COLORECTAL MUCOSAL LESIONS USING ENDOSCOPIC SUBMUCOSAL DISSECTION (ESD) FROM A SINGLE CENTER FROM A REGION NON ENDEMIC FOR COLORECTAL CANCER – ASSESSING THE PREDICTIVE FACTORS FOR DIFFICULT ESD AND LEARNING CURVE FOR ESD

J. Ansari¹, H. Bapaye², H. Raina¹, M. Borkar¹, A. Gandhi¹, P. Bharambe¹, S. Gokhale¹, J. Bapaye³, R. Pujari¹, H. Gadhihar¹, A. Bapaye¹

¹Deenanath Mangeshkar Hospital, Shivanand Desai Center for Digestive Diseases, Pune, India, ²Byramjee Jeejeebhoy Medical College, Department of Internal Medicine, Pune, India, ³Rochester General Hospital, Internal Medicine, New York, United States

Contact E-Mail Address: jaseem10ansari@gmail.com

Introduction: Large >2cm colorectal mucosal neoplasms can be resected using endoscopic submucosal dissection (ESD) or endoscopic mucosal resection (EMR). Enbloc resection is desirable to provide accurate post-resection histological assessment; and to minimize risk of recurrence. EMR for larger lesions often requires piecemeal resection (EMR-p) and ESD has superior enbloc resection rates.

Colorectal ESD, however, is technically difficult, time consuming, and is associated with a steep learning curve. There is limited data evaluating predictors associated with difficult colorectal ESD. The current single center clinical audit of colorectal ESD identifies factors predicting difficulty to perform colorectal ESD and those increasing risk of failure of enbloc resection; and calculates the learning curve to achieve competency to perform colorectal ESD for large (>2cm) colorectal mucosal neoplasms.

Aims & Methods: Single center retrospective evaluation of a prospectively maintained database. Study duration – 10 years (2012 – 2021). Data of 149 consecutive patients with large >2cm colorectal mucosal neoplasms undergoing ESD was abstracted. Parameters studied included colonic segment (rectum, left, right, anastomotic site), prior resection attempt, dissection speed (S), adverse events (AE), enbloc and R0 resection rates. Primary outcome was to identify factors predicting difficulty while performing ESD. Secondary outcomes were to identify risk factors for failure of enbloc resection and to assess the learning curve based on enbloc resection rate, S and AE.

Results: N = 149; mean age – 61.36 years, 101 males (67.8%). Mean size of colorectal neoplasm –46.62mm (±25.46), Median 40mm (IQR 30-60, Range 20-125). Successful enbloc resection – 141/149 (94.6%), (EMR-p = 7, failure – 1) and successful R0 resection – 132/142 (92.9%). AEs = 6 (4%) – Bleeding – 1 (Endotherapy), deep muscle injury – 2 (Endotherapy – 1, Surgery – 1), Others-3 (unrelated, treated conservatively). Mean S for cohort was 9.03 ± 7.94 mm²/min. Speed was fastest for rectum – 10.9 and slowest for right colon – 4.22 with sigmoid – 5.72, anastomotic site – 4.72 being in between. Mean procedure time was significantly prolonged in patients with previous resection attempt (298.44 min ±161.1) compared to naïve lesions (209.77 min ±146.44) ($p<0.009$).

Increase in procedure time showed a significant positive correlation with increase in area of the lesion ($\rho = 0.64$, $p = <0.001$); with procedure time increasing by a mean 3min for every 100mm² increase in area of the lesion. ROC curve analysis estimated lesion size of ≤ 68 (mm) as a predictor for enbloc resection (PPV 95.8%, OR 14.06, $p<0.001$). Univariate regression analysis identified size of the lesion as the single independent predictive factor for enbloc resection (OR 0.96; 0.95–0.98; $p < 0.001$).

Tumor location and prior resection attempt were associated with dissection speed and AEs, but not with enbloc resection. Learning curve analysis revealed a minimum 47 procedures to attain competency in colorectal ESD.

Conclusion: This clinical audit of colorectal ESD from a non-endemic population for lower GI polyps and mucosal cancers revealed that lesion size was the single most important determinant of success for enbloc resection. Lesions in the right colon, anastomotic site and patients with history of previous resection attempts were associated with longer procedure times. The learning curve to attain competency in ESD was approximately 47 procedures.

Disclosure: Nothing to disclose.

P0617

CLINICAL OUTCOMES OF ENDOSCOPIC STENT INSERTION OR BYPASS OPERATION FOR MALIGNANT COLONIC OBSTRUCTION DUE TO PANCREATOBILIARY CANCER

C.S. Park¹, J. Park², E.A. Kang², S.J. Park³, M.-J. Chung³, J.Y. Park⁴, J.H. Cheon⁴, S. Bang², S.W. Park², T.I. Kim², S.-Y. Song⁴, J.J. Park²

¹Yonsei University, Seoul, Korea (Republic of), ²Severance Hospital, Yonsei University College of Medicine, Internal Medicine, Seoul, Korea (Republic of), ³Yonsei University, Gastroenterology, Seoul, Korea (Republic of), ⁴Yonsei University, College of Medicine, Internal Medicine, Seoul, Korea (Republic of)

Contact E-Mail Address: wpakcs@yuhs.ac

Introduction: Although self-expandable metal stent (SEMS) insertion has been shown to be an effective therapy for palliation of obstruction from pancreatobiliary malignancy, Studies on comparative clinical outcomes to bypass surgery is limited.

Aims & Methods: This is a retrospective, single tertiary-center study that involved all consecutive patients with pancreatic cancer or biliary tract cancer who were treated with SEMS (n=58) or emergency surgery (n=5) for palliation of malignant colorectal obstruction between January 2005 and December 2021. Time to recurrent obstruction requiring additional intervention and stent patency was analyzed by Kaplan-Meier analysis. Factors related to clinical outcomes were analyzed by log-rank test and Cox regression analysis.

Results: The types of cancer included were 48 patients (82.8.2%) with pancreatic cancer, 3 patients (5.2%) with biliary cancer, and Gallbladder cancer is 7 (12.1%). The technical succession rate of the SEMS group and emergency surgery group was 98.1% (52/53) and 100%(5/5), and the clinical success rate was 91.4%(53/45) and 100%(5/5), respectively. There was no significant statistical difference between SEMS and the bypass operation group (p=0.349). Regarding the time to recurrent obstruction required additional intervention, there was no marginally improved longer duration of time to recurrent obstruction in the bypass operation group. (p=0.101)

When we analyzed in a subgroup of the stent population, palliative chemotherapy after stenting was associated with increased duration of stent patency(p=0.019, Log-rank).

Conclusion: In patients with colorectal obstruction due to pancreatobiliary malignancy, the short-term clinical outcomes of the bypass surgery group were comparable to the stent group. However, the surgery group showed a trend for favorable long-term outcomes in terms of reintervention-free survival. Palliative chemotherapy was associated with an increased duration of stent patency.

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Disclosure: Nothing to disclose.

P0618

THE ENGLISH BOWEL CANCER SCREENING PROGRAMME: DESIGNED FOR AN ASYMPTOMATIC POPULATION, BUT IS THIS THE CASE?

S. Serna¹, R. Granville¹, T. Baldwin¹, A.M. Verma¹

¹Kettering General Hospital, Department of Digestive Diseases, Kettering, United Kingdom

Contact E-Mail Address: ajay.verma@nhs.net

Introduction: The English Bowel Cancer Screening Programme(BCSP) was designed to screen an asymptomatic middle-aged population for pre-malignant colonic adenomas and early colorectal cancer (CRC). Whilst the programme is considered a success, ~40% of those diagnosed with CRC are still having adverse outcomes with advanced disease which is non-curable.¹ When informing patients of a CRC diagnosis at colonoscopy, it is not uncommon to hear that they have had suggestive symptoms for many months. We aim to evaluate the proportion of patients diagnosed with CRC at BCSP, who have suggestive symptoms.

Aims & Methods: Data from the BCSP reporting database on symptoms recorded by the specialist screening nurse practitioners at pre-endoscopy assessments for patients diagnosed with CRC were analysed. Symptoms were classified as red flag(based on urgent cancer pathway referral criteria in England); change in bowel habit, rectal bleeding, weight loss, abdominal pain, and other; chronic diarrhoea, constipation, mucous discharge, urgency of defecation, rectal irritation.

Results: Data were analysed on symptoms recorded pre-endoscopy from 316 patients diagnosed with CRC in BCSP 2015-2021 (7 years) in the Northamptonshire County BCSP.

- 180 males (57.0%) / 132 female (41.8%) / 4 unrecorded (1.3%)
- Mean / median age = 68.0 / 68.7 years
- 69 patients were asymptomatic (21.8%)
- 247 patients were symptomatic (78.2%), **HR 3.58** (95% CI 2.63-4.88; **p <0.0001**)
- 166 had red flag symptoms (52.5%), **HR 2.41** (95% CI 1.75-3.32; **p <0.0001**)
- The most common reported symptom reported by patients was urgency of defecation (49.9%)
- The most common reported "red flag" symptom was change in bowel habit (45.8%)

Conclusion: This analysis significantly shows that the vast majority of patients diagnosed with CRC in the English BCSP were symptomatic, with over half having red flag symptoms. Those patients should have ideally been managed on symptomatic pathways (especially those with "red flag" symptoms) in a timely manner.

Despite the BCSP in England being aimed at an asymptomatic population, it is possibly acting as a safety net for those with suggestive symptoms for weeks or months. It is sobering to contemplate that without a BCSP colonoscopy diagnosing CRC, some of these patients may have presented later as an emergency with a severe complication such as bowel obstruction or metastatic disease.

The English population awareness about symptoms of CRC, and the effectiveness of symptomatic pathways in identifying symptoms and managing patients with CRC needs to improve.

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Disclosure: None.

P0619

ACTION OF 4-THIAZOLIDINONE DERIVATIVES ON FREE RADICAL OXIDATION IN RAT'S COLON MUCOSA UNDER THE CONDITIONS OF COLORECTAL CANCER

N. Denysenko¹, I. Lozynska (Ilkiv)¹, I. Fomenko², I. Yushyn³, R. Lesyk³

¹Danylo Halytsky Lviv National Medical University, Department of Biochemistry, Lviv, Ukraine, ²Danylo Halytsky Lviv National Medical University, Department of Biochemistry, Lviv, Ukraine, ³Danylo Halytsky Lviv National Medical University, Department of Pharmaceutical, Organic and Bioorganic Chemistry, Lviv, Ukraine

Contact E-Mail Address: denysenko.natalia@gmail.com

Introduction: Colorectal cancer (CRC) is the third most common malignancy and the second most deadly cancer worldwide. This makes the search of promising drugs be an actual objective for biomedical sciences. Management of malignancies is frequently accompanied with activation of free radical oxidation. On the one hand this effect provides efficiency of chemotherapy, on the other hand – the side effects.

Aims & Methods: The aim of this research was to investigate the changes of free radical oxidation in colon mucosa (CM) of rats with CRC after the action of compounds with anticancer properties (Les-6485, Les-5303). Male Wistar rats were divided into 4 groups: 1 – control, 2 – CRC, 3 – CRC + Les-6485, 4 – CRC + Les-5303. CRC was induced by administration of dimethylhydrazine in a dose 20 mg/kg/week for 20 weeks.

The experimental compounds are the derivatives of 4-thiazolidinone, were tested for their anticancer activity *in vitro* and showed a selective effect on the growth of several colon cancer cell lines, especially COLO-205, HCC-2998, HCT-116, HCT-15, HT29, KM12, SW-620. It is assumed that mechanism of anticancer properties of tested compounds involves activation of caspase 3 and Nrf2-Keap1 pathway.

After euthanasia specimens of colon for histological investigation were taken. Homogenates of CM were used for determination of superoxide dismutase (SOD), glutathione peroxidase (GPO), myeloperoxidase (MPO) activity, concentration of reduced glutathione (GSH), TBA-active products and products of proteins oxidation (aldehydes and ketones).

Results: CRC caused threefold increase of MPO activity whereas activity of both GPO and SOD decreased by 25% compared to control group. Concentration of GSH was reduced by 12%, both MDA and neutral ketones content raised by 14%, concentration of basic aldehydes – by 24% compared to control group.

Dimethylhydrazine model of CRC is based on inflammation, which stimulates the activity of MPO and thus cause the oxidative stress. Compound Les-6485 increased the level of GSH by 13% which might raise the antioxidant capacity.

This lowered the accumulation of products of proteins oxidation, mainly basic aldehydes by 21% compared with CRC group. Compound Les-5303 augmented SOD activity by 34% compared with CRC group. Nevertheless, higher SOD activity in Les-5303 group was not enough to normalize the rest indices.

Conclusion: Considering the obtained data, we suppose that compound Les-6485 might have more potent antioxidant properties due to its structure which included extra group with anticancer properties. Being a Michael acceptor, compound Les-5303 can bind sulfhydryl groups including GSH and have less pronounced antioxidant properties.

Disclosure: Nothing to disclose.

P0620

A DUAL STRAIN *BIFIDOBACTERIUM LONGUM* PROBIOTIC IS ASSOCIATED WITH SIGNIFICANT IMPROVEMENTS IN GASTROINTESTINAL AND PSYCHOSOCIAL SYMPTOMS IN PEOPLE WITH IRRITABLE BOWEL SYNDROME – A REAL-WORLD EXPERIENCE PROGRAMME

F. Kinnear¹, K. Sorensen¹, N. Power², K. Sanders³, J. MacRae⁴, B. Bishop⁵

¹Novozymes, Medical Affairs, Cork, Ireland, ²Ulster Hospital, Department of Nutrition & Dietetics, Belfast, United Kingdom, ³University Hospital Lewisham, Department of Nutrition & Dietetics, London, United Kingdom, ⁴County Community Hospital, Department of Nutrition & Dietetics, Invergordon, United Kingdom, ⁵Novozymes, Data Science, Lyngby, Denmark

Contact E-Mail Address: fjak@novozymes.com

Introduction: Irritable bowel syndrome (IBS) has been described as a disorder of the microbiome-gut-brain axis, associated with both gastrointestinal (GI) and psychosocial symptoms¹. The gut microbiota may differ between people with IBS and those without², and may be a potential therapeutic target. Clinical trials have demonstrated improvements in GI symptoms, depression, anxiety, and quality of life following supplementation with *Bifidobacterium longum* 35624 and 1714 individually and in combination³⁻⁵, however real-world evidence is limited.

Aims & Methods: This real-world experience programme aimed to evaluate GI and psychosocial symptoms of people with IBS who received a supplement containing *Bifidobacterium longum* 35624 and 1714 (Dual Strain). Participants were referred to the 12-week programme by UK registered dietitians, to receive Dual Strain (1x10⁹ colony-forming units, once-daily). Abdominal pain, distension, bowel habit dissatisfaction (frequency and ease), stress, fatigue, mood and impact to daily life over the previous 2 weeks were assessed at baseline and 4-week intervals by 10-point Likert scale in an online survey. Interim statistical analysis compared data from baseline and week 4 using Wilcoxon signed-rank test.

Participants prescribed antibiotics during the programme were excluded from the primary analysis but included in a sensitivity analysis. Results are presented as percentage of participants, mean±SD scores, and calculated percentage change over time.

Results: 63 participants (75% female, 24% male, 1% other; 55% aged <34y, 22% 35-54y, 23% ≥55y) completed surveys at baseline and week 4, of whom 8 (13%) were prescribed antibiotics during the programme and excluded from primary analysis.

Outcome	Baseline	Week 4	Mean percentage change	p-value
Abdominal distension	6.15±2.80	4.67±2.44	24%	p=0.0002
Abdominal pain	5.42±2.53	4.04±2.28	25%	p<0.0001
Bowel habit dissatisfaction	6.38±2.06	4.82±2.33	24%	p<0.0001
Stress	6.49±2.28	5.78±2.42	11%	p=0.02
Fatigue	7.24±2.10	6.35±2.24	12%	p=0.01
Mood*	4.85±1.84	5.82±1.99	20%	p=0.005
Impact to daily life	6.36±2.15	4.51±2.29	29%	p<0.0001

*For all outcomes except 'mood', lower Likert scale scores indicate positive outcomes, whilst higher scores indicate negative outcomes (e.g. abdominal pain 0=no pain, 10=severe pain). For 'mood', scores were inverted (0=low mood, 10=good mood).

Table. Mean±SD 10-point Likert scale symptom scores before and 4 weeks after supplementation with Dual Strain.

All participants (n=55, 100%) reported being affected by GI symptoms (abdominal distension 85%; abdominal pain 73%; diarrhoea 65%; constipation 45%); 85% also reported psychosocial symptoms (stress from con-

dition 67%; fatigue 65%; anxiety/low mood 49%; sleep disruption 45%). At week 4, significant improvements ($p \leq 0.02$) were observed for all symptoms, including abdominal pain (1.38 ± 2.51), distension (1.47 ± 2.59), bowel habit dissatisfaction (1.56 ± 2.55), stress (0.71 ± 2.39), fatigue (0.89 ± 2.44), mood (0.96 ± 2.36), and impact to daily life (1.85 ± 2.36) (Table).

Overall, the mean percentage improvement for all symptoms was 21% (range 11–29%), with impact to daily life improving by the greatest increment. Results of the sensitivity analysis ($n=63$), including those prescribed antibiotics, were similar and remained statistically significant.

Conclusion: These real-world data are consistent with clinical research findings that supplementation with *Bifidobacterium longum* 35624 and 1714 may produce strain-specific clinical benefits in people with IBS. Further research investigating the mode of action of these combined probiotic strains is warranted.

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P0621

DO IRRITABLE BOWEL SYNDROME PATIENTS WITH AND WITHOUT HYPERMOBILITY SPECTRUM DISORDERS DIFFER IN GASTROINTESTINAL SYMPTOMS, PSYCHOLOGICAL COMORBIDITIES, AND QUALITY OF LIFE?

L. Vork¹, B. Beckers¹, Z.Z. Weerts², A. Fikree³, A.D. Farmer⁴, Q. Aziz⁵, M.A.M. Hesselink¹, D.M. Jonkers⁶, A.A. Masclee¹, D. Keszthelyi¹

¹Maastricht University Medical Center +, Gastroenterology-Hepatology, Maastricht, Netherlands, ²Maastricht University Medical Center, Zuyderland Medical Center, Division of Gastroenterology and Hepatology, Maastricht, Netherlands, ³Barts Health NHS Trust, Dept. of Gastroenterology, London, United Kingdom, ⁴Wingate Institute of Neurogastroenterology, Barts and the London School of Med., Gastroenterology, London, United Kingdom, ⁵Wingate Institute for Neurogastroenterology - Centre for Neuroscience and Trauma, Centre for Neuroscience, Surgery and Trauma, London, United Kingdom, ⁶Maastricht University Medical Center, Department of Internal Medicine, Division of Gastroenterology-Hepatology, Maastricht, Netherlands

Contact E-Mail Address: l.vork@maastrichtuniversity.nl

Introduction: Hypermobility spectrum disorders (HSD), previously known as joint hypermobility syndrome, have been associated with disorders of gut brain interaction (DGBIs) such as irritable bowel syndrome (IBS). HSD encompasses a spectrum of disorders – on the one end there is symptomatic generalized joint hypermobility (gJHM)(i.e. the capability of a joint to move beyond normal limits) –hypermobile Ehlers Danlos Syndrome

(hEDS) on the other. Joint hypermobility is the key characteristic of all subjects along the entire spectrum. Disordered autonomic regulation has been suggested as a possible underlying mechanism in symptom genesis in hypermobile patients with DGBIs, but the exact mechanisms behind these overlapping syndromes still need to be unraveled.

Aims & Methods: The aim of this study was to determine the prevalence of generalized joint hypermobility and HSD in an IBS population, and to evaluate differences in clinical presentation between subjects with and without gJHM or HSD. 258 (Rome III) IBS patients were included.

Patients included prior to 2015 were screened retrospectively for gJHM and HSD using a validated questionnaire (JHM Questionnaire) and subsequently assessed by physical examination, using the Beighton score and Brighton criteria. Those included after 2015 were assessed prospectively by physical examination.

Subjects were categorized as non-hypermobile, gJHM, or HSD. Subjects also completed the Gastrointestinal Symptom Rating Scale for gastrointestinal symptom severity, Hospital Anxiety and Depression Scale to screen for (subclinical) depression and anxiety, and RAND 36-item Short-Form Health Survey for quality of life.

Results: Of the 258 subjects, 195 were screened using the JHM questionnaire, and 63 subjects were directly assessed by physical examination. In the questionnaire group, 58 subjects (29.7%) scored positive and in total 35 subjects (15.6%) had gJHM. In the prospective group, 20 subjects (31.7%) had HSD. Hypermobile subjects were more often female and significantly younger than non-hypermobile subjects, but these differences were not found for HSDvs.no HSD. No differences could be demonstrated in gastrointestinal symptom severity, subclinical anxiety/depression, or quality of life when comparing gJHM/HSD tonon-hypermobile/non-HSD counterparts.

Conclusion: gJHM and in particular HSDs are present in substantial numbers (~30%) in a heterogeneous group of IBS patients. However, when comparing IBS patients with gJHM or HSD to their non-hypermobile/non-HSD counterparts, no apparent differences in gastrointestinal symptoms, depression, anxiety, and quality of life were found.

Future studies should focus on differences in additional somatic symptoms (including overlapping DGBIs), autonomic symptoms, and somatization scores, in order to unravel the question of whether IBS patients with a comorbid diagnosis of joint hypermobility or HSD represent a specific subgroup within the IBS population.

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P0622

NETWORK MODELLING IN CHRONIC CONSTIPATION: DELINEATING DISEASE PHENOTYPES

R. Rajiah¹, C.E. Ng², R.L. Embleton², Y. Yiannakou², J. Ruffle³

¹Brighton & Sussex Medical School, Brighton, United Kingdom,

²County Durham and Darlington NHS Foundation Trust, Durham, United Kingdom, ³Queen Square Institute of Neurology, University College London, London, United Kingdom

Contact E-Mail Address: rebekah.rajiah@gmail.com

Introduction: Chronic constipation (CC) is a common condition affecting 14% of adults worldwide. Attributed to a complex and multifactorial underpinning pathophysiology, CC remains both incompletely understood and difficult to treat. Patients with CC experience an array of debilitating symptoms, which may interact to worsen quality of life. Yet, the impact on a patient's overall health and quality of life caused by interacting symptoms is unknown. To address this, we applied graphical modelling to characterise these symptom interactions and better interrogate the disease process. By treating this complex heterogeneity in clinical features as a network, we aimed to delineate the core connective features in CC symptomology and outline the structure of the underlying symptom constellations such that key links may be revealed and constituent disease phenotypes better understood.

Aims & Methods: Objective: To characterise the network constellation of symptoms afflicting patients with CC and identify constituent disease phenotypes.

Methods: Patient assessment of constipation symptoms (PAC-SYM) and quality of life (PAC-QOL) questionnaires were collected in 786 CC patients prospectively from a tertiary centre over 7 years. We investigated the interplay between symptoms and quality of life (QOL) domains in a graphical domain, utilising weighted undirected graphical networks, quantifying centrality metrics and applying Bayesian inference to derive the community structure of underpinning symptom and QOL domains.

Results: Statistically significant positive correlations were found between many common CC features, including abdominal discomfort and eating less ($r>0.42$), painful bowel movements and rectal burning ($r>0.53$), and stress with decreased self-confidence ($r>0.70$) (all $p<0.0001$). Features with the greatest eigenvector centrality comprised factors relating to mental wellbeing, including the presence of stress, irritability, sadness, decreased self-confidence and worry over lack of bowel movements. Use of the Bayesian generative stochastic block model revealed six distinct phenotypic symptom/QOL clusters spanning the following domains: abdominal symptom burden, rectal symptom burden, treatment dissatisfaction, mental health impact, and impact upon daily life.

Conclusion: Network modelling reveals the associations between symptoms and quality of life disruptors in an unprecedented sample size of patients afflicted with chronic constipation. The results yield an improved understanding of this patient population, wherein stratification of symptom and QOL impacts is apparent across distinct domains.

Future work should evaluate if these graphical representations can be used to facilitate personalised medicine, with treatment allocation based upon targeted therapies to a given symptom cluster.

Disclosure: Nothing to disclose.

P0623

FECAL CALPROTECTIN IS CORRELATED WITH SERUM CYTOKINES IN DIARRHEA SUBTYPE IRRITABLE BOWEL SYNDROME

M.M. Piskorz¹, N. Litwin², H. Hashimoto¹, T.N. Uehara³, F. Bazan¹, A. Tevez¹, J.I. Olmos⁴, E. Gonzalez Ballerga⁴, J. Olmos¹

¹Hospital de Clinicas Universidad de Buenos Aires, Neurogastroenterology, Buenos Aires, Argentina, ²LABORATORIO LITWIN, Buenos Aires, Argentina, ³Hospital de Clínicas "José de San Martín"/ University of Buenos Aires, Neurogastroenterology, Ciudad de Buenos Aires, Argentina, ⁴Hospital de Clinicas Universidad de Buenos Aires, Gastroenterology, Buenos Aires, Argentina

Contact E-Mail Address: juan.ignacio.olmos@gmail.com

Introduction: The pathophysiology of irritable bowel syndrome (IBS) is not completely understood; however, dysregulation of the brain-gut axis is believed to lead to IBS. Various central and peripheral mechanisms are indicated to be involved, such as altered GI motility, visceral hypersensitivity, alteration of the intestinal microbiota, low-grade immune activation, and intestinal inflammation, which may be linked to enhanced exposure to antigens due to increased intestinal permeability. Fecal calprotectin (FC) is a marker of intraluminal intestinal inflammation that could have a clinical utility in identifying IBS patients with more inflammation.

Aims & Methods: Aims: To explore the levels of FC in IBS-diarrhea (IBS-d) patients and healthy controls (HC) and to correlate the levels of FC with clinical characteristics and inflammatory and anti-inflammatory cytokines.

Material and methods: We included 129 patients aged over 18 years referred to tertiary hospital outpatient with Rome IV criteria for IBS-d, in whom normal colonoscopy and appropriate tests had excluded organic disease, and 53 HC (mainly patients relatives) with no history of gastrointestinal disorders and no bowel-related symptoms. None of the subjects included in the study was taking any medications known to affect the gastrointestinal tract or the immune system.

Clinical, laboratory data, blood and stool samples were collected. FC was measured quantitatively using a commercially available enzyme immunoassay ((Bühlmann Laboratories, Shönenbuch, Switzerland). 27- pro and anti-inflammatory cytokines (Bio-Plex Pro™, Bio- Rad) were measured in serum. IBS-d patients completed the Bristol scale and IBS severity score. FC levels adjusted for age, sex, and BMI among patients with IBS-d and HC were analyzed by linear regression. Correlations between IBS severity, levels of cytokines and FC were analyzed through the Spearman correlation coefficient.

Results: IBS-d patients has a mean age of 56 ± 16 , ($F=79\%$). HC 52 ± 7 , ($F=60\%$). Compared with HC, IBS-d patients had significantly higher median FC levels after adjusting for age, sex, and BMI ($63 \mu\text{g/g}$ [IQR 40-127] vs $33 \mu\text{g/g}$ [IQR 22-49], $p=0.000$). 29 (22%) patients with IBS-d had calprotectin values greater than $150 \mu\text{g/g}$.

In IBS-d patients, no significant correlation was observed between IBS severity and FC levels. Neither between the number of bowel movements per day and FC levels. There was a positive correlation between FC levels and the levels of IL-8 ($\text{Rho } 0.27$, $p=0.007$), IL-10 ($\text{Rho } 0.28$, $p=0.005$) and IP-10 ($\text{Rho } 0.21$, $p=0.04$).

There was a negative correlation between FC levels and distension Likert scale ($\text{Rho } -0.25$, $p=0.01$)

Conclusion: The FC level was significantly higher in patients with IBS-d than in HCs, regardless age, sex, and BMI. In IBS-d patients, no positive correlation was observed between FC levels and IBS severity or the number of bowel movements. FC levels was positive correlated with the levels of some serum cytokines, supporting the notion that IBS is a type of low-grade bowel inflammation.

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P0624

BENIGN JOINT HYPERMOBILITY SYNDROME IN IRRITABLE BOWEL SYNDROME

I. Midenfjord¹, A. Polster¹, S. Lindholm¹, H. Törnblom¹, M. Simrén^{1,2}
¹Institute of Medicine, Department of Molecular and Clinical Medicine, Gothenburg, Sweden, ²Centre for Functional GI and Motility Disorders, University of North Carolina, Chapel Hill, NC, United States

Contact E-Mail Address: irina.midenfjord@gu.se

Introduction: Previous literature suggests a higher prevalence of irritable bowel syndrome (IBS) in hypermobility disorders (Beckers et al 2017), but few studies exist evaluating the prevalence of benign joint hypermobility syndrome (BJHS) in IBS. Hence, our aim was to assess the prevalence of BJHS in IBS and to characterize IBS patients with and without BJHS.

Aims & Methods: Patients with a prior IBS diagnosis and actively seeking health care for IBS (N= 68), and subjects without documented or self-reported chronic diseases volunteering for participation in research (N=124) were included 2015-2020 and completed the Rome III diagnostic questionnaire. They were divided into groups with or without IBS according to the Rome III criteria for the subsequent analyses.

The presence of BJHS was assessed through the revised Brighton criteria (Grahame et al 2000). The subjects also completed questionnaires to assess severity of IBS symptoms (IBS-SSS), anxiety (HAD-A), depression (HAD-D), somatic non-GI symptoms (PHQ12), GI-specific anxiety (VSI) and pain catastrophizing (PCS).

Results: In total, 99 subjects with IBS and 93 without IBS were included. The participants with IBS were older and more likely female than the subjects without IBS, and reported more severe GI and non-GI symptoms overall (table). A trend towards a higher prevalence of BJHS in the IBS group was seen (p=0.06), and the IBS subjects more often had hypermobile backs (58% vs. 41%, p=0.04) and arthralgia in 1-3 joints (36% vs. 17%, p=0.07) or in 4 or more joints (9% vs. 1%, p=0.02). Subjects with IBS and BJHS were not clearly different from subjects with IBS alone regarding GI and non-GI symptoms (table). A numerical difference, although not reaching statistical significance, was seen in the IBS subtype distribution comparing those with and without BJHS.

Conclusion: Benign joint hypermobility syndrome is relatively common among subjects with IBS, and they frequently report hypermobile backs and arthralgia. However, clear differences in other symptoms were not evident in subjects with IBS with or without joint hypermobility. Acknowledging the presence of joint symptoms in patients with IBS seem to be one important aspect of the holistic management approach recommended in this patient group.

	Subjects with IBS (N=99)	Subjects without IBS (N=93)	P-value	Subjects with IBS alone (N=63)	Subjects with IBS and BJHS (N=36)	P-value
Female gender	73 (74%)	55 (59%)	0.05	47 (75%)	26 (72%)	0.98
Age	28 [24-39]	23 [21-27]	<0.001	27 [23-39]	28 [25-38]	0.44
IBS subgroups (C/D/M/U)	25/33/28/11 (26%/34%/29%/11%)		0.01	18/18/18/8 (29%/29%/29%/13%)	7/15/10/3 (20%/43%/29%/9%)	0.54
IBS-SSS	260 [179-349]	10 [0-63]	<0.001	249 [173-348]	279 [194-355]	0.53
Brighton score	4 [2-5]	3 [2-5]	0.58	3 [2-4]	6 [4-7]	<0.001
Brighton criteria fulfilled	36 (36%)	21 (23%)	0.06	0 (0%)	36 (100%)	
HAD-A*	8 [5-10]	1 [1-2]	0.003	7 [5-9]	9 [5-11]	0.31
HAD-D*	5 [3-8]	1 [0-1]	<0.001	5 [3-7]	7 [4-10]	0.11
PHQ12*	8 [5-10]	4 [3-5]	0.03	7 [4-9]	9 [6-11]	0.08

* Data available in 68 subjects with IBS and 11 healthy.

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P0625

PREVALENCE OF ANTIGLIADIN IGG ANTIBODIES (AGA IGG) AND THE ASSOCIATION WITH SYMPTOMS IN IRRITABLE BOWEL SYNDROME

J. Algera¹, T. Kathirkamanathan¹, M. Sapnara², M.M. Magnusson², S. Störsrud¹, H. Törnblom¹, M. Simrén^{1,3}, L. Öhman²
¹Institute of Medicine, Sahlgrenska Academy, University Of Gothenburg, Molecular and Clinical Medicine, Gothenburg, Sweden, ²Institute of Biomedicine, Sahlgrenska Academy, University Of Gothenburg, Immunology and Microbiology, Gothenburg, Sweden, ³University of North Carolina at Chapel Hill, Center for Functional GI & Motility Disorders, Chapel Hill, United States

Contact E-Mail Address: joostalgera@gmail.com

Introduction: Antibody reactivity to gluten has been suggested to be linked to symptoms of patients with irritable bowel syndrome (IBS) (Uhde et al. *Gastroenterology*, 2020).

Aims & Methods: We aimed to assess the prevalence of serum antigliadin (AGA) specific Immunoglobulin-G (IgG) antibodies in IBS, and to identify associations between AGA IgG, including subclasses, and gastrointestinal symptoms in IBS.

IBS patients (n=506; 78% females; all with negative tissue transglutaminase IgA antibody tests) provided serum samples as well as recordings of gastrointestinal symptoms (GSRS-IBS), bowel habits (BSF), and psychological distress (HADS). Demographics included sex, age, and body mass index (BMI). Levels of total AGA IgG and subclasses (IgG1-4) were assessed by Gliadin IgG ELISA (IBL International Hamburg, Germany). IgG subclass

profiles were assessed in those with a positive AGA IgG test (>14.0 U/mL) and in a set of IBS patients with negative AGA IgG test (n=11). The IgG values were normalized by the mean of the negative controls. AGA IgG1–4 tests were considered as positive when the concentrations were at least two standard deviations higher than the mean concentrations of the negative controls.

Associations between AGA IgG, IgG1–4 and demographics/IBS symptoms/psychological distress were assessed with Mann Whitney U tests and followed by false discovery rate (FDR) correction (q<.05). Data are presented as medians with interquartile range.

Results: In total, 11% (n=54) of the IBS patients had a positive AGA IgG test. Demographics, IBS symptoms and psychological distress did not differ between patients with a positive versus negative AGA IgG test. A lower BMI was associated with a positive AGA IgG test (Table). Among IgG subclasses, a positive test was observed in 8% (n=43) for AGA IgG1, 10% (n=51) for AGA IgG2, 1.6% (n=8) for AGA IgG3, and 9% (n=48) for AGA IgG4. No associations were observed between gastrointestinal symptoms and positive AGA IgG1–4 tests.

Table	AGA IgG total		P
	Positive (n=54) (≥14.0 U/mL)	Negative (n=452) (<14.0 U/mL)	
Female sex, %	77	76	.80
Age, years	21 (26–47)	35 (27–47)	.37
BMI, kg/m ²	22 (21–24)	24 (21–27)	<.01#
IBS-C/D/nonCnonD), %	37/26/37	35/35/30	.63
Stool frequency/day	1.6 (1.2–2.2)	1.7 (1.3–2.4)	.38
Stool consistency (BSF)	3.7 (2.6–4.4)	3.8 (2.8–4.8)	.39
GSRS-IBS total	3.8 (3.4–4.2)	3.8 (3.4–4.4)	.68
Abdominal pain	4.5 (3.5–5.0)	4.0 (3.5–5.0)	.78
Abdominal bloating	4.7 (3.7–5.3)	5.0 (4.0–5.7)	.13
Diarrhea	3.8 (2.9–4.0)	3.5 (2.8–4.5)	.76
Constipation	3.0 (1.5–4.5)	3.0 (1.5–4.6)	.78
Satiety	3.5 (2.0–4.0)	2.5 (1.5–4.0)	.28
Psychological distress (HADS)	10 (7–15)	11 (7–16)	.85

AGA, antigliadin antibodies; BSF, Bristol stool form; BMI, body mass index; GSRS-IBS, Gastrointestinal Symptom Rating Scale – IBS version; HADS, hospital anxiety and depression scale; IgG, immunoglobulin-G; IBS, irritable bowel syndrome; IBS-C, IBS with predominant constipation; IBS-D, IBS with predominant diarrhea; IBS-nonCnonD; IBS with mixed bowel habits or unspecified IBS. Significant results are shown in bold. # q<.05 after false discovery rate correction

Table.

Conclusion: A positive AGA IgG test, including IgG subclasses, does not have a clear association to common gastrointestinal symptoms in IBS. Follow-up studies are needed to understand the relevance of IgG antibody responses to gliadin for symptom generation in IBS.

Disclosure: Nothing to disclose.

P0626

INTESTINAL PERMEABILITY, ABDOMINAL SYMPTOMS AND PSYCHOLOGICAL COMORBIDITIES IN IBS-D PATIENTS

M.R. Barbaro¹, G. Marasco², C. Cremon¹, L. Rotondo¹, D. Fuschi¹, M. Palombo³, F. Bonomini³, V. Stanghellini², G. Barbara²
¹IRCCS Azienda Ospedaliero-Universitaria di Bologna, Bologna, Italy, ²IRCCS Azienda Ospedaliero-Universitaria di Bologna, Department of Medical and Surgical Sciences, Bologna, Italy, ³University of Bologna, Department of Medical and Surgical Sciences, Bologna, Italy

Contact E-Mail Address: maria.barbaro2@unibo.it

Introduction: The pathophysiology of Irritable bowel syndrome (IBS) is multifactorial and includes alterations in intestinal permeability contributing to symptom generation. The present study aimed to assess: intestinal permeability of the gastrointestinal tract in a well-characterized IBS-D cohort and asymptomatic controls (AC); the correlations between intestinal permeability alterations and abdominal symptoms, psychological functioning and general health; the diagnostic accuracy of sugar test in discriminating between IBS-D and AC.

Aims & Methods: Eighteenand 31 patients with IBS-D have been enrolled. Rome IV criteria, Bowel disease questionnaire, Short Form 36, Hospital Anxiety Depression Scale were used to phenotype patients. Mannitol, lactulose, sucralose, and sucrose urinary excretion was assessed by HPLC-MS. The lactulose/mannitol ratio (L/M ratio) was calculated. Correlation analyses were performed between demographic and laboratory data. Receiver operating characteristic (ROC) curve analyses were used to evaluate the accuracy of sugar test in discriminating between IBS-D and AC.

Results: Compared to AC, lactulose (P<0.05), sucralose (P<0.01), sucrose (P<0.01) excretion and the L/M ratio (P<0.01) were significantly increased in IBS-D patients. Abdominal pain and bloating scores correlated with the excretion of all sugars. Anxiety score correlated with sucrose (P=0.026; rs:0.324) and lactulose (P=0.022; rs:0.333) excretion and with L/M ratio (P=0.001; rs:0.462). Depression score correlated with L/M ratio (P<0.0001; rs:0.552), sucrose (P=0.033; rs:0.311), lactulose (P=0.003; rs:0.420) and sucralose (P=0.039; rs:0.303) excretion.

Physical and mental health-related quality of life inversely correlated with L/M ratio, sucrose, lactulose and sucralose excretion. L/M ratio had the highest diagnostic accuracy in discriminating IBS-D from AC (AUROC: 0.773).

Conclusion: Intestinal permeability is increased along the entire gastrointestinal tract and correlates with abdominal and psychological symptoms and with health related quality of life. L/M ratio has the highest diagnostic accuracy in discriminating IBS-D from AC.

Disclosure: Nothing to disclose.

P0627

GASTROINTESTINAL SYMPTOMS AND AUTONOMIC DYSFUNCTION IN HEREDITARY TRANSTHYRETIN AMYLOIDOSIS: EARLY DETECTION AND MONITORING THROUGH THE COMPASS 31 SCORE

D. Brinch¹, V. Di Stefano^{2,3,2}, S. Muscarella¹, M. Saladino¹, F. Brighina³, M. Cappello¹

¹University of Palermo, Gastroenterology and Hepatology Section, Promise, Palermo, Italy, ²University of Palermo, Palermo, Italy,

³Unit of Neurophysiopathology, Department of Biomedicine, Neuroscience and advanced Diagnostic (BIND), Palermo, Italy

Contact E-Mail Address: danielebrinch@gmail.com

Introduction: Hereditary transthyretin amyloidosis (hATTR) is a rare multisystemic hereditary disease which manifests mostly as sensorimotor polyneuropathy but can involve also the heart, the kidney and the eye and the gastrointestinal (GI) system. hATTR is a progressive and fatal disease, death occurs within ten years from the onset but novel gene silencing therapies are potentially able to arrest progression and prevent disability if used in early stages.

Data on the prevalence of GI disturbances are discrepant, they are common (56-69 %) but often misleading being non-specific: they can be the presenting symptoms and their underrecognition can cause diagnostic delay.

The aim of our study was to assess the prevalence and burden of GI involvement in a ethnically homogeneous cohort of patients with hATTR.

Aims & Methods: The aim of our study was to assess the prevalence and burden of GI involvement in a ethnically homogeneous cohort of patients with hATTR. We studied a cohort of sicilian patients with hATTR, diagnosed at our referral center for rare neuromuscular disease, focusing From January 2019 to December 2021 on the GI involvement and analysing distribution of symptoms and age of onset in relation to the age of diagnosis and to the onset of neurological disturbances. The burden of GI symptoms related to autonomic dysfunction was objectively assessed by the Compass 31 score, in particular 12 to 23 item were evaluated.

Results: 21 sicilian patients with hATTR were studied. All received genetic testing and 16 (76,2%) have the Phe84Leu mutation. 13/21 (62%) patients present GI symptoms (diarrhea 38 %), unintentional weight loss (38 %), constipation (23 %) and nausea (30%). GI involvement appeared before the diagnosis in 11/13 (85%) of patients (mean diagnostic delay 22 months); 9/11 (75 %) had also neurological symptoms (mostly bilateral carpal tunnel) suggestive of ATTR amyloidosis: mean global and GI COMPASS-31 score, evaluated at diagnosis, was 20 and 10, respectively.

Conclusion: Our experience confirm that GI involvement in hATTR is frequent (62%) but often underrecognized in spite of the presence of neurological red flags, thus leading to a diagnostic delay than can blunt the effectiveness of the new therapies. The Compass score for GI items confirms that autonomic dysfunction is the main pathogenetic mechanism and will be an effective monitoring toll for follow up.

Awareness of this rare disease must increase among gastroenterologists, who should be able to recognize the red flags that raise clinical suspicion. Their role in a multidisciplinary team could be relevant also in providing supportive measures to improve symptoms.

Disclosure: Nothing to disclose.

P0628

STW 5-II COUNTERACTED STRESS-INDUCED INFLAMMATION AND TIGHT JUNCTION DISRUPTION IN IBS-LIKE MODEL USING INTESTINAL ORGANOID

M. Elbadawi¹, R.M. Ammar², S. Rabin², T. Efferth¹

¹Johannes Gutenberg University-Mainz, Department of Pharmaceutical Biology, Institute of Pharmaceutical and Biomedical Sciences, Mainz, Germany, ²Bayer Consumer Health, Global Medical Affairs, Darmstadt, Germany

Contact E-Mail Address: melbadawi@uni-mainz.de

Introduction: Disturbance of the bidirectional brain-gut axis is increasingly recognized as a conceptual model of IBS pathophysiology, involving abnormal function in the enteric, autonomic and/or central nervous systems. Chronic stress is one of the confounding factors for gut brain miscommunication and pathogenesis of disorders of gut-brain interaction (DGBI) such as irritable bowel syndrome. Stress stimulates the HPA axis and then triggers the release of corticotropin-releasing factor (CRF) and cortisol, which directly or indirectly affect gut function, influences the composition and the growth of microbiota, and also stimulates the sympathetic nervous system. CRF enhances the release of mast cell mediators such as pro-inflammatory cytokines by acting on CRF receptors on the mucosal mast cells in the gastrointestinal tract.

These mediators act on intestinal epithelium to increase permeability and induce visceral hypersensitivity, representing two major pathophysiological features of IBS. STW 5-II, a combination of 6 herbal extracts, is a clinically proven treatment option for IBS and functional dyspepsia.

Aims & Methods: In this study we aimed to establish an organoid-based IBS-like model. This model has been used to investigate the molecular mechanisms of STW 5-II on CRF and stress-related inflammatory parameters in stress-induced IBS-like model.

Mouse intestinal organoids were cultured in Matrigel domes. The organoids were pretreated with increasing concentrations of STW 5-II (10, 20, 30 µg/ml) for 24 h followed by treatment with CRF (100 nM) for 48 h. Afterward, the effects of CRF and STW 5-II were studied using several *in vitro* and *in silico* approaches. We have investigated the expression of many pro-inflammatory mediators and cytokines such as NF-κB, TLR4, MYD88, IL-6, IL-1β, and TNFα using quantitative real-time PCR and microarrays analyses. The expression of NF-κB was additionally assessed via whole-mount immunofluorescence staining.

Moreover, the expression of the tight junction protein claudin-2 has been evaluated. ELISA was performed to study the activity of STW 5-II on CRF-mediated elevation of serotonin. Such activity towards CRF signaling was further confirmed by PyRx screening and molecular docking of the major 52 constituents in STW 5-II against both CRF receptors, CRFR1 and CRFR2.

Results: Stress-induced IBS-like model was successfully established in rat organoids.

Exposure to CRF has induced inflammation, as evidenced by the increased expression of the inflammatory mediators TLR4, MYD88, IL-1β, IL-6, TNFα, and NF-κB. STW 5-II was able to reverse these effects in a dose-dependent manner. STW 5-II was able to reduce CRF-mediated claudin-2 upregulation that could play a role in leaky gut. Moreover, STW 5-II inhibited CRF-mediated serotonin secretion in a dose-dependent manner.

Conclusion: STW 5-II counteracted stress-induced inflammation and tight junction disruption, one of the major predisposing factors for the development of DGBIs such as IBS. These multi-targets activities could substantiate and explain the clinically proven efficacy of STW 5-II in IBS.

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P0629

IMPORTANCE OF BOWEL HABITS AS A RISK FACTOR OF INADEQUATE BOWEL PREPARATION IN COLONOSCOPY: A PROSPECTIVE QUESTIONNAIRE-BASED OBSERVATIONAL STUDY

N. Maeda^{1,2}, A. Higashimori¹, M. Nakatani², Y. Nakamura², A. Hashimoto², K. Morimoto², T. Fukuda², Y. Fujiwara¹
¹Osaka Metropolitan University Graduate School of Medicine, Gastroenterology, Osaka, Japan, ²Minami Osaka Hospital, Gastroenterology, Osaka, Japan

Contact E-Mail Address: natsu072407@yahoo.co.jp

Introduction: Inadequate bowel preparation (IBP) negatively affects the efficacy and quality of colonoscopy. Although constipation has already been reported as one of the most important predictors of IBP, there is limited information about the relation of IBP to bowel habit factors including symptoms, medications, and severity of constipation.

Aims & Methods: We aimed to investigate predictors of IBP focusing on symptoms, medications, and severity of constipation. This was a questionnaire-based prospective observational study in single institution. Between March and December 2019, 1157 consecutive outpatients underwent afternoon colonoscopy.

All patients received low-volume polyethylene glycol solution with ascorbate (Moviprep®) on the same day as the examination. Bowel preparation cleansing was evaluated using Boston Bowel Preparation Scale (BBPS). IBP was defined by BBPS<2 per each segment. Chronic constipation was diagnosed by ROME 4 criteria, which includes six questions regarding constipation-related symptoms. Severity of constipation was scored by Constipation Scoring System (CSS; range 0-30). Chronic use of laxatives was defined as uses more than 3 days per week for at least 3 months.

The potential predictors for IBP were age, male sex, high body mass index (BMI), abdominal/pelvic surgery, constipation, tricyclic antidepressant use, diabetes mellitus, stroke, Parkinson's disease, and cirrhosis. Exclusion criteria were incomplete total colonoscopy, colectomy, and active inflammatory bowel disease.

Results: A total 1049 patients were included. Their average patient age and BMI were 63.8±12.8 years old and 23.5±4.9 kg/m². IBP was found in 104 patients (10%) and chronic constipation was found in 290 patients (28%). At multivariate analysis, age, chronic constipation, and diabetes mellitus were independent risk factors for IBP. By dividing patients into 3 equal groups by CSS score (mild [CSS: 0-2], moderate [CSS: 3-8], and severe constipation [CSS: >9]), IBP rate was 15% in mild group, 18% in moderate group, and 23% in severe constipation group and IBP increased with CSS score (P for trend=0.01).

Among constipation-related symptoms, straining during defecations was a significant predictor of IBP (odds ratio (OR)=1.62, 95% confidence interval [CI] 1.03-3.36) after adjusting cofounders. Furthermore, chronic use of stimulant laxatives is an independent predictor of IBP (OR=2.57, 95% CI 1.59-4.17), whereas chronic use of non-stimulant laxatives was not related to IBP.

Conclusion: Chronic constipation was a risk factor of IBP, as expected. The risk of IBP increased with the severity of constipation. Straining and chronic use of stimulant laxatives were significant predictor of IBP. For severe constipated patients with straining and chronic use of stimulant laxatives, an intensified preparation regimen should be especially considered.

Disclosure: Nothing to disclose.

P0630

STUDY OF THE DIAGNOSTIC ABILITY OF ULTRASONOGRAPHY COMPARED TO CT FOR FECES IN THE RECTUM

N. Misawa¹, S. Tamura¹, T. Kessoku¹, T. Higurashi¹, A. Nakajima¹
¹Yokohama City University School of Medicine, Department of Gastroenterology and Hepatology, Yokohama, Japan

Contact E-Mail Address: nobomisa@yokohama-cu.ac.jp

Introduction: Chronic constipation is a common functional gastrointestinal disorder in older adults, and it is very important to manage chronic constipation. Computed tomography (CT) has been used to evaluate fecal masses in the rectum, but there are problems such as radiation exposure, cost, and the inability to evaluate at facilities where CT cannot be performed.

Ultrasonography (US) can be broadly applied in clinical practice because of its low cost, high safety, high speed and use of non-ionising radiation, and it is known that US observation of colonic faecal retention is useful for diagnosing constipation and evaluating the effectiveness of treatment. However, it is not yet known whether feces in the rectum can be accurately assessed by US.

Aims & Methods: In this study, we investigated the evaluation of fecal mass retention in the rectum using US. US was performed within 1 hour before and after CT in patients scheduled to undergo CT. Background information (age, gender, BMI), history (presence of chronic constipation, presence of diabetes mellitus), and findings of rectal stool (US and CT) were evaluated. Stool findings in the rectum were evaluated on three levels: no stool (R1), presence of stool (R2), and hard stool filling (R3), and the degree of agreement between CT and US findings was evaluated.

Results: A total of 96 cases (52 males and 44 females) were included in the study, of which 47 cases were constipated. 79 cases (R1: 45 cases, R2: 26 cases, R3: 8 cases) were matched with CT and US findings, and 17 cases were not matched, showing high statistical agreement (kappa coefficient 0.711, P<0.001). When evaluated in the constipation group and non-constipation group, all cases with R3 were found in the constipation group, while more than half of the cases with R1 were found in the non-constipation group. CT and US findings showed high agreement in both constipation and non-constipation groups (constipation group: kappa coefficient 0.717, P<0.001; non-constipation group: kappa coefficient 0.651, P<0.001). Cases that did not match were considered to have low urine volume or high gas.

Conclusion: CT and US showed a high degree of agreement in the evaluation of fecal mass retention in the rectum, indicating that US may be a substitute for CT.

In addition, many cases in the non-constipation group showed no stool in the rectum, whereas many cases in the constipation group showed stool accumulation findings. US was considered to be a simple, bedside, and objective method of diagnosing rectal fecal conditions without radiation exposure or other invasive procedures.

Disclosure: Nothing to disclose.

P0631 WITHDRAWN

P0632

PREVALENCE AND PATHOPHYSIOLOGY OF FECAL CONSISTENCY DISORDERS AND THEIR IMPACT ON CLINICAL SEVERITY AND QUALITY OF LIFE IN PATIENTS WITH FECAL INCONTINENCE

A. Raventós¹, S. Carrión Bolorino¹, P. Clavé^{1,2}, L. Mundet^{1,2}

¹Hospital de Mataró (Consorci Sanitari del Maresme), GI Motility Unit, Mataró, Spain, ²Centro de Investigación Biomédica En Red de Enfermedades Hepáticas y Digestivas (CIBERehd), Instituto de Salud Carlos III, Madrid, Spain

Contact E-Mail Address: alba.ravens92@gmail.com

Introduction: Fecal incontinence (FI) affects up to 24% of middle-aged and older women, seriously impacting their health and quality of life (QoL). Pathophysiological studies have focused more on sphincter and anorectal dysfunctions than on the role of changes in fecal consistency.

Aims & Methods: To compare the impact of sphincter dysfunctions with changes in fecal consistency on pathophysiology, clinical severity and QoL in women with FI.

Cross-sectional observational study. We evaluated sociodemographics, medical history, anorectal physiology (HR anorectal manometry, endo-anal ultrasound, neurophysiology with pudendal nerve terminal motor latency (PNTML)) and fecal consistency (Bristol Scale). In patients with stools on Bristol Scale ≥ 5 we performed: a) breath-test to detect lactose, fructose/sorbitol malabsorption, bacterial overgrowth (SIBO), and an empirical test using cholestyramine (4g/12h for 2 weeks) to assess the presence of bile salt malabsorption. We compared anorectal physiology, clinical severity (Wexner/St.Mark's) and QoL (EQ5D/FIQL) of the group with Bristol ≥ 5 vs the rest.

Results: We studied 74 women with FI (St.Mark's 13 ± 3.59 /Wexner 10.82 ± 3.44), mean age 64.81 ± 11.96 . A total of 64.38% had emergency FI, 15.06% passive FI and 19.18% both. Up to 56.2% had soft stool consistency (Bristol ≥ 5) associated with: 20.5% bile acid malabsorption, 17.9% lactose intolerance, 14.3% fructose/sorbitol malabsorption, and 14.3% SIBO.

The sphincter dysfunction of the patients was homogeneous regardless of fecal consistency. A 66.6% had insufficiency of the external anal sphincter, 38.8% internal and 27.7% both, 37.5% had altered Valsalva reflex and 25.45% delayed PNTML. A 17.5% showed rectal hypersensitivity and 8.9% showed hyposensitivity.

Clinical severity (St. Mark's) worsened with Bristol ≥ 5 (14.2 ± 3 vs 12.3 ± 3.6 $p < 0.05$) as did QoL in the FIQL dimensions of lifestyle, coping, depression/self-perception ($2.7 \pm 0.8/2.2 \pm 0.8/2.6 \pm 0.7$ vs $3.3 \pm 0.6/2.8 \pm 0.7/3.1 \pm 0.5$ $p < 0.05$) and in the anxiety/depression dimension of the EQ5D (51.6% vs 24.7% $p < 0.05$).

Conclusion: More than 50% of patients with FI have excessively soft stools (Bristol ≥ 5). Sphincter dysfunction is severe and similar in patients with or without loose stools, but their presence worsens clinical severity and QoL significantly, requiring a specific diagnostic and therapeutic approach.

Disclosure: Nothing to disclose.

P0633

EFFECTIVE DIAGNOSIS OF DYSSYNERGIC DEFECATION IN REFRACTORY CONSTIPATION BY MINIMALLY INVASIVE PROTOCOL

G. Chiarioni¹, C. Lambiase², W.E. Whitehead³, R. Morganti⁴, S.L. Popa⁵, M. Bellini²

¹Division of Gastroenterology B, AOUI Verona, Verona, Italy and UNC Center for Functional GI and Motility Disorders, University of North Carolina at Chapel Hill, USA, Gastroenterology, Verona, Italy, ²Gastrointestinal Unit, Department of Translational Sciences and New Technologies in Medicine and Surgery, University of Pisa, Pisa, Italy, ³UNC Center for Functional GI and Motility Disorders, University of North Carolina at Chapel Hill, Chapel Hill, NC, United States, ⁴Clinical Trial Statistical Support Unit, Azienda Ospedaliero Universitaria Pisana, Pisa, Italy, ⁵2nd Medical Department, Iuliu Hațieganu University of Medicine and Pharmacy, Cluj-Napoca, Romania

Contact E-Mail Address: christian.lambiase93@gmail.com

Introduction: Dyssynergic Defecation (DD) is prevalent etiology of refractory Chronic Constipation (CC) which can be managed successfully by biofeedback therapy. DD diagnosis requires focused anorectal physiology testing not available outside specialized Center thus delaying effective management. Easy-to-perform tools would be key to improve referral of CC patients.

Aims & Methods: Aim of this study was to evaluate the accuracy and Odds Ratio (OR) of a minimally invasive protocol consisting of a:

1. Straining questionnaire (SQ),
2. Digital rectal examination on straining (DRE) and
3. Balloon Expulsion Test (BET) on predicting a Rome III DD diagnosis in refractory CC patients.

Two hundred and thirty-eight CC patients (Rome III) failing fiber/laxatives for 4 weeks were enrolled. A SQ (What muscles do you mainly use when you push to defecate?) was administered to patients before entering the study (T0) and after the 30-day fiber/laxative trial (T30). The possible answers were: "belly muscles"; "anal muscles"; "both muscles"; "Prefer not to answer/I don't know".

DRE and BET were again performed at T0 and at T30.

At T30, all patients underwent anorectal manometry (ARM).

OR, sensitivity, specificity, positive and negative predictive values (PPV and NPV) were calculated for the SQ, DRE and BET in predicting a DD, alone and in combination.

Sixty healthy volunteers underwent SQ and BET, but not DRE.

Results: One hundred nine patients (45.8%) showed features of DD according to Rome III criteria: paradoxical contraction or failure to relax pelvic floor muscles on straining at physiology and failed BET.

The most significant response to the SQ in predicting a DD was "anal muscles" (SQ+). At T30, the OR of this response in predicting a DD was 32.6 ($p < 0.001$). This response had sensitivity:72.1%, specificity:92.7%, PPV:92.1%, and NPV:73.7% in diagnosing DD.

The most significant DRE pattern in predicting a DD was failure of anal relaxation during push (DRE+). At T0, the OR of this pattern in predicting a DD was 15.6 ($p < 0.001$). This pattern had sensitivity:83.72%, specificity:75.23%, PPV:80%, and NPV:79.61% in diagnosing DD.

The most significant outcome on BET in predicting a DD was a failed balloon expulsion within 2 minutes. The OR of this response in predicting a DD was 3.5 ($p < 0.001$). This response had sensitivity:72.87%, specificity:56.88%, PPV:66.67%, and NPV:63.93% in diagnosing DD.

Cohen's Kappa was calculated to establish the concordance at T0 and T30 for the SQ (0.97), DRE (0.517), and BET (1).

When considering the combination, the most significant in predicting a DD are summarized in the table.

Combination	Sensitivity	Specificity	PPV	NPV	OR	p-value
SQ+,DRE+,BET+	53.12%	95.41%	93.15%	72.57%	38	<0.001
SQ+,DRE+,BET-	15.62%	99.08%	95.24%	50%	23	<0.001

Table.

Interestingly, combinations where pathological outcomes do not appear are not associated with DD: SQ-,DRE+,BET+ has an OR of 0.24 ($p=0.004$) in predicting DD; SQ-,DRE-,BET- has an OR of 0.04 ($p<0.001$) in predicting DD. All 60 HC could evacuate the rectal balloon. Only one of them had SQ+.

Conclusion: In our sample of 238 refractory CC patients, 45.8% showed features of DD according to Rome III criteria. Our data support screening CC patients for DD at any level of care by SQ, DRE and BET to improve management and facilitate the referral to anorectal physiology testing.

Moreover, our protocol may offer an opportunity to consider biofeedback treatment in the community without additional physiology testing. It is intriguing to speculate DD patients are conscious of their maladaptive behavior thus suggesting faulty learning as potential disorder etiology.

Disclosure: Nothing to disclose.

P0634

CHARACTERIZATION OF DEFECATION DISORDERS FROM A STRUCTURAL AND A FUNCTIONAL PERSPECTIVE IN A COHORT OF 588 PATIENTS

L. Mundet^{1,2}, A. Raventós¹, S. Carrión Bolorino¹, C. Bascompte Jurado¹, P. Clavé^{1,2}

¹Hospital de Mataró (Consorci Sanitari del Maresme), GI Motility Unit, Mataró, Spain, ²Centro de Investigación Biomédica en Red de Enfermedades Hepáticas y Digestivas, Instituto Carlos III, Madrid, Spain

Contact E-Mail Address: lluismundetp@gmail.com

Introduction: Evacuation disorders are the result of sphincter dysfunction and/or structural alterations of the rectal ampulla during evacuation. They are studied with anorectal manometry (ARM) and evacuation defecography (ED), which allow the assessment of defecation from a dual perspective: pressure dynamics and dynamic imaging of the posterior compartment.

Aims & Methods: Characterize functional (FDD) and structural (SDD) defecation disorders with ARM and ED, along with clinical manifestations of obstructive defecation.

Retrospective study with 588 patients with obstructive defecation who underwent ED (2012-2020). Diagnosis, pelvic dynamics during defecation (anorectal angle (ARA)) and perineal descent (PD) were collected and quantified; in a subsample of 294 patients, anorectal function was evaluated with ARM, and clinical manifestations were collected.

Results: Five hundred and eighty-eight patients (90.3% women) were evaluated, with a mean age of 58.39 ± 13.11 .

Structural study.

Mean age was 58.5 ± 12.4 , mostly women (90.1%). Most had some SDD (76.5% rectocele (43.7% significant), 45.3% some type of prolapse, 19.3% enterocele, and 8.5% megarectum). The percentage of women with rectocele was significantly higher than in men (78.4%—21.1%, respectively; $p<0.001$), and the same was true for prolapse (48.9%—12.3%; $p<0.001$), and enterocele (20.2%—8.9%; $p=0.041$). Megarectum was more prevalent in men (7.7%—15.8%; $p=0.038$).

Functional study.

ED: The ARA was not rectified in 66.3% of the patients (64.7% of women and 80.7% of men; $p=0.015$). PD was poor in 31.6% of the patients (30.7% of women—40.9% of men; ns), and excessive in 32.2%.

ARM: From the 294 patients evaluated with ARM, 40.4% showed hyper-tonicity of internal anal sphincter, 21.2% abnormal RAIR (19.1% of wom-

en—36.7% for men; $p=0.027$), 33.3% rectal hyposensitivity (30.5% women—54.3% men; $p=0.020$). PD was poor in 57.5% of women and 62.9% of men (ns).

Overall, 16.3% of the patients had FDD (women—men) (12.3%—54.5%), 46.4% SDD (48.2%—29.1%) and 37.3% both (39.5%—16.4%); $p<0.001$.

Symptoms.

The most frequent symptoms were straining (86.8%), sense of incomplete defecation (84.8%), anal blockage (58.3%), and hard stools (38.9%). Digitation was present in 35.8% of them. More than 20 years with symptoms was reported by 44.8% of the patients.

Expulsive capacity was impaired in 66.2% of SDD, 71.3% of FDD and in 78% of patients with both ($p=0.017$).

Conclusion: Coexistence of SDD and FDD is common. Isolated SDD is much more common in females, with rectocele being the most prevalent disorder. Pure FDD is more prevalent in men, and is manifested primarily by high MRP, rectal hyposensitivity and dyssynergic defecation. It is very common that expulsive difficulty is accompanied by an incomplete evacuation, especially in those patients in whom SDD coexist with FDD, followed by those who present Isolated FDD.

Disclosure: Nothing to disclose.

P0635

IMPACT ON QUALITY OF LIFE BEFORE AND AFTER TREATMENT INTERVENTION FOR CHRONIC INTESTINAL PSEUDO-OBSTRUCTION

K. Takahashi^{1,2}, T. Kessoku^{2,3}, K. Tanaka^{2,3}, T. Ogata², T. Jono², A. Yamamoto², A. Ozaki², Y. Kasai², M. Iwaki², A. Fuyuki², H. Okubo³, A. Nakajima³

¹Yokosuka General Hospital Uwamachi, Gastroenterology, Yokosuka, Japan, ²Yokohama City University Hospital, Palliative Medicine, Yokohama, Japan, ³Yokohama City University Graduate School of Medicine, Gastroenterology and Hepatology, Yokohama, Japan

Contact E-Mail Address: takahashi1700pk9@gmail.com

Introduction: Chronic intestinal pseudo-obstruction (CIPO) is a rare and intractable disease of the gastrointestinal tract that presents with abdominal symptoms such as abdominal pain, abdominal bloating, and pathological dilation of the intestinal tract without any organic obstruction. Many patients have difficulty in controlling their symptoms, so our challenge is to improve the symptoms and quality of life (QOL). In this study, we assessed QOL before and after the treatment intervention.

Aims & Methods: 41 patients with CIPO diagnosed by cine-MRI (1) and treated with treatment intervention were included in this study. Therapeutic interventions were defined as dietary restriction, intestinal sterilization, and decompression therapy such as percutaneous endoscopic gastro-jejunostomy (PEG-J) (2).

Patient background, treatment, desire for palliative care intervention, numerical rating scale (NRS) for abdominal pain/abdominal bloating, Japanese version of the Patient Assessment of Constipation QOL (JAPC-QOL) and Short Form (SF)-36 were prospectively sampled and collected. JAPC-QOL subscales were categorized into physical, mental, anxiety and satisfaction. SF-36 was classified into Physical component summary (PCS), Mental component summary (MCS) and Role/Social component summary (RCS).

Results: The mean age of onset of the target patients was 42 years, 29 were female (71%), and 30 were willing to undergo palliative care intervention (73%). Effective treatment included intestinal sterilization in 18 patients, decompression therapy with PEG-J in 8 patients, dietary restriction in 5 patients, and others in 11 patients. The mean NRS for abdominal distention was 8.7 before treatment, but improved to 2.7 after treatment, and the mean NRS for abdominal pain improved from 7.6 to 2.2 ($P<0.0001$).

SF-36 showed a change from an average of 30.1 to 38.1 for PCS ($P=0.0231$), an average of 42.0 to 47.9 for MCS ($P=0.0073$), and an average of 28.7 to 39.0 for RCS ($P=0.0079$). JPAC-QOL subscales showed a change from 2.6 to 1.2 for physical ($p<0.0001$), 1.9 to 1.4 for mental ($p=0.0022$), 2.1 to 1.5 for anxiety ($p<0.0001$), and 3.0 to 1.6 for satisfaction ($P<0.0001$).

Conclusion: The majority of CIPO patients were those who requested palliative care intervention, and were suffering from holistic distress that combined physical, mental, and social aspect.

This study suggested that appropriate treatment intervention for CIPO not only reduced physical suffering, but also improved mental and financial quality. In the future, it will be necessary to standardize treatment strategies for CIPO by searching for the invasiveness of treatment of CIPO and the effectiveness of different treatments.

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Disclosure: Nothing to disclose.

P0636

CHARACTERISTIC PATTERNS IN HIGH RESOLUTION ANORECTAL MANOMETRY IN PATIENTS WITH FECAL INCONTINENCE AFTER LOW ANTERIOR RESECTION SURGERY

I. Blanco Nodal¹, C. Ciriza de Los Rios¹, M. Aparicio Cabeza², A. Zatarain Valles¹, E. Velasco Martínez¹, S. Molina Tejedor¹, J. Casado Hernández¹, E. Rey Díaz-Rubio²

¹Hospital Universitario Clínico San Carlos, Gastroenterology, Madrid, Spain, ²Hospital Clínico San Carlos, Vice President of society, Madrid, Spain

Contact E-Mail Address: ignaciobnov37@gmail.com

Introduction: Low anterior resection syndrome (LARS) is a very common pathology among patients that had a sphincter-preserving surgery for rectal cancer. The most frequent complication is fecal incontinence (FI), which can be found in up to 95% of patients, with a huge impact on patients quality of life. This syndrome has a multifactorial origin, and thus, there are no clear manometric patterns so far.

Aims & Methods: Our aim was to assess and describe the anorectal manometric parameters found in patients who suffered FI following a low anterior resection (LAR) surgery.

Observational and cross-sectional study in 19 patients consecutively studied for FI after LAR. Epidemiological, clinical, and severity data were obtained with structured medical history followed by a high-resolution anorectal manometry (HRAM) (Manoscan®, Medtronic). Severity of FI was graded according to the Wexner score, establishing a moderate-severe disease when it was ≥ 9 . Severity of LARS was quantified with the LARS score, describing severe disease values ≥ 30 .

Results: 19 patients were included, of which 13 (68.4%) were male. Mean age and BMI were 63.2 (57.8-68.5) and 27 (24.8-29.2) respectively. Most of them suffered comorbidities 12 (63.2%), most frequently diabetes 7 (31.6%). Self-reported bowel habit was altered in 16 (84.2%) patients with more than 3 stools per day, and 13 (68.4%) had loose stools (Bristol scale ≥ 5). FI was frequently passive in 13 (72.2%) and on a daily basis in 14 (82.4%) patients. Seventeen (94.4%) had a Wexner score of ≥ 9 , and 14 (73.7%) had a LARS score ≥ 30 . Within parameters related to surgery, the anastomosis mean distance was 8.5 cm (6.5-10.5) and the mean time until surgical reconstruction was 17.5 months (7.7-27.4). All of them had received radiotherapy before the intervention.

As for the manometric parameters (Table 1), internal anal sphincter (IAS) was hypotensive in 14 (73.7%), with spontaneous relaxations of the anal canal in 15 (78.9%) of them. External anal sphincter (EAS) was hypoten-

sive in 4 (21.1%) patients, and 4 (21.1%) had hypotensive sphincter with shorten squeeze duration. Rectal volume tolerability (first sensation, urge to defaecate and discomfort volume) were reduced in 16 (84.2%) of them. Cough reflex was normal in 11 (57.9%) patients and RAIR was present in 17 (89.5%). Simulated defecation was normal in all of them except in one patient that was not studied.

Characteristic anal canal spontaneous relaxation was correlated with lower anal canal pressures ($p=0.028$). No other parameters studied included the anastomosis distance and the time until surgical reconstruction were associated with them. No other correlations were found with the anastomosis distance and the time until surgical reconstruction.

PARAMETER	MEAN VALUE	CI 95%
Anal canal length	4.7	1.3-7.9
Mean Resting pressure (mmHg)	44.9	33.2-56.7
Maximum Resting pressure (mmHg)	63.6	50.1-77.2
Maximum Squeeze pressure (mmHg)	162.1	128.6-195.6
Pressive increase (%)	77.8	46.5-119.2
Squeeze duration (seconds)	13.2	9.5-16.9
First sensation	14	8.9-19
Urge	35.3	29.1-41.6
Discomfort	48.7	40.9-56.5

Table.

Conclusion: Severe and daily FI is one of the most devastating problems in patients suffering LARS. HRAM is very useful to understand the anorectal function in these with the most common pattern being hypotensive IAS with spontaneous relaxations of the anal canal that explain passive FI. Decreased rectal volume tolerability is also very frequently found.

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Disclosure: Nothing to disclose.

P0637

PROSPECTIVE ASSESSMENT OF ANAL DISTENSIBILITY USING ENDOFLIP IN HEALTHY VOLUNTEERS

A. Rasijeff¹, C.H. Knowles¹, S.M. Scott¹

¹Queen Mary University of London, Blizard Institute, London, United Kingdom

Contact E-Mail Address: a.rasijeff@qmul.ac.uk

Introduction: Only a proportion of patients with faecal incontinence (FI) have abnormal anal tone (Rasijeff, Colorectal Dis 2022). Anal distensibility, measured by EndoFLIP, has been proposed as a viable alternative to manometry for assessing anal sphincter competence. A lower distensibility index (DI) has been observed in FI patients compared with healthy volunteers (HV) previously (Gourcerol, Neurogastroenterol Motil 2016; Zifan, Neurogastroenterol Motil 2012).

Aims & Methods: Aim: to describe distensibility of the anal canal using EndoFLIP in HV, and to define normal ranges for opening pressure, opening volume and DI, as well as to compare the results of manual data processing with data from commercially available software (EndoVizX [Motilityviz, California]). In total, 51 normal subjects without bowel symptoms underwent EndoFLIP at the Wingate Institute of Neurogastroenterology,

London, UK, as previously described (Alqudah, Neurogastroenterol Motil 2012). Opening (or yield) pressure (the pressure at which the diameter of the most narrow region of the anal canal first began to increase continuously during constant inflation of the EndoFLIP bag from 0 – 50 ml at a rate of 40 ml/minute), opening volume (the bag volume at opening pressure), opening DI (the narrowest CSA at opening, divided by the opening pressure), and DI at rest (median CSA at the narrowest anal canal location at rest, divided by the median pressure over the same time period) were calculated. Results were compared between sexes and according to female parity, and the impact of age and BMI was also assessed.

Results: Distensibility parameters were analysed in 46 subjects (35 F; mean age 38.5). At 50 ml, no significant differences in opening pressure (mean 49 mmHg, 95% CI: 45–54, $p=0.270$), opening volume (38 ml, 95% CI: 37–40, $p=0.232$), opening DI (0.49, 95% CI 0.4–0.6, $p=0.313$), or DI at rest (2.1, 95% CI: 1.7–2.6, $p=0.244$) were observed between men ($n=11$), nulliparous women ($n=19$), and parous women ($n=16$). There was no statistically significant linear association between distensibility parameters during inflation and age ($p=0.15$, $R^2=4.9\%$, 95% CI= -0.001 to 0.009) or BMI ($p=0.823$, $R^2=1.2\%$, 95% CI= -0.02 to 0.01). DI at rest increased by 0.4 units (95% CI 0.1–0.7) for every 10 year increase in age. Normal ranges are presented in Table 1. Statistically significant ($p<0.001$) linear relationships were observed between the results of manual data processing and results analysed using EndovizX software.

	Median	5 th percentile	95 th percentile
Opening pressure (mmHg) during inflation	47	22	75
Opening volume (ml) during inflation	38	30	45
Opening DI (cm ² /mmHg) during inflation	0.5	0.4	0.6
Distensibility index (cm ² /mmHg) at rest	1.9	0.8	4.8

Table.

Conclusion: Evaluation of the biomechanical properties of gastrointestinal sphincters using EndoFLIP technology to delineate function is gaining popularity. This study describes anal canal resistance to opening (during inflation) and DI at rest in a group of 46 HV - the largest HV cohort, including both sexes, studied to date. Normal cut-offs were defined based on 5th and 95th percentiles in health.

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P0638

EFFECT OF BIFIDOBACTERIUM BIFIDUM G9-1 ON FECAL SHORT-CHAIN FATTY ACIDS IN PATIENTS WITH CHRONIC CONSTIPATION: A MULTICENTER, OBSERVATIONAL STUDY

T. Ogata¹, T. Kessoku^{1,2}, T. Jono¹, K. Tanaka^{1,2}, A. Yamamoto¹, K. Takahashi¹, Y. Kasai¹, A. Ozaki¹, M. Iwaki¹, T. Kobayashi¹, N. Misawa¹, A. Fuyuki¹, A. Nakajima¹

¹Yokohama City University Graduate School of Medicine, Gastroenterology and Hepatology, Yokohama, Japan, ²Yokohama City University Graduate School of Medicine, Palliative Medicine, Yokohama, Japan

Contact E-Mail Address: tomo1993baske@gmail.com

Introduction: Constipation is a common and occasionally disabling digestive problem with an estimated prevalence ranging from 2% to 28% in adults. In previous reports, short chain fatty acids(SCFAs) has been decreased in constipated patients (1).

SCFAs enhance colonic fluid and sodium absorption and thus may aggravate the symptoms of constipation; however, the effect of SCFAs on colonic contractility, motility, and transit time remains unclear. *Bifidobacterium bifidum G9-1 (BBG9-1)* is a probiotic that has been used as an intestinal medicine for decades and has been shown to be effective for treating constipation in animal and human study (2,3).

Furthermore, few studies that have assessed the effect of probiotics on SCFAs in patients with constipation are available.

Aims & Methods: In our report, we showed that *BBG9-1* is effective for constipation, and we investigated whether one of the mechanisms is the alteration of SCFAs. This was a prospective, multicenter, observational study. Chronic constipation with patients diagnosed as Rome IV criteria were enrolled from the 4 institutions from July 2018 to February 2022. After baseline period, patients received 72 mg daily of *BBG9-1* for 8 weeks. We evaluated the effects on bowel function, changes in fecal SCFAs concentrations before and after *BBG9-1* administration.

Results: In the 87 patients analyzed, the frequency of pre- and post-treatment bowel movements per fortnight was 7 and 10 ($P < 0.001$), respectively. Not only bowel movement but also sense of incomplete evacuation, straining and stool form were significantly improved before and after *BBG9-1* administration.

The pre-treatment fecal n-butyrate concentration increased significantly from 0.76 to 1.03 mg/g stool post-treatment ($P < 0.0001$), with a significant increase in fecal iso-butyrate (pre-treatment 0.18 mg/g stool to post-treatment 0.21 mg/g stool, $P = 0.003$) and in acetic acid (pre-treatment 2.9 mg/g stool to post-treatment 3.2 mg/g stool, $P = 0.008$).

Conclusion: 8-week treatment with *BBG9-1* increased the concentrations of n-butyrate, iso-butyrate and acetic acid.

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Disclosure: Nothing to disclose.

P0639

VALIDATION OF THE RAPID BAROSTAT BAG (RBB) PUMP AND COMPARISON WITH CONVENTIONAL ELECTROMECHANICAL BAROSTAT

A. Rasijeff¹, A. Choudhary², R. Fried³, C.H. Knowles¹, S.M. Scott¹

¹Queen Mary University of London, Blizard Institute, London, United Kingdom, ²Queen Mary University, Wingate Institute of Neurogastroenterology, London, United Kingdom, ³University Hospital Zurich, Klinik für Gastroenterologie und Hepatologie, Zurich, Switzerland

Contact E-Mail Address: a.rasijeff@qmul.ac.uk

Introduction: Awareness of rectal filling is critical to normal bowel function. A tenth of women and 1 in 4 men with FI exhibit abnormal sensory thresholds to balloon distension (Rasijeff, Colorectal Dis 2022), however balloon distension alone cannot determine the *cause* of abnormal thresholds. While the electromechanical barostat is the gold-standard method for assessing rectal sensorimotor function, the Rapid Barostat Bag pump (Mui Scientific) seeks to enable accurate and consistent measurement of rectal capacity, compliance and sensory thresholds in a more timely fashion, using a portable device.

Aims & Methods: Aim: to compare measures of rectal sensorimotor function in health using the RBB pump against the standard electromechanical barostat (G&J Electronics). Healthy volunteers (n=19, mean age 37 [sd: 13], 13 F) were recruited prospectively to undergo standard barostat and RBB assessment on the same day in randomised order. Each method incorporated an infinitely compliant rectal barostat bag (600 ml for standard barostat, 700 ml for RBB). Compliance was defined as the slope of the line of best fit of the steepest part of a pressure-volume curve plotted using raw data from each method. Capacity (volume at 40 mmHg or maximum tolerable volume) and sensory threshold volumes for first sensation, urge and maximum tolerable volume (MTV) were also obtained. Bland and Altman plots were generated to assess agreement between methods and assess inter- and intra-rater agreement.

Results: Data on sensory thresholds, capacity and compliance for standard and rapid barostat are summarised in Table 1.

		Mean difference (SD)	95% CI	Limits of agreement		Outer Confidence Limits of LoA	Inner Confidence Limits of LoA
				Lower limit	Upper limit		
Standard barostat vs RBB	First sensation (ml)	-38.7 (47.6)	-65.1 - (-12.4)	-133.9	56.3	-191.5 - 113.8	-108.7 - 31.1
	Urge (ml)	-19.5 (63.5)	-54.6 - 15.7	-146.5	107.5	-223.1 - 184.1	-112.7 - 73.7
	MTV (ml)	-10.2 (46.2)	-35.8 - 15.4	-102.5	82.3	-158.3 - 138.1	-77.9 - 57.7
	Compliance	-2.4 (5.1)	-5.3 - 0.4	-12.7	7.8	-18.8 - 14.0	-9.9 - 5.1
	Capacity	-10.9 (40.5)	-33.4 - 11.5	-91.8	70.2	-140.7 - 119.1	-70.3 - 48.7
RBB vs RBB	Intra-observer	0.1 (2.7)	-1.2 - 1.4	-5.3	5.5	-8.0 - 8.1	-4.0 - 4.1
	Inter-observer	2.6 (4.6)	0.4 - 4.8	-6.5	11.7	-11.0 - 16.2	-4.3 - 9.5

Table 1.

Sensory threshold volumes measured by RBB were significantly higher for first sensation (112 ml vs 74 ml; $p=0.007$), but similar for other thresholds (urge: 221 ml vs 202 ml; MTV: 345 ml vs 335 ml). Mean compliance (17.9 ml/mmHg, 95% CI: 14.7-21.1 for RBB, and 16.8 ml/mmHg, 95% CI: 14.7-19.0 for standard barostat) and mean capacity (312 ml for RBB vs 301 ml) were also similar between methods. Although mean differences were clinically insignificant, the wide Limits of agreement (LoA) suggest-

ed poor agreement between the two methods (Table 1). Generally, the wider the inner and outer limits of LoA, the more inaccurate either (or both) methods are.

Conclusion: The RBB pump has been developed to facilitate routine measurement of compliance, capacity, and rectal sensation. Despite clinically insignificant differences between mean measurements by standard barostat and RBB pump, wide limits of agreement suggest that the two methods do not provide entirely comparable measures of rectal compliance (i.e. elasticity). The RBB pump showed excellent intra- and inter-rater agreement for compliance. However, while the RBB may be clinically useful as an alternative to balloon distension or conventional barostat, these data preview the need for the development for a larger normative RBB dataset.

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P0640

TSH RECEPTOR ANTIBODIES (TRAB) – A POTENTIAL NEW BIOMARKER TO DIFFER BETWEEN IRRITABLE BOWEL SYNDROME AND ENDOMETRIOSIS

B. Ohlsson¹, B. Roth¹, A. Svensson¹

¹Skanes Universitetssjukhus, Department of Clinical Sciences, Malmö, Sweden

Contact E-Mail Address: Bodil.Ohlsson@med.lu.se

Introduction: Irritable bowel syndrome (IBS) is common in the society, especially in young women. Before the diagnosis is set, other organic diseases have to be excluded. Endometriosis is defined by endometrial cells and stroma growing outside of the uterus. The disease affects 5–10% of women in reproductive age; thus affecting the same group which suffer from IBS. Endometriosis is causing symptoms such as pelvic pain, gastrointestinal symptoms and infertility.

The prevalence of gastrointestinal symptoms is as common as other symptoms, and was present in 85% during the last year (Ek et al. 2015). One-third of endometriosis patients also suffer from IBS (Ek et al. 2021). It is a great challenge for the clinicians, to differ between IBS and endometriosis. Endometriosis demands ultrasound examination or laparoscopy for diagnosis, and the disease demands quite a different treatment compared with IBS.

Thus, it is very important for the clinicians to have access to biomarkers that can differ the two conditions, and suggest more examinations in one or the other direction. Several autoimmune diseases, including thyroid dysfunction, has been reported to be increased in patients with endometriosis, which has not been observed in IBS. Upregulated thyroid-stimulating hormone (TSH) receptors in ectopic endometrium and elevated serum titers of TSH receptor antibodies (TRAb) IgG in endometriosis patients indicates an overlap in pathophysiology (Ek et al. 2018).

Aims & Methods: The objective of this study was to compare the expression of autoantibodies in women with endometriosis, IBS and controls to evaluate the potential of TRAb IgG as a diagnostic marker to exclude endometriosis at a Department of Gastroenterology or in primary care. This cross sectional study was carried out in 172 women with surgically confirmed endometriosis and two control groups consisting of 50 healthy

female blood donors and 114 women from the general population with known IBS prevalence, respectively. Serum levels of TRAb IgG antibodies, TSH and thyroid hormones were analyzed by standardized methods at the Division of Clinical Chemistry, whereas serum levels of IgM were evaluated by in-house enzyme-linked immunosorbent assays (ELISA).

The endometriosis patients and controls from the general population answered a questionnaire and estimated their gastrointestinal symptoms using the Visual Analogue Scale for Irritable Bowel Syndrome (Bengtsson et al. 2007).

Results: There was no difference in TRAb titers between population-based controls who had IBS (N=25, 21.9%; p=0.655) or reported gastrointestinal symptoms in the past two week (N=30, 26.3%; p=0.885) compared to those without symptoms. Of the endometriosis patients, 29.1% had TRAb IgG above the present detection limit of 1.0 IE/L compared to 2.6% of the population-based controls (p<0.001) and 94.5% had levels of TRAb over the previous detection limit 0.3 IE/L compared to 7.9% of the controls (p<0.001).

Titers of both TRAb IgG and IgM were increased in patients compared to population-based controls and healthy controls (p<0.001). TRAb titers did not correlate with age, disease duration, TSH, thyroid hormones or gastrointestinal symptoms. The prevalence of TRAb IgG as defined as grey-zone (1.2-1.7) and positive (>1.7 IE/L) was higher in endometriosis than controls (p<0.001), whereas positive for IgM did not differ (p=0.162) between endometriosis and controls.

Conclusion: TRAb IgG and IgM are slightly elevated in patients with endometriosis, but not in IBS. The results indicate that TRAb is truly elevated in endometriosis and thereby has the potential to support the diagnosis. Thus, TRAb could be used to help the clinician to exclude endometriosis in women with gastrointestinal symptoms. Very low levels of TRAb support the diagnosis of IBS.

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Disclosure: No conflicts of interest is present.

P0641

SYMPTOM CLUSTERS OUTSIDE THE ROME IV CONSENSUS CAN BE IDENTIFIED IN BOTH EASTERN AND WESTERN PATIENTS WITH A DISORDER OF GUT-BRAIN INTERACTION: PRELIMINARY RESULTS OF AN ONGOING INTERNATIONAL MULTICENTER STUDY

E. Colomier^{1,2}, L. Holvoet¹, F. Carbone¹, T. Bai³, J. Liu³, C.K. Huat⁴, S. Mahadeva⁴, K.T.H. Siah⁵, R. Nakov⁶, P. Liptak⁷, P. Banovcin⁷, G.J. Holtmann⁸, H. Suzuki⁹, T. Ueda⁹, I. Midenfjord², M. Simrén^{2,10}, K.A. Gwee⁵, J. Tack^{1,2}

¹Translational Research Center for Gastrointestinal Disorders (TARGID), Department of Chronic Diseases, Metabolism and Aging (CHROMETA), Leuven, Belgium, ²Department of Molecular and Clinical Medicine, Institute of Medicine, Sahlgrenska Academy, University of Gothenburg, Gothenburg, Sweden, ³Gastroenterology Department of Wuhan Union, Tongji Medical College of Huazhong Science & Technology University, Wuhan, China, ⁴Department of Medicine, University of Malaya, Kuala Lumpur, Malaysia, ⁵Department of Medicine, National University of Singapore and Gleneagles Hospital, Tanglin, Singapore, ⁶Tsaritsa Yoanna University Hospital, Medical University of Sofia, Department of Gastroenterology, Sofia, Bulgaria, ⁷Clinic of Internal Medicine-Gastroenterology, University hospital in Martin, Jessenius faculty of Medicine in Martin, Comenius University, Martin, Slovakia, ⁸Princess Alexandra Hospital, Gastroenterology & Hepatology, Brisbane, Australia, ⁹Department of Gastroenterology and Hepatology, Tokai University School of Medicine, Isehara, Japan, ¹⁰Center for Functional GI and Motility Disorders, University of North Carolina-Chapel Hill, Chapel Hill, NC, United States

Contact E-Mail Address: esther.colomier@kuleuven.be

Introduction: Disorders of gut-brain interaction (DGBI) are characterized by symptoms clusters emanating from the gastrointestinal (GI) tract in the absence of explanatory organic findings on routine examination. The diagnostic Rome IV criteria, mainly validated in Western countries, classify DGBI based on the anatomical section of the GI tract where the predominant symptoms originate from.

However, a study in Eastern patients using an Enhanced Asian Rome III questionnaire (EAR3Q) identified symptom clusters involving more than one anatomical section:

1. Meal-related bowel symptom cluster,
2. Upper abdominal pain with constipation cluster, and
3. Bloating, fullness, belching, and flatulence cluster (1).

Our aim was to compare Eastern and Western DGBI patients and investigate if these three symptom clusters were reproducible in a Western cohort.

Aims & Methods: We conducted descriptive analyses on the first data of an ongoing international survey study comparing symptom patterns and clusters in both Eastern and Western participating centers. We included consecutive adult patients who were diagnosed with a DGBI by their treating physician. In addition to a primary DGBI diagnosis, the physician identified potential overlapping symptoms of other DGBI based on the Rome IV classification (secondary diagnosis). Patients completed the Adult Diagnostic Rome IV questionnaire supplemented with questions from the EAR3Q that identified the aforementioned three symptom clusters. Patients were appointed to symptom clusters if they reported presence of the respective GI symptoms in the Rome IV and EAR3Q for more than six months. The subjects' quality of life (QoL) (mental and physical health) was measured with the validated PROMIS Global-10 questionnaire.

Results: We included 375 Eastern and 89 Western DGBI patients from respectively 3 and 5 centers (Western: 75% female, age: 39±14 years, BMI: 23±4 kg/m² and Eastern: 55% female, age: 43±13 years, BMI: 22±4 kg/m²).

In both the Western and Eastern cohort, the most prominent DGBI diagnoses were functional dyspepsia (34% vs. 37%), irritable bowel syndrome (33% vs. 29%), functional constipation (6% vs. 10%), and functional diarrhea (2% vs. 8%).

The most common secondary diagnoses in the Western and Eastern cohort included functional dyspepsia (18% vs. 3%), irritable bowel syndrome (14% vs. 2%), functional bloating (7% vs. 4%), and functional constipation (6% vs. 4%). The proportion of patients without overlapping symptoms was 21% vs. 67% in the Western and Eastern cohort, respectively. The Western cohort reported better physical QoL (Western physical QoL: 12±3 vs. Eastern physical QoL: 10±2, $p<0.001$). In total, 83% vs. 33% of the Western and Eastern patients could be appointed to one of the three previously reported Eastern symptom clusters.

Within the three symptom clusters outside the current Rome IV consensus, the largest proportion of both Eastern and Western patients reported symptoms representing cluster 1 (Table). Patients could also be appointed to more than 1 symptom cluster with the largest overlap between clusters 1 and 3.

	Cluster 1	Cluster 2	Cluster 3	Overlap cluster 1 and 2	Overlap cluster 1 and 3	Overlap cluster 2 and 3
Western cohort (n=87)	76%	27%	33%	24%	29%	11%
Eastern cohort (n=468)	31%	5%	4%	4%	4%	2%

Table.

Conclusion: The previously found Eastern GI symptom clusters involving more than one anatomical section are also present in a Western DGBI cohort. The anatomical basis for disorder classification as used in the Rome IV consensus may not cover the full symptom spectrum of patients with DGBI.

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Disclosure: Nothing to disclose

P0642

COMPARISON OF THE HABITUAL DIETARY INTAKE AND DIET QUALITY IN PATIENTS WITH IRRITABLE BOWEL SYNDROME AND THE GENERAL POPULATION

E. Colomier^{1,2}, S. Nybacka¹, S. Störsrud¹, J. Tack^{1,2}, H. Törnblom¹, M. Simré^{1,3}

¹Institute of Medicine, Sahlgrenska Academy, University of Gothenburg, Molecular and Clinical Medicine, Gothenburg, Sweden, ²Translational Research Center for Gastrointestinal Disorders (TARGID), Chronic Diseases, Metabolism and Aging (CHROMETA), KU Leuven, Leuven, Belgium, ³Center for Functional GI and Motility Disorders, University of North Carolina-Chapel Hill, Chapel Hill, United States

Contact E-Mail Address: esther.colomier@kuleuven.be

Introduction: Food hypersensitivity is of importance in the pathophysiology of irritable bowel syndrome (IBS). To improve gastrointestinal symptoms, patients with IBS tend to avoid triggering foods, which might influence their habitual dietary intakes and diet quality. Therefore, we aimed to determine and compare the habitual diet quality and dietary intake of IBS patients and controls.

Aims & Methods: We used baseline data of patients with IBS who were recruited for a dietary intervention study or a study investigating pathophysiological factors. For the age and gender-matched control sample, we used data from a Swedish population-based study that collected data during the same period, the Riksmaten study (2010-2015).

The habitual dietary intake was assessed with consecutive 4-day food diaries, during Wednesday-Saturday in the patient cohort, and with an equal distribution of weekdays and weekend days in the control group. A dedicated software (DIETIST XP V.3.1) was used to calculate the mean daily energy, macronutrient, and fiber intake.

The food group categorization was based on the classification of the Swedish National Food Administration. Diet quality was assessed using a diet quality index (DQI) based on adherence to the Swedish nutrition recommendations and dietary guidelines (1).

The index considered the intake of saturated and polyunsaturated fatty acids, fish, fiber, fruit and vegetables, and sucrose. Per component, adherence vs. non-adherence to the recommendations resulted in a score of 1 vs. 0, leading to a sum score ranging from 0-6.

Results: We included 197 patients with IBS and 197 controls (both cohorts: 77% female, age: 37±14 years, BMI: 24±4 kg/m²). Controls had a significantly lower total energy intake compared to patients with IBS (1858±616 kcal vs. 2127±550 kcal, $p<0.001$), including a higher intake of carbohydrates (43±7 E% vs. 40±8 E%, $p=0.003$) and lower intake of protein (16±4 E% vs. 17±4 E%, $p=0.01$) and fat (38±8 E% vs. 36±7 E%, $p=0.003$). In both patients and controls the intake of carbohydrates was lower than the recommendations, i.e. 45-60 E%. The intake of other macronutrients adhered to the Swedish national nutrition recommendations.

Patients had a higher cereal, egg, fish, meat, nuts and seeds intake, and a lower coffee, and mixed dishes intake compared with controls. Reported intake of alcohol, dairy, fruits, and vegetables did not differ between patients and controls.

The mean DQI did not differ between the patients and controls (2.8±1.3 vs. 2.8±1.3, $p>0.99$), but the proportion of patients adhering to the recommended cut-offs of DQI components fish and dietary fiber differed from the proportion of controls adhering to these recommendations (37% vs. 26%, $p=0.02$ and 46% vs. 62%, $p=0.001$, respectively) (Table).

Description of DQI	Adherence			
	Index component	Cut-off	IBS patients	Controls p-value
Short-chain fatty acids (non-alcohol Energy %)	≤14	43%	44%	>0.99
Polyunsaturated fatty acids (non-alcohol Energy %)	5-10	68%	68%	>0.99
Fish (gram/week)	≥300	37%	26%	0.02
Dietary fiber (gram/Megajoule)	2.2	46%	62%	0.001
Fruit and vegetables (gram/day)	≥400	14%	13%	>0.99
Sucrose (non-alcohol Energy %)	≤10	73%	68%	0.26

Table.

Conclusion: The reported habitual dietary intake in patients with IBS included a higher energy intake with slight differences in macronutrient composition compared with a population-based control group. More patients adhered to the recommended fish intake, but less patients adhered to the recommended dietary fiber intake compared to controls. Habitual dietary intakes should be monitored in clinical practice to assure healthy eating habits.

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Disclosure: Nothing to disclose.

P0643

IDENTIFYING DIFFERENT IRRITABLE BOWEL SYNDROME SUBGROUPS BASED ON BOWEL HABITS AND PSYCHOLOGICAL COMORBIDITY: A REPLICATION STUDY USING MIXTURE MODELLING

I.A. Trindade¹, I. Midenfjord¹, E. Colomier¹, J. Hreinsson², S. Störsrud², H. Törnblom¹, M. Simrén^{1,3}

¹University of Gothenburg, Department of Molecular and Clinical Medicine, Institute of Medicine, Sahlgrenska Academy, Gothenburg, Sweden, ²Sahlgrenska University Hospital, Department of Molecular and Clinical Medicine, Gothenburg, Sweden, ³University of North Carolina-Chapel Hill, Center for Functional GI and Motility Disorders, Chapel Hill, North Carolina, United States

Contact E-Mail Address: ines.trindade@gu.se

Introduction: Previous studies have identified subgroups of irritable bowel syndrome (IBS) patients based on bowel habits, and comorbid extraintestinal and psychological symptoms [1]. Different group profiles regarding combinations of bowel habits and low/high comorbidities were identified. This study aims to replicate these findings while also considering additional relevant aspects.

Aims & Methods: IBS patients completed self-report questionnaires as measures of gastrointestinal symptom severity (GSRS-IBS), stool consistency and frequency (BSF), anxiety and depression (HADS), extraintestinal somatic symptoms (PHQ-12), GI-specific anxiety (VSI), trait anxiety (STAI-T), stress (PSS), sexual and physical abuse (Leserman et al. [2]), fatigue (MFI), and pain catastrophizing (PCS). A mixture model analysis was performed to identify latent classes based on questionnaire scores. The subgroups were then compared regarding demographic variables, other disease diagnoses, IBS severity (IBS-SSS), post-traumatic stress (SQ-PTSD), and work absenteeism and impairment (WPAI), using analysis of variance, chi-squared tests, or Fisher's exact tests.

Results: We included 181 IBS patients; 70.7% female; mean age 35.9 (range 19-66) years. Five latent subgroups were identified and characterized by:

- constipation with low level of severity of somatic/psychological comorbidities;
- constipation with high comorbidities;
- diarrhea with low comorbidities;
- diarrhea with high comorbidities, high pain catastrophizing, and history of sexual and/or physical abuse; and,
- mild symptoms with low comorbidities.

The high comorbidities groups had a higher proportion of females ($p < .001$) and higher IBS severity ($p < .001$), work absenteeism ($p = .008$), impairment while working ($p < .001$), and general activity impairment ($p < .001$). Post-traumatic stress was more prevalent in the diarrhea with high comorbidities group ($p = .041$), and chronic fatigue was more prevalent in constipation with high comorbidities ($p < .001$). No differences were found between subgroups regarding age ($p = .215$), duration of symptoms ($p = .061$), fibromyalgia ($p = .603$), and overall work impairment ($p = .054$).

Conclusion: This study confirms previous findings of latent IBS subgroups based on bowel habits combined with somatic/psychological comorbidity and the association of these subgroups to other important clinical, demographic, and outcome parameters. This study also contributes with novel findings by considering variables such as abuse history, pain catastrophizing, and fatigue to identify these subgroups.

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Disclosure: Outside of the present work, IAT has served as consultant for Pfizer Inc. CM has received speaker fees from Kyowa Kirin, Norgine, Biocodex, Mayoly spindler, Tillots, and Ipsen, and has served as Advisory Board member for Kyowa Kirin. HT has served as Consultant/Advisory Board member for Almirall, Danone and Shire.

MS has received unrestricted research grants from Danone Nutricia Research, Glycom, and Ferring Pharmaceuticals, and served as a Consultant/Advisory Board member for AstraZeneca, Biocodex, Danone Nutricia Research, Genetic Analysis AS, Menarini, Nestlé, Chr Hansen, Almirall, Allergan, Arena, Adnovate Albireo, Glycom, and Shire, and as a speaker for Tillotts, Menarini, Kyowa Kirin, Takeda, Shire, Biocodex, Alfasisigma, Falk Foundation, and Almirall.

P0644

KOMBUCHA-BASED SPECIALIZED FOOD PRODUCT FOR TREATMENT OF CONSTIPATION

V. Pilipenko¹, S. Morozov², V. Isakov²

¹Federal Research Centre of Nutrition, Gastroenterology and Hepatology, Moscow, Russian Federation, ²Federal Research Center of Nutrition and Biotechnology, Gastroenterology & Hepatology, Moscow, Russian Federation

Contact E-Mail Address: pilipenkovork@rambler.ru

Introduction: Aim: To assess the efficacy of kombucha-based specialized food product, enriched with inulin in patients with constipation-predominant irritable bowel syndrome.

Aims & Methods: The study (NCT05164861) was approved by LEC and enrolled subjects with constipation-predominant irritable bowel syndrome (according to ROME IV). The subjects were randomized to receive either 220 ml of a non-alcoholic drink, based on pasteurized kombucha (KG), enriched with inulin (1.15 g/100ml) or 220 ml water (control group, CG), for 10 days.

Except study product, subjects were advised to follow their usual diet. Standard examination included evaluation of stool frequency (bowel movements per day), stool form (with the Bristol stool scale) and evaluation of concomitant symptoms (abdominal pain/discomfort, abdominal fullness, bloating, and feeling of incomplete bowel emptying) with the use of 5-point Likert scale before (BL) and 10 days after the start of intervention (EOT).

Results: The complete data of 40 subjects were available for the analysis. Significant increase of stool frequency was found at the EOT compared to BL in KG ($n = 20$), Mean $\pm$ SD: 0.60 ± 0.31 to 0.85 ± 0.19 times/day; $p = 0.004$, while there was no change in CG ($n = 20$): 0.63 ± 0.33 vs 0.72 ± 0.28 , $p > 0.05$. Mean values of stool scale form increased in KG (2.95 ± 1.15 to 4.4 ± 0.97 ; $p = 0.001$), while remained unchanged in CG (2.94 ± 1.2 vs 3.4 ± 1.2 , $p = 0.6$). Mean values of the Bristol stool scale in KG and CG differed significantly at EOT ($p = 0.018$).

Significant decrease in mean values of incomplete bowel emptying feeling was found in KG (1.88 ± 0.78 at BL vs 1.41 ± 0.56 points at EOT, $p = 0.015$), but not in the control group. There was no difference in patient's reports for other symptoms between KG and CG.

Conclusion: New specialized kombucha-based drink enriched with inulin is well-tolerated and increases stool frequency and consistency in patients with constipation-predominant irritable bowel syndrome.

Disclosure: Nothing to disclose.

P0645

NON-COELIAC GLUTEN SENSITIVITY APPEARS TO BE THE MAJOR PRESENTING AETIOLOGY BEHIND IBS

T. Su^{1a}, J. Ye², C. Montoya^{3,4}, D. Luo⁵, K. Rostami²

¹University of Otago, Christchurch, New Zealand, ²MidCentral DHB Palmerston North Hospital, Department of Gastroenterology, Palmerston North, New Zealand, ³AgResearch Limited, Smart Foods and Bioproducts Innovation Centre of Excellence, Palmerston North, New Zealand, ⁴Massey University, Riddet Institute, Palmerston North, New Zealand, ⁵AgResearch Limited, Ruakura Research Centre, Hamilton, New Zealand

Contact E-Mail Address: suata871@student.otago.ac.nz

Introduction: Non-coeliac gluten sensitivity diagnosis has improved the therapy approach for many patients diagnosed with irritable bowel syndrome (IBS). The polymorphisms of gluten and other food antigens implicated in the modern lifestyle could act as strong epigenetic factors with a spectrum of different severity. Identifying and addressing food sensitivities in patients presenting with IBS like symptoms are currently underemphasised in clinical guidelines. Yet have the potential to provide major benefits for patients.

Aims & Methods: This observational study aimed at assessing the efficacy of targeted interventions addressing common food sensitivities and lifestyle factors that commonly contribute to the presentation of gastrointestinal symptoms identified as IBS.

Information was collected from the medical records of patients that were referred to the Gastroenterology Unit of Palmerston North DHB with unexplained gastrointestinal (GI) symptoms with or without other GI comorbidities between September 2018 and November 2021. A diagnosis of coeliac disease was excluded. The main management option offered to the 121 patients included in this study, was a trial of 6 weeks, eliminating gluten according to Salerno expert criteria and lactose exclusion from the diet and/or lifestyle adjustment recommendations.

Results: The most prevalent symptoms were abdominal pain (79%), and diarrhoea (69%), followed by bloating and constipation. Seventy-eight patients had the outcomes of their improvement available. A total of 42 out of 78 patients (54%) were treated exclusively with a gluten and lactose-free diet, in this group of patients 86% (36/42) reported a significant improvement in their symptoms with a score in the range of 40-100%.

Conclusion: The improvement score between 40-100% of symptoms following gluten elimination advocates that gluten represents a major pathogenic factor behind IBS presentation. But the disunity and variability of the response indicate that gluten might not be the only noxious factor implicated in these patients' conditions.

Nevertheless, gluten elimination for treating IBS patients' symptoms is non-toxic and highly effective in achieving optimal outcomes and improving many of these patients' quality of life.

Disclosure: Nothing to disclose.

P0646

ROLE OF DIETARY HABITS ON SYMPTOM CONTROL AND GUT MICROBIOTA COMPOSITION IN PATIENTS WITH IRRITABLE BOWEL SYNDROME WITH CONSTIPATION (IBS-C)

S. Crucillà¹, A. Altomare², C. Di Rosa³, L. Putignani⁴, S. Emerenziani⁵, M.V. Ristori⁴, C. Calò³, R. Nicolò⁵, M. Ciccozzi⁶, M. Cicala², M.P.L. Guarino²

¹Azienda Ospedaliera Universitaria Integrata Verona, Gastroenterology Unit, Verona, Italy, ²Campus Bio Medico University, Gastroenterology Unit, Rome, Italy, ³Campus Bio Medico University, Department of Sciences and Technologies for Human and Environment, Rome, Italy, ⁴Children's Hospital and Research Institute "Bambino Gesù", Units of Parasitology and Human Microbiome, Rome, Italy, ⁵Campus Biomedico University of Rome, Unit of Nutrition, Rome, Italy, ⁶Campus Bio Medico University, Unit of Medical Statistics and Molecular Epidemiology, Rome, Italy

Contact E-Mail Address: salvatore.crucilla1@gmail.com

Introduction: The pathophysiology of Irritable Bowel Syndrome (IBS) has not been clearly understood but diet and intestinal dysbiosis appear to be involved. The aim of the present pilot study was to observe the interaction between Mediterranean diet (MD), gastrointestinal (GI) symptoms and gut microbiota changes in prevalent constipation IBS (IBS-C) patients.

Aims & Methods: 15 IBS-C were underwent to a targeted nutritional protocol for 4 weeks, filling a food diary and an IBS symptoms questionnaire 2 weeks before and at the end of the nutritional intervention.

Moreover a fecal sample was collected 2 weeks before and at the end of the nutritional protocol performing the microbiota analysis by 16S rRNA targeted-metagenomics.

The control group, composed by 17 healthy subjects, received a food diary and a symptoms questionnaire to exclude gastrointestinal disorders. The nutritional protocol was elaborated respecting the macronutrient percentage and the quantity of fiber indicated by LARN 2014 guidelines (Reference Levels of Nutrients and Energy Intake for the Italian population). MD adherence was calculated using the MDSS score.

Results: MDSS index was significantly reduced in IBS patients compared to controls ($p > 0.0001$). The analysis of food diaries at T0 showed a significant increase of protein intake ($p = 0.0229$) in IBS patients compared to controls as well as a less intake of carbohydrates and fiber without a significant difference.

After the nutritional intervention, the MDSS index was significantly increased in IBS patients, showing a better adherence to MD ($p < 0.0001$). The percentage of proteins, lipids, carbohydrates, simple sugars and grams of fibers intake were checked before and after the nutritional protocol. Up to these five items checked a significant improvement from T0 to the endpoint was observed ($p = 0.0199$).

Gut microbiota analysis showed, at phylum level, an increase of *Bacteroidetes* and a decrease of *Firmicutes* in IBS patients after the nutritional protocol (T1) with an increase of *Bacteroidaceae* and a decrease of *Ruminococcaceae*, *Lachnospiraceae*, *Clostridiales* and *Prevotellaceae* at the family level.

A significant reduction in pre-evacuation abdominal pain ($p = 0.0004$), in the daily frequency of abdominal pain ($p = 0.0020$) and in the abdominal pain during the evacuation ($p < 0.0001$) was observed in IBS patients following the nutritional intervention.

Conclusion: These preliminary results show a significant role of a right dietary lifestyle in controlling IBS symptoms; further investigations, increasing the number of patients, are needed to confirm these data.

Disclosure: Nothing to disclose.

P0647

GENERAL LIFE SATISFACTION IN IBS PATIENTS IS ASSOCIATED WITH PSYCHOLOGICAL SYMPTOM BURDEN AND QUALITY OF LIFE, RATHER THAN GASTROINTESTINAL SYMPTOM SEVERITY

J.T.W. Snijkers^{1,2}, B. Winkens³, Z.Z.R.M. Weerts^{1,2}, L. Vork^{1,2}, Z. Mujagic^{1,2}, M.A.M. Hesselink^{1,2}, C. Leue^{4,5}, J.W. Kruimel^{1,2}, J.W.M. Muris⁶, D.M.A.E. Jonkers^{1,2}, A.A. Masclee^{1,2}, D. Keszthelyi^{1,2}
¹Maastricht University Medical Center+, Division of Gastroenterology-Hepatology, Department of Internal Medicine, Maastricht, Netherlands, ²Maastricht University, NUTRIM, School of Nutrition and Translational Research in Metabolism, Maastricht, Netherlands, ³Maastricht University, Department of Methodology and Statistics, CAPHRI, Care and Public Health Research Institute, Maastricht, Netherlands, ⁴Maastricht University Medical Center+, Department of Psychiatry and Psychology, Maastricht, Netherlands, ⁵Maastricht University, MHeNS, School for Mental Health and Neuroscience, Maastricht, Netherlands, ⁶Maastricht University, Department of Family Medicine, CAPHRI Care and Public Health Research Institute, Maastricht, Netherlands

Contact E-Mail Address: j.snijkers@maastrichtuniversity.nl

Introduction: Irritable bowel syndrome (IBS) is a disorder of gut-brain interaction. IBS symptoms have major impact on a person's emotional, social, and professional life. Previous research showed the high disease burden in IBS patients, but studies on general life satisfaction in IBS populations are lacking.

Aims & Methods: The current study aims to evaluate general life satisfaction in IBS patients and to determine which factors are associated with higher life satisfaction. IBS patients (n=195, median age 53 years (interquartile range 29 years), 73.8% female) recruited from primary and secondary/tertiary care completed questionnaires regarding gastrointestinal symptoms (Gastrointestinal Symptom Rating Scale-IBS), quality of life (36-item Short-Form Health Survey, physical and mental composite score), psychological factors (Hospital Anxiety and Depression Scale), gastrointestinal-specific anxiety (Visceral Sensitivity Index), and life satisfaction. Life satisfaction was measured by the Satisfaction With Life Scale (SWLS, 5 items, range 5-35). This instrument assesses the judgement of one's life as a whole and does not measure satisfaction in specific life domains. Multivariable linear regression was used to identify variables associated with life satisfaction.

Results: Overall, 76.4% of the patients had a SWLS-score ≥ 20 , corresponding with a neutral score or higher on life satisfaction. When a cut-off of SWLS-score ≥ 21 was used, corresponding with scores between slightly satisfied and extremely satisfied, 71.3% of the patients scored satisfied about their life.

The mean of the SWLS-score was 23.9 (standard deviation 6.4). Female gender (B (unstandardized coefficient)=1.926, $p=0.025$), higher physical quality of life (B=0.229, $p<0.001$), higher mental quality of life (B=0.216, $p<0.001$), and fewer general anxiety symptoms (B=-0.334, $p=0.032$) were associated with higher life satisfaction. No significant association was found between gastrointestinal symptom severity and life satisfaction.

Conclusion: Higher quality of life and less anxiety symptoms, but not gastrointestinal symptom severity, were associated with higher general life satisfaction in IBS. These findings support the clinical need in IBS treatment to take psychological factors and quality of life into account in order to enhance life satisfaction.

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P0648

IRRITABLE BOWEL SYNDROME SYMPTOM SEVERITY AND ASSOCIATION WITH SHORT-CHAIN FERMENTABLE CARBOHYDRATES CONSUMPTION AFTER BARIATRIC SURGERY: AN OBSERVATIONAL PROSPECTIVE STUDY

P. Van Ouytsel^{1,2}, A. Szalai², K. Buedts², M. Barea², V. Huberty¹, J. Closset³, P. Loi³, H. Piessevaux⁴, H. Louis¹
¹Hopital Erasme, Department of Gastroenterology, Hepatopancreatology and Digestive Oncology, Bruxelles, Belgium, ²Hopital Erasme, Dietetic, Bruxelles, Belgium, ³Hopital Erasme, Digestive Surgery, Bruxelles, Belgium, ⁴Cliniques Universitaires Saint-Luc, Department of Hepato-Gastroenterology, Brussels, Belgium

Contact E-Mail Address: pauline.vanouytsel@gmail.com

Introduction: Irritable Bowel Syndrome (IBS)-like symptoms such as diarrhoea, constipation, bloating, and gas are frequent following bariatric surgery. Since short-chain fermentable carbohydrates (FODMAPs) can trigger symptoms in IBS, we aimed to prospectively evaluate the frequency of IBS symptoms severity before and after bariatric surgery and their link with FODMAPs consumption.

Aims & Methods: The primary outcome was to evaluate the IBS symptom severity in a cohort of obese patients before, 6 and 12 months after bariatric surgery by validated questionnaires and tools (Irritable Bowel Syndrome Severity Scoring System (IBS SSS), Bristol Stool Scale (BSS), Quality of Life Short-Form-12 (SF-12), Hospital Anxiety and Depression scale (HAD)).

The secondary outcome was to evaluate the FODMAPs consumption and its association with IBS symptom severity, using a food frequency questionnaire focused on high-FODMAPs food consumption.

Results: Fifty-one patients were included (41 female; mean age 41 years (SD: 12) ; 10 with a previous bariatric surgery), 84% benefited from a sleeve gastrectomy, and 16% from a Roux-en-Y gastric bypass. IBS SSS score was not significantly different before, 6 and 12 months after surgery (83.5 ± 81.6 vs 105.8 ± 91.3 vs 83.3 ± 95.0 ; NS).

Nevertheless, compared to pre-surgery score, IBS symptoms severity increased in one third of the patients 6 months following surgery, and in one quarter of the patients at 12 months.

According to the IBS SSS score, no severe IBS was diagnosed before surgery, but was observed in 5 % of the patients at 6 and 12 months. Forty-three percent of the patients had a mild to moderate IBS before surgery, compared to 53 % and 29% of the operated patients after 6 and 12 months respectively.

In a multivariate model, a significant association was found between the IBS SSS score and lactose consumption at 6 months ($\beta = + 58, 1; p = 0.03$), and with polyols consumption at 12 months ($\beta = + 112, 6; p = 0.01$).

Conclusion: Mild to moderate IBS symptoms are frequent in obese patients before bariatric surgery. Despite anatomical and physiological alterations induced by surgical procedures, IBS symptom severity does not seem to increase significantly after surgery.

However, a significant association between lactose and polyols consumption after operation and IBS SSS score was observed after bariatric surgery suggesting a potential link between the severity of IBS symptoms and some specific FODMAPs consumption, such as lactose and polyols.

Disclosure: Nothing to disclose.

P0649

EFFECT OF IBEROGAST (STW5) ON TOLERANCE TO COLONIC GAS IN PATIENTS WITH IRRITABLE BOWEL SYNDROME

A. Aguilar^{1,2}, B. Benslaiman¹, J. Serra²

¹University Hospital Germans Trias i Pujol, Motility Unit, Badalona, Spain, ²University Hospital Vall d'Hebron, Digestive System Research Unit, Barcelona, Spain

Contact E-Mail Address: ariadna.agca@gmail.com

Introduction: Patients with irritable bowel syndrome (IBS) have a poor tolerance to colonic gas that has been related to visceral hypersensitivity. STW5 is a medicinal product composed of 9 herbal extracts that has shown clinical efficacy in relieving symptoms in IBS patients, including abdominal pain and sensation of tension and fullness¹.

Further, STW 5 promotes changes in gastric tone, gastrointestinal motility, intestinal inflammation and visceral sensitivity. The effect of STW5 on tolerance to colonic gas in IBS has never been studied.

Aims & Methods: The aim of the present study is to determine the effect of STW5 on tolerance to colonic gas in patients with IBS. In 10 IBS patients (1 IBS-C; 7 IBS-D and 2 IBS-M) with bloating (8 female and 2 male, age range 22-61 yrs), we designed a controlled, randomized, double blind, cross-over study. On separate days, two gas challenge tests were performed in each patient: a) after two weeks on STW5 20 drops t.i.d. and b) after 2 weeks on placebo.

The gas challenge test consisted in an infusion period, with continuous infusion of a mixture of gases into rectum at 24 mL/min for 60 minutes, followed by a 30-min period of free rectal gas evacuation period. Gas evacuation was recorded by means of a barostat, abdominal symptoms were scored using a 0-6 perception questionnaire and abdominal distension was measured using a tape measure.

Results: Colonic gas infusion was associated to a progressive and significant increment in abdominal symptom perception, which was significantly greater when gas infusion was performed on placebo than when gas was infused on STW5.

At the end of the infusion period, when 1440 ml of gas were infused into the colon, abdominal perception score had increased by 4.0 ± 0.3 in the studies performed on placebo, and by 3.2 ± 0.4 when gas infusion was performed on STW5 ($p=0.034$).

In parallel, gas infusion was also associated to a progressive abdominal distension, that was similar at the end of the infusion period in the studies performed on placebo (2.3 ± 0.4 cm) and on STW5 (2.2 ± 0.3 cm; $p=0.434$).

During the evacuation period, opening of the rectal cannula was followed by a massive gas evacuation, and after 30 min of free gas evacuation only 408 ± 99 ml and 359 ± 70 ml of gas were still retained into the colon (placebo and STW5, respectively; $p=0.309$). Gas evacuation was associated to a rapid decrease in symptom perception and abdominal distension, which was faster when patients were on STW5 than on placebo.

Hence, at the end of the evacuation period, abdominal perception (score increment 0.5 ± 0.3 ; $p=0.048$ vs basal) and distension (girth increment 0.8 ± 0.3 mm; $p=0.016$ vs basal) remained significantly greater when compared to basal levels in the studies performed on placebo, whereas both had returned to basal levels in the studies performed on STW5 (perception score increment -0.1 ± 0.4 ; $p=0.399$ vs basal, and girth increment 0.3 ± 0.2 cm vs basal; $p=0.112$).

Conclusion: STW5 improves tolerance to increments in colonic gas in patients with IBS. This medicinal product may be beneficial for management of gas-related symptoms, like bloating, in patients with IBS. EudraCT: 2019-003976-38.

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Disclosure: Nothing to disclose.

P0650

INTESTINAL METHANOGEN OVERGROWTH IN AN IRISH COHORT - A CHALLENGING PROBLEM

L. Barry¹, D. Houlihan^{2,3}, W. Stack^{2,3}, L. Jackson^{2,3},

A.M. Keane McCarthy³

¹Bon Secours Hospital, GI Physiology Laboratory & Dept. of Gastroenterology, Cork, Ireland, ²Bon Secours Hospital, Dept. of Gastroenterology, Cork, Ireland, ³University College Cork, Department of Medicine, Cork, Ireland

Contact E-Mail Address: 119301866@umail.ucc.ie

Introduction: Small Intestinal Bacterial Overgrowth (SIBO) & Intestinal Methanogen Overgrowth (IMO) are recognized but poorly defined conditions which are increasingly recognized to play a role in the clinical manifestations of IBS. Recent meta-analysis² data shows high prevalence of SIBO/IMO in 31% IBS patients. Recent AGA Clinical Practice update acknowledges that there is limited data to guide clinicians on optimum treatment of SIBO/IMO¹. Data has suggested that a combination of Rifaximin and Neomycin was effective treatment strategy in those with Intestinal Methanogen Overgrowth.³

Aims & Methods: To assess the efficacy of recommended antibiotic treatment strategies for the eradication of IMO in an Irish cohort. Retrospective review of results of Glucose Breath Tests & medical records of 201 consecutive patients (153F, 48M), who attended our unit between Feb'21 & Feb'22 was undertaken.

Results: 58/201 (28.8%) patients (46F, 12M) referred with IBS symptoms were found to have abnormal Hydrogen (7/58 -12%) and Methane (51/58-87.9%) Breath Tests. All patient identified with intestinal methanogenic overgrowth (the presence of methane levels of >10 ppm CH₄ any time during the breath test) were prescribed antibiotic therapy. The importance of addressing the constipation was reiterated. All of the treated IMO patients were scheduled follow up glucose Breath Test to confirm "eradication" ~12 weeks post cessation of treatment. 26/51 patients with IMO have returned for repeat breath testing to date. 17/26 (65.4%) of returning IMO patients were treated with dual antibiotic therapy (Rifaximin & neomycin), 5/26 (19.2%) were treated with single agent Rifaximin and 4 with metronidazole (15.4%)

Remission was observed in 8/26 (30.7%) patients who returned for repeat breath test post antibiotic treatment. There was no significant difference between remission in dual vs single agent antibiotic therapies (35.2% vs. 22.2%, $p=0.66$).

Conclusion: We have demonstrated high prevalence of IMO/SIBO in an Irish population similar to that reported in large meta-analysis². This represents a high burden of care. Treatment with current recommended therapies resulted in sustained eradication in only 30.7% of those treated to date. This is significantly lower than previously reported³. With increasing mindfulness of need for antibiotic stewardship urgent further studies are required to determine better therapeutic strategies for this cohort

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Disclosure: Nothing to disclose.

P0651

IMPACT OF INTEGRATED MULTIDISCIPLINARY MANAGEMENT ON SUBSEQUENT HEALTH CARE UTILISATION BY COMPLEX PATIENTS WITH DISORDERS OF BRAIN-GUT INTERACTION: A PROSPECTIVE 12-MONTH CONTROL COHORT STUDY

B. McKillen¹, N. Moy², C.-y. Chao³, A. Ahmadvand¹, A. Taylor¹, A. Shah¹, G.J. Holtmann¹, N. Talley⁴, M. Jones⁵

¹Princess Alexandra Hospital, Gastroenterology Department, Brisbane, Australia, ²Queensland University of Technology, Brisbane, Australia, ³Princess Alexandra Hospital, Brisbane, Australia, ⁴University of Newcastle, Newcastle, Australia, ⁵MacQuarie University, Sydney, Australia

Contact E-Mail Address: benjamin.mckillen@hotmail.com

Introduction: An integrated approach for the management of patients with functional gastrointestinal disorders (FGID) has recently been shown to result in superior reductions in both symptom burden and psychological morbidity compared to standard care.⁽¹⁾ It is not clear, however, whether this results in a subsequent reduction in healthcare utilisation.

Aims & Methods: **Aims:** To assess the impact of a 3 month structured treatment in a dedicated integrated care clinic (ICC) versus standard care on subsequent healthcare utilisation among patients with functional gastrointestinal disorders (FGID) who had failed to respond to conventional treatment modalities available in the outpatient setting.

Methods: A cohort of 100 consecutive patients with FGID were matched with 200 FGID control patients according to age, gender, FGID diagnosis and symptom severity at a large tertiary hospital. ICC patients received 3 months of a highly structured treatment program provided by a multidisciplinary team of gastroenterologists, general practitioners, dietitians, psychologists, and exercise physiologists. Historic controls (before the ICC program commenced) received standard care at the same facility meeting established clinical guidelines with access to allied health interventions but no standardised multidisciplinary approach.

Healthcare utilisation including hospital admissions, emergency department presentations, outpatient clinic attendances, procedures, imaging studies and allied health reviews were assessed by review of the statewide integrated electronic medical record (iEMR), capturing service events 12 months before and after the ICC intervention or standard care in the case of the controls.

Healthcare utilisation by each group was compared by category (hospital admissions, emergency department presentations, outpatient visits, allied health reviews, diagnostic and therapeutic procedures and imaging) and the overall cost of healthcare utilisation was estimated using Australian costing (MBS) data.

Results: Healthcare utilisation by ICC patients decreased by a mean of 2.4 service occasions per patient compared to controls, resulting in a cost delta of approximately \$2,600 for the 12 months after the intervention. This change was driven by a statistically significant decrease in OPD attendances, allied health reviews and a reduced number of imaging studies in the ICC group.

	ICC Patients	Controls
Mean age (years)	45.8	43.2
Gender (percentage female)	81	81
Gastrointestinal Symptom Score (SAGIS) prior to ICC or standard care	30.3	31.2
Mean service encounters in 12 months post intervention	3.02	5.385

Conclusion: This matched cohort study demonstrates that an intensive 3 month integrated treatment program results in a significant reduction in healthcare utilisation when compared to a standard model of care in patients with treatment resistant FGID.

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P1034

THE LOW FODMAP DIET IS EFFECTIVE IN IBS-C TERTIARY CARE NORMAL CLINICAL PRACTICE AND DOES NOT INCREASE CONSTIPATION

L.D. Martin¹, N. Canga², A. Alolyan²

¹University College London Hospital, Nutrition & Dietetics, London, United Kingdom, ²University College London, London, United Kingdom

Contact E-Mail Address: lee.martin1@nhs.net

Introduction: The low fermentable oligosaccharides, disaccharides, monosaccharides and polyols (FODMAP) diet is an effective treatment for irritable bowel syndrome (IBS). However the majority of randomised controlled trials have focused on those with a diarrhoea predominant subtype (IBS-D) and efficacy in IBS with constipation (IBS-C) still requires further evaluation¹.

Additionally there are concerns the diet could increase (or not improve) constipation symptoms² and taken together these factors may cause trepidation in offering a low FODMAP diet to IBS-C in clinical practice.

Aims & Methods: This study utilised a relatively large IBS data set from normal clinical practice and aimed (1) to evaluate the effectiveness of FODMAP Restriction across the range of IBS sub-types and (2) to describe the impact of diet had on stool patterns in IBS-C and how this related to diet effectiveness.

An observational, prospective study of patients with IBS (n=272) aged 18 to 86 years (44.6 ± 15.5), 226 females (83%). All patients attended FODMAP Restriction (baseline) and FODMAP Reintroduction (follow up) dietetic-led group education sessions.

Primary outcome of effectiveness was assessed using the global symptom question (GSQ)³ measuring 'satisfactory relief of gut symptoms'. Secondary outcomes assessed changes in stool consistency and related IBS sub-type using Bristol Stool Form Scale (BSFS)⁴.

To determine any differences in satisfactory relief at baseline and follow up across IBS sub-types a Bonferroni Mann Whitney U test was applied. Descriptive analyses identified changes in IBS sub-type at follow up while satisfactory relief at follow up was compared using Chi-squared.

Results: In the entire cohort (n=272), IBS-C represented 23%. Both IBS-C (n=63) and IBS-D (n=98) achieved similar satisfactory relief from FODMAP Restriction (p=NS). IBS-U (n=83) were more likely to have satisfactory relief at baseline compared to IBS-D (p=0.012) and IBS-C (p=0.011) but similar relief at follow up (p=NS). IBS-M (n=28) experience significantly less satisfactory relief compared to IBS-C (p=0.006) and IBS-U (p=0.008) but not IBS-D (p=0.073).

Following FODMAP Restriction in patients with IBS-C 51% (n=32) remained IBS-C while 44% (n=28) changed to IBS-U, the remaining 5% changed to IBS-M (n=2) or IBS-D (n=1).

Satisfactory relief was achieved in 50% (n=16) of 'IBS-C to IBS-C' but in 71% (n=20) of 'IBS-C to IBS-U' although this did not reach significance (p=0.091).

Conclusion: Overall 60% of IBS-C achieved satisfactory relief of symptoms following FODMAP Restriction. 44% changed stool pattern from abnormal (IBS-C) to normal (IBS-U) consistency, highlighting FODMAP Restriction does not necessarily increase constipation in IBS-C.

Higher rates of satisfactory relief were achieved in those who improved stool consistency. In tertiary care clinical practice patients with IBS-C should be offered the low FODMAP dietary treatment.

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Disclosure: Nothing to disclose.

P0652

13C-BUTYRATE AND 13C-GLUCOSE BREATH TESTING TO DETECT MESENTERIC ISCHEMIA, A PROOF OF PRINCIPAL STUDY IN HEALTHY VOLUNTEERS

D. Harmankaya¹, L. Terlouw¹, D. Leemreis- van Noord², A. Moelker³, M.J. Bruno¹, M.P. Peppelenbosch¹

¹Erasmus Medical Center, Gastroenterology and Hepatology, Rotterdam, Netherlands, ²Franciscus Gasthuis & Vlietland, Gastroenterology and Hepatology, Rotterdam, Netherlands, ³Erasmus Medical Center, Radiology and Nuclear Medicine, Rotterdam, Netherlands

Contact E-Mail Address: d.harmankaya@erasmusmc.nl

Introduction: Chronic mesenteric ischemia (CMI) is an incapacitating disease that can progress to potentially fatal acute mesenteric ischemia. A gold standard diagnostic test to diagnose CMI is currently lacking, causing both undertreatment and overtreatment of patients.

Since CMI is accompanied by a switch of the intestinal epithelium from butyrate-dependent oxidative phosphorylation to anaerobic glucose metabolism and oxygen is needed to absorb and metabolize butyrate and glucose in the enterocyte, a labelled-butyrate and labelled-glucose breath test could theoretically quantify mucosal oxygen content and thereby detect ischemia.

Aims & Methods: This study is a multi-center randomized interventional proof of principal study, conducted in healthy volunteers without gastrointestinal complaints and with an unremarkable medical history. Two control groups and two intervention groups each consisting of five volunteers received either 13C-butyrate or 13C-glucose.

The control groups performed breath tests without performing any physical exercise. The intervention groups performed a 30 minute standardized bicycle ergometer exercise test, which has been proven to elicit mesenteric ischemia. Breath samples of expired 13CO₂ were collected during a period of 4 hours.

Results: A total of twenty volunteers were included in this study. In the control and intervention group butyrate reached the peak concentration of expired 13CO₂ faster than glucose (65 min. vs. 130 min). Compared to the control group butyrate and glucose were metabolized less in the intervention group (T30 min p=0.0043, T60 min p=0.0171, T75 min p=0.0360).

Conclusion: Glucose/butyrate breath testing can identify exercise-induced mesenteric ischemia by measuring mucosal oxygen consumption. This holds great promise for the development of a new diagnostic tool to detect and quantify mesenteric ischemia.

Disclosure: No conflict of interest

P0653

AGE-ADJUSTED CHARLSON COMORBIDITY INDEX PREDICTS COLONIC DIVERTICULAR REBLEEDING

H. You¹, D.H. Kim¹, S.-Y. Park¹, H. Kim¹

¹Chonnam National University Hospital and Medical School, Department of Gastroenterology and Hepatology, Gwangju, Korea (Republic of)

Contact E-Mail Address: go6003@naver.com

Introduction: Colonic diverticular bleeding (CDB) is a common cause of acute lower gastrointestinal bleeding.¹ Patients with CDB are at increased risk for recurrence.²⁻⁵ Its reported risk factors are similar but inconsistent, as previous studies included a small number of patients, and related clinical situations at each period may be different.

Here, we aimed to evaluate the clinical course of patients with CDB and identify risk factors, including the age-adjusted Charlson comorbidity index (ACCI), for recurrent CDB (rCDB).

Aims & Methods: We retrospectively included patients who were hospitalized at the Chonnam National University Hospital for management of CDB between January 2005 and March 2020, and data on the underlying disease, drug history, treatment method, post-discharge rCDB, and death were checked.

The primary and secondary outcomes were rCDB and mortality after diverticular bleeding, respectively. Rebleeding free days were calculated from the date of first bleeding to the date of recurrence or death using the Kaplan-Meier method.

Results: Among 221 investigated patients (mean age, 68.1 years; 56 females), 56 and 165 had definite and presumptive CDB, respectively, 122 (55.2%) had a right-sided CDB, and 51 (23.3%) experienced rCDB throughout a median period of 339 days (range, 3-4817 days).

Variables	cHR	95% CI	p-value	aHR	95% CI	p-value
Male sex	1.73	0.96-3.10	0.07			
ACCI ≥ 7	2.11	1.05-4.22	0.04	2.76	1.30-5.88	0.03
Number of antithrombotics	1.00	0.71-1.43	0.99			
Steroids	0.31	0.07-1.38	0.12			
NSAIDs	0.81	0.29-2.26	0.69			
Hemostasis	1.03	0.55-1.90	0.94			
Location of bleeding	0.80	0.33-1.91	0.61			

Table 1. Univariate and multivariate analyses of the risk factors for increase in diverticular rebleeding using Cox regression.

The most common comorbidities were hypertension (62.4%) and diabetes (33.5%). The median length of hospitalization was 5 days (range, 2-119 days). The CDB-related mortality rate was 0.9% at first admission. The cumulative incidence rates of rCDB after 1, 6, 12, 24 months were

4.6%, 9.1%, 12.3%, and 16.9%, respectively. In Cox regression analysis, rCDB more frequently occurred in patients with ACCI ≥ 7 than in patients with ACCI < 7 (adjusted hazard ratio, 2.76; 95% confidence interval, 1.30–5.88; $p = 0.03$).

Conclusion: This study presented the clinical course of 221 patients with CDB over 13 years in a tertiary referral center. The recurrence rate was as high as 23%. rCDB occurred frequently at any time in patients with previous CDB. ACCI was effective for predicting rCDB. ACCI ≥ 7 was found to be significantly associated with an increased risk of rCDB. Clinicians need to consider possible rCDB for patients with high ACCIs.

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P0654

CURRENT TREATMENT AND MANAGEMENT OF DIVERTICULAR DISEASE IN GERMANY: CHALLENGING DIAGNOSIS AND SUCCESSFUL PROBIOTIC THERAPY

M. Gross¹, U. Beckenbauer²

¹Internistisches Klinikum München Süd, Klinik für Allgemeine Innere Medizin und Gastroenterologie, Munich, Germany,

²Internistische Praxisgemeinschaft & Zentrum f. Präventivmedizin, Munich, Germany

Contact E-Mail Address: gross@muellerklinik.de

Introduction: The symptomatic uncomplicated diverticular disease (SUDD) is the most common type of diverticular disease, but guidelines provide only a few treatment options.

Aims & Methods: The aim of the present German-wide survey was to evaluate the current medical care situation for patients with diverticula in primary care and to record the grade of satisfaction with available therapeutic options. A questionnaire was sent to 13,790 German general physicians (GP). It contained questions concerning the diagnosis and medical care of patients with diverticula, the evaluation of available treatment options, and the challenges for the daily medical routine.

Results: In total, 526 questionnaires were sent back for analysis. The biggest challenge for GPs handling patients with chronic diverticular disease (SUDD) is making an accurate diagnosis (37%), including difficulties with the clear demarcation to the irritable bowel syndrome (22%). In line with that, only 6% of the medical practitioners feel themselves sufficiently informed about SUDD, despite the high prevalence of this disease.

The support for GPs by medical specialist such as gastroenterologists is relatively limited: After referring a patient with suspected acute diverticulitis or SUDD, the GP sometimes receive a therapy plan (27%), infrequently

advice for diverticulitis relapse prevention (18%), and rarely assisting information for patient education (4%). For primary prevention of symptoms in asymptomatic patients with diverticula, 41% of the GPs give nutritional advice, 37% recommend lifestyle changes and 18% recommend probiotics.

After an acute diverticulitis, 42% recommend lifestyle changes and nutritional measures, 26% probiotics. In agreement with the German guideline that does not recommend the use of mesalazine or rifaximin in this situation, these drugs are only recommended by 7% and 3%, respectively.

The most popular treatment options used by GPs for SUDD, are lifestyle and diet modification (45%) as well as the use of probiotics (30%). Mesalazine (8%) and rifaximin (2%) are seldom prescribed for SUDD.

Of the GPs who answered the survey, 72% and 74% are satisfied or very satisfied with the effect of lifestyle recommendations and dietary measures, respectively. 62% of the physicians are satisfied or very satisfied with the therapeutic effect of probiotics for SUDD. 47% of the participating GPs use probiotics to treat SUDD often or always.

Another 15% stated that they have not yet used probiotics to treat SUDD. The reasons given were the lack of reimbursability for probiotics by German health insurances (31%), the poor adherence of patients to therapy because of the delayed onset of the therapeutic effect (20%) and the difficulty of selecting an appropriate evidence-based probiotic (16%).

Conclusion: In daily medical routine, the accurate diagnosis of SUDD is a major challenge for GPs and supporting information provided by gastroenterologists is limited. Lifestyle and diet recommendations, as well as probiotics, are common and satisfying interventions in SUDD.

After acute diverticulitis, many GPs also give lifestyle and diet recommendations and around every fourth recommends probiotics after acute diverticulitis.

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P0655

PRIOR ABDOMINAL SURGERY: A POTENTIAL RISK FACTOR FOR COLONIC DIVERTICULOSIS OR DIVERTICULITIS

E. Ariam¹, H. Shirin¹, A. Bermont¹, D.E. Cohen¹, V. Richter¹, Y. Sandler²

¹Shamir (Assaf Harofeh) Medical Center, Gastroenterology, Zerifin, Israel, ²Shamir (Assaf Harofeh) Medical Center, Surgery, Zerifin, Israel

Contact E-Mail Address: haimsh@shamir.gov.il

Introduction: Abnormal colonic pressure profiles have been associated with an increased risk of colonic diverticulosis. A surgical history is a known risk factor for abdominal adhesions, and these may lead to increased intraluminal colonic pressure. We assessed whether previous abdominal surgery is associated with colonic diverticulosis or diverticulitis.

Aims & Methods: We analyzed data from a prospective study of patients undergoing colonoscopy for different indications from 2020 through 2021. Patients completed a structured questionnaire concerning previous abdominal surgeries, dietary and lifestyle exposures including smoking and alcohol use, and co-morbidities.

Results: 359 patients were included in the study. The mean age was 67.6 and 46% were females. Diabetes mellitus, hypertension, ischemic heart disease, chronic obstructive pulmonary disease, chronic renal failure, and BMI were similar in the diverticulosis and control groups.

The overall prevalence of colonic diverticulosis was 25% (91/359) and 48% of the patients had previous abdominal surgery. As expected, the prevalence of diverticulosis increased with age. There was no difference in the rate of previous abdominal surgery between patients with or without diverticulosis (49% vs 47%, $p=0.78$).

In regards to specific surgeries, inguinal hernia repair was significantly associated with diverticulosis (52% vs 20%, $p=0.001$), but not diverticulitis. In contrast, appendectomy was found to have a protective effect for diverticulosis (6% vs 14%, $p=0.048$).

Conclusion: These findings suggest that post-operative abdominal adhesions inducing high colonic intraluminal pressures do not appear to be the mechanism for diverticula formation. Rather, inguinal hernia and diverticulosis probably share similar connective tissue pathologies with no causative relationship between them.

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P0656

DIVERTICULOSIS IS ASSOCIATED WITH FUTURE EXTRA-GI HEALTH CARE UTILISATION BUT NOT GI HEALTH CARE UTILISATION

A. Andreasson^{1,2,3}, D. McNaughton², M.P. Jones², N.J. Talley⁴, M.M. Walker⁵, L. Agréus⁶, P.L. Schmidt³

¹Stockholm University, Stress Research Institute, Stockholm, Sweden, ²Macquarie University, Psychology, North Ryde, Australia, ³Karolinska Institutet, Dept of Medicine, Solna, Stockholm, Sweden, ⁴University of Newcastle, Faculty of Health & Medicine, New Lambton Heights, Australia, ⁵University of Newcastle, Dept. of Anatomical Pathology, Newcastle, Australia, ⁶Karolinska Institutet, Division of Family Medicine and Primary Care, Huddinge, Sweden

Contact E-Mail Address: mike.jones@mq.edu.au

Introduction: Diverticulosis is common in the general population and is generally a benign disease although diverticulitis can be complicated. As the exact prevalence of diverticular disease in the general population is largely unknown, the association with future health care use in non-health care seekers is uncertain. Here, we investigate if diverticulosis is associated with future health care use (HCU) in a population-based colonoscopy study.

Aims & Methods: This study is based on the PopCol study¹ in which 745 individuals from the general population had an ileocolonoscopy for research purposes. 130 individuals (55% women, mean age 61 years) had diverticulosis at the time of the investigation, and they were older than the individuals without diverticulosis (58% women, mean age 49 years). The study was later linked with registry data on health care use over the sub-

sequent 10 years. Health care use was classified based on ICD-10 codes for the health encounter. Since many patients do not seek some categories of health care, the association between diverticulosis and HCU was modelled using a zero-inflated negative binomial model which simultaneously estimates the association of any HCU (reported as log-odds ratio [ln-OR]) as well as the quantum of HCU (reported as incidence rate ratio [IRR]).

Results: Diverticulosis was associated with increased future extra-GI health care use, so that those that had sought care had more encounters, both in outpatient and tertiary care, but not GI or psychiatric health care (Table 1).

	IRR (SE) p-value	ln-OR (SE) p-value
Outpatient Extra-GI	1.25 (0.11) p = .02	-
Outpatient Psych	1.23 (0.44) p = .54	-1.19 (2.30) p = .61
Outpatient GI	1.42 (0.32) p = .15	-16.95 (7631.25) p = .99
In-patient Extra-GI	1.21 (0.11) p = .04	0.05 (22851.55) p = .99
In-patient GI	1.22 (0.48) p = .61	-1.16 (1.00) p = .25
In-patient Psychiatric	2.55 (5.31) p = .65	0.34 (1.68) p = .84

Table 1. Association between diverticular disease and future health care use, adjusted for age and gender

Conclusion: These novel data suggest extra-GI health care use was more common among those with diverticulosis than those without. The reasons remain to be clarified but the association between diverticulosis and extra-GI health care use will be further investigated in relation to extra GI symptom burden.

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P0657

ETIOLOGIC AND PHYSIOLOGIC CHARACTERISTICS OF FECAL INCONTINENCE IN MEN

R. Margalit Yehuda^{1,2}, C. Maradey-Romero^{1,2}, Y. Davidov^{3,2}, D. Carter^{1,2}

¹Sheba Medical Center, Department of Gastroenterology, Tel Hashomer, Israel, ²Tel Aviv University, Sackler Faculty of Medicine, Tel Aviv, Israel, ³Sheba Medical Center, Liver Diseases Center, Tel Hashomer, Israel

Contact E-Mail Address: dr.dancarter@gmail.com

Introduction: Fecal incontinence (FI) is a common chronic debilitating condition, diagnosed both in men and women. FI is often underreported and underestimated in men.

Aims & Methods: Our aim was to clarify the causes and the physiologic characteristics of FI in men and to compare these factors to those of women diagnosed with FI.

The study cohort encompassed 200 men and 200 women who were evaluated for FI in a tertiary referral center specializing in pelvic floor disorders. All patients underwent endoanal ultrasound and anorectal manometry. Demographic, medical, anatomic and physiologic parameters were compared between the 2 study groups.

Results: Urge incontinence was the most frequent type of FI both in men and women. Diagnosis of anal fistulas and history of anal surgeries, rectal tumors and pelvic radiotherapy were more common in men while

history of pelvic surgeries was more common in women. Associated urinary incontinence was reported more frequently by women. External anal sphincter defects, usually anterior, were more common in women (M:1.5%, W:24%, $p<0.0001$). Decreased resting and squeeze pressures were more common in women (M:29%, W:46%, $p<0.0001$: M:44%, W:66%, $p<0.0001$).

The incidence of rectal hyposensitivity was higher in men (M:33%, W:18%, $p<0.0001$), while rectal hypersensitivity was higher in women (M:29%, W:49%, $p<0.0001$). Anorectal dyssynergia was more common in men (M:66%, W:37%, $p<0.0001$). Ninety-one percent of patients had decreased maximal tolerance volume without significant difference between genders.

	Women	Men	p value
Age (years), median (IQR)	66 (55-72)	63(52-73)	0.8000
Anal surgery, n(%)	20 (10.9)	47 (25)	<0.0001
Pelvic surgery, n(%)	49 (26.5)	28 (14.9)	0.0060
EAS defect, n (%)	49 (24.5)	3 (1.5)	<0.0001
Resting pressure (mmHg), median (IQR)	52.9 (39.0-72.9)	62.5 (45.6-83.4)	0.004
Squeeze pressure (mmHg), median (IQR)	90.4 (69.5-123.2)	125.1 (96-162)	0.001
First sensation volume (ml), median (IQR)	30 (20-40)	40 (30-50)	<0.0001
Desire to defecate (ml), median (IQR)	80 (60-110)	100 (70-145)	<0.0001
Anismus, n (%)	74 (37.0)	132 (66.3)	<0.0001

Conclusion: FI in men has different etiologic factors and physiologic characteristics when compared with women. Acknowledging these differences is significant and may yield better treatment options.

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P0658

SCLEROTHERAPY WITH POLIDOCANOL FOAM VERSUS HEMORRHOIDAL ARTERY LIGATION WITH RECTO ANAL REPAIR IN THE TREATMENT OF SECOND AND THIRD-GRADE HEMORRHOIDAL DISEASE: A RANDOMIZED, PILOT STUDY

S. Neves¹, D. Falcão², A. Povo³, F. Castro Poças², J. Oliveira⁴, P.S. Salgueiro²

¹Instituto de Ciências Biomédicas Abel Salazar, Porto, Portugal,

²Centro Hospitalar Universitário do Porto, Gastroenterology,

Porto, Portugal, ³Centro Hospitalar Universitário do Porto, General

Surgery, Porto, Portugal, ⁴Escola Superior Agrária de Viseu e

Centro de Recursos Naturais, Ambiente e Sociedade, Instituto

Politécnico de Viseu, Viseu, Portugal

Contact E-Mail Address: danielateixeirafalcao@gmail.com

Introduction: Hemorrhoidal disease (HD) therapy comprises office-based treatments as well as surgery.(1,2) This pilot study aimed to compare the efficacy and safety of polidocanol foam sclerotherapy (SP) with the surgical technique doppler-guided hemorrhoidal artery ligation with recto-anal repair (HAL-RAR).

Aims & Methods: Prospective, randomized, single centre study including patients with HD grades II and III. Participants were randomly assigned (1:1) into one of two groups (SP or HAL-RAR), stratified according to Goligher classification, during a recruitment period of six months. Therapeutic success, using Sodergren's score and a bleeding score, was the primary efficacy outcome. Primary and secondary safety outcomes evaluated complications and implication in professional life, respectively.

Results: A total of 46 eligible patients were allocated either to SP (n=22; 47.8%) or HAL-RAR (n=24; 52.2%). Most patients achieved therapeutic success (SP 100% vs. HAL-RAR 90.9%, $p=0.131$). However, complete success was higher in SP group (91.7% vs. 68.2%, $p=0.045$). SP treated patients had less complications (25%), when compared to HAL-RAR (68.2%) ($p=0.003$). Additionally, HAL-RAR revealed a higher rate of mild complications ($p=0.003$). HAL-RAR had a greater negative impact in patients' work activity, measured in days of absence from work (SP 0.6 ± 0.2 vs. HAL-RAR 9.5 ± 10.1 , $p\leq0.001$).

Conclusion: SP was more effective when considering complete success, and had fewer complications than HAL-RAR. Patients undergoing SP had less impact on their work activity.

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P0659

CELL SHAPE CHARACTERISTICS OF HUMAN SKELETAL MUSCLE CELLS AS A PREDICTOR OF MYOGENIC COMPETENCY: A NEW PARADIGM TOWARDS PRECISION CELL THERAPY FOR INCONTINENCE

C. Desprez¹, D. Danovi², C.H. Knowles³, R. Day¹

¹Centre for Precision Healthcare, UCL Division of Medicine, University College London, London, United Kingdom,

²Centre for Gene Therapy and Regenerative Medicine, King's College London, London, United Kingdom, ³Queen Mary University of London School of Medicine NCBRSI, NBRC, London, United Kingdom

Contact E-Mail Address: charlotte-desprez@orange.fr

Introduction: Skeletal muscle derived cells (SMDC) hold tremendous potential for replenishing dysfunctional muscle associated with incontinence. Autologous SMDC-based therapy for faecal incontinence (FI) is reported to be safe, but the level of efficacy reported in previous studies suggests that heterogeneity in the proposed therapy may contribute to inconsistent clinical outcomes.

Improved methods for patient stratification to identify patients who are (un)likely to respond well to regenerative therapies are advocated to ensure the potential benefits of cell-based regenerative medicine can be fully exploited.

Aims & Methods: Here, we report on the development of a novel SMDC profiling tool to examine populations of cells *in vitro* derived from different donors.

The primary aim of the study was to evaluate the applicability of multi-parametric imaging-based phenotypic characterization to distinguish myogenic potency of SMDC. Heterogeneity in the formation of myotubes from different donors was correlated with cell shape descriptors.

Commercially available human SMDC (Cook MyoSite) consisting of non-differentiated primary human muscle cells were derived from 14 individual human donors. Image acquisition of SMDC growth was performed using a CytoSMART Lux2 microscope. Images were acquired every 5 minutes over a period of 72 hours.

CellProfiler software was used to create an image analysis pipeline for analysis of different cell shape characteristics during 2 hours of tracking at 12- and 24-hours post-culture. The Konstanz Information Miner (KNIME; open-source data analytics) software was used to calculate the mean and SD of the characteristic for all the objects identified in one image.

These data were then used for statistical correlation with the fusion index calculated from myotube formation assays established in the same cultures after 5 days of subsequent incubation in differentiation medium. The fusion index was calculated as the ratio of nuclei number in myocytes with 2 or more nuclei divided by the total number of nuclei. Correlation studies used the Spearman test with $r < -0.5$ or $> +0.5$ indicating correlation.

Results: Several early cell shape characteristics were found to negatively correlate with the fusion index. Images collected at 12 hours after initiating culture revealed that 5 cell shape characteristics negatively correlated with the fusion index, including the total area occupied by cells ($r = -0.815$, $p = 0.001$), area shape ($r = -0.631$; $p = 0.028$), bounding box area ($r = -0.576$; $p = 0.049$), minimum ferret diameter ($r = -0.589$; $p = 0.044$) and minor axis length ($r = -0.614$; $p = 0.034$). Images collected at 24 hours after initiating culture revealed 8 cell shape characteristics that negatively correlated with the fusion index.

These included: total area occupied by cells ($r = -0.686$; $p = 0.007$), area shape ($r = -0.709$; $p = 0.005$), bounding box area ($r = -0.563$; $p = 0.036$), compactness ($r = -0.534$; $p = 0.049$), equivalent diameter ($r = -0.576$; $p = 0.031$), minimum ferret diameter ($r = -0.620$; $p = 0.018$), minor axis length ($r = -0.590$; $p = 0.026$) and perimeter ($r = -0.654$; $p = 0.011$). There was a high correlation between all these characteristics at 24 hours of imaging after initiating culture.

Conclusion: Results indicate that monitoring of cell shape during the early stages of bioprocessing using real-time imaging could be used to predict cellular competency necessary for differentiation and myofibre formation *in vivo*.

Further studies could establish whether selection of either patients or cell populations on this basis have a higher probability of yielding better outcomes in cell-based therapy for incontinence.

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P0660

A SYSTEMATIC REVIEW OF OUTCOMES ASSOCIATED WITH SETON PLACEMENT AND OTHER NON-INVASIVE TECHNIQUES FOR COMPLEX CRYPTOGLANDULAR FISTULA

D. Bennett^{1,2}, X. Zhang^{3,4}, M.D. Kappelman⁴, K. Iglay³, M. Aldridge³, C. Karki¹, S.F. Cook³

¹Takeda Pharmaceuticals USA, Inc., Cambridge, United States,

²University of Pennsylvania Perelman School of Medicine, Philadelphia, United States, ³CERobs Consultancy LLC, Chapel Hill, United States, ⁴University of North Carolina, Chapel Hill, United States

Contact E-Mail Address: dimitri.bennett@takeda.com

Introduction: Complex cryptoglandular fistulas (CCFs) are abnormal passages arising from inflammation of the proctodaeal glands in the intersphincteric space, which can be associated with substantial disease burden in affected patients. Treatment options include surgical and non-surgical interventions. Regardless of treatment strategy, seton placement is used to facilitate fistula drainage, promote fistula healing and prevent recurrent abscess formation.

Aims & Methods: The aim of this systematic literature review (PROSPERO registration: CRD42020177732) was to assess treatment outcomes of interest (fistula healing, recurrence, faecal incontinence and pain) associated with seton placement, selected biomaterial approaches (plug, collagen paste and plasma) and non-operative techniques (laser ablation, video-assisted anal fistula treatment and over-the-scope clip) in patients with CCF. Embase and PubMed were searched for CCF observational studies published between 1 January 2015 and 25 March 2020 reporting the outcomes of interest.

Articles were screened for inclusion by two trained reviewers using PI-COTS criteria and data on outcomes of interest were extracted from included articles. Articles were assessed for risk of bias using the Risk of Bias in Non-randomized Studies – of Interventions (ROBINS-I) tool. Data were summarized using descriptive statistics.

Results: After screening, 18 studies were included (Table). In total, 17 articles reported rates of fistula healing or success, with notable heterogeneous or absent outcome definitions. Healing/success rates were intervention-dependent (Table), ranging from 39% to 98% with mean and median follow-up times ranging from 6 months to 9.4 years. Recurrence/treatment failure was reported in 14 articles (Table).

Rates of recurrence/treatment failure were also variable and dependent on intervention type (range: 3%–44%; Table), with the same follow-up times as for healing. Rates of faecal incontinence were reported in 16 articles using a variety of faecal incontinence scales.

Overall, faecal incontinence was minimal during post-operative follow-up (range: 6–24 months) regardless of intervention. Few studies (n = 8) reported pain as a clinical outcome. The majority used a mix of clinician- and patient-reported scales with limited evidence of long-term post-operative pain (follow-up range: 6–24 months). Most articles (89%) included had a moderate risk of bias.

Intervention	Overall number of articles included in the systematic literature review (n)	Rate of healing/success ^a (range, % [number of articles, n])	Rate of recurrence/treatment failure ^b (range, % [number of articles, n])
Seton use	2	90–98 (2)	7–10 (2)
Biomaterial approaches	9	41–70 (8)	3–44 (7)
Non-operative techniques	7	39–90 (7)	10–40 (5)

^aHealing was generally defined as closure of the fistula opening or lack of fistula drainage
^bRecurrence/treatment failure was generally defined as persistence or reappearance of fistula with or without symptoms such as pain or purulent discharge

Table: Rates of healing and recurrence in patients with complex cryptoglandular fistula by intervention

Conclusion: Rates of healing/success and recurrence/treatment failure in patients with CCF varied widely among and within most interventions. The variability observed is potentially due to the heterogeneous outcome definitions, follow-up duration, patient characteristics and study designs, which highlight a need for consistent approaches to study CCF and produce comparable outcomes.

Despite limited evidence, the low to modest rates of recurrence and rare reports of long-term post-operative incontinence or pain suggest non-invasive procedures may help to relieve the substantial burden of CCF.

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CK is an employee and shareholder of Takeda Pharmaceuticals International Co.

SFC consulted on this project through CERobs Consulting, LLC, which received funding from Takeda Pharmaceuticals International Co. and is currently an employee and shareholder of Takeda Pharmaceuticals International Co.

P0661

RELATIONSHIP BETWEEN ANAL FUNCTIONAL LUMEN IMAGING PROBE (ENDOFLIP®) RESULTS AND THE CLINICAL PRESENTATION OF FAECAL INCONTINENCE

C. Desprez¹, G. Gourcerol¹, C. Savoye-Collet², V. Bridoux³, T. Duflo⁴, A.M. Leroi¹
¹Rouen University Hospital, Digestive Physiology Unit, Rouen, France, ²Rouen University Hospital, Radiology Unit, Rouen, France, ³Rouen University Hospital, Visceral Surgery Unit, Rouen, France, ⁴Rouen University Hospital, Pharmacology Unit, Rouen, France

Contact E-Mail Address: charlotte-desprez@orange.fr

Introduction: Faecal incontinence (FI) subtypes (urge, passive, mixed) are linked to the physiopathological mechanism of FI. Previous studies have failed to demonstrate a consistent relationship between FI subtypes and anal sphincter dysfunctions. Our aim was to evaluate the relationship between anal sphincter function assessed using the new EndoFLIP® technology and FI subtypes.

Aims & Methods: Patients referred for FI were prospectively enrolled between October 2015 and May 2021 in a registry, and data were retrospectively examined. Each patient underwent a clinical assessment as well as 3D-high resolution or water-perfused anorectal manometry, anal EndoFLIP®, anorectal electrophysiological, and endoanal ultrasound tests. The results of the investigations were compared across FI subtypes.

Results: The cohort included 133 patients, 54 (41%) meeting the criteria for urge FI, 40 (30%) for passive FI, and 39 (29%) for mixed FI. The resting anal distensibility index (DI) at 50 mL of distension was significantly lower in patients with urge FI than in patients with passive FI (p=0.04). At rest, a DI at 50 mL of distension ≥7.3 mm².mmHg⁻¹ and a DI at 40 mL of distension <1.3 mm².mmHg⁻¹ were associated with the passive and urge FI subtypes, respectively, with poor discriminatory power (accuracy of 0.49 compared to 0.33 for random assignment).

There were no differences in anorectal manometry, endoanal ultrasound, electrophysiologic test results among the urge, passive, and mixed FI subgroups (all p>0.05).

Conclusion: The anal sphincter DI using the EndoFLIP® system displayed poor predictive performance in distinguishing among FI subtypes. The EndoFLIP® system can distinguish among FI subtypes in some extreme cases but is not powerful enough to be used alone to diagnose an FI subtype.

Disclosure: Nothing to disclose.

P0662 WITHDRAWN

P0663 WITHDRAWN

P0664 WITHDRAWN

P0665 WITHDRAWN

P0666

THE EFFECTIVENESS OF PERSONALIZED COLORECTAL CANCER SCREENING BASED ON PRIOR FECAL HEMOGLOBIN CONCENTRATION: PERFECT-FIT STUDY PROTOCOL

E. Toes-Zoutendijk¹, E. Brekvelde¹, L. de Jonge¹, M.C.W. Spaander², A. van Vuuren², F. van Kemenade³, C. Ramakers⁴, E. Dekker⁵, I.D. Nagtegaal⁶, M. van Leerdam⁷, I. Lansdorp-Vogelaar¹

¹Erasmus MC University Medical Center, Public Health, Rotterdam, Netherlands, ²Erasmus MC University Medical Center, Gastroenterology & Hepatology, Rotterdam, Netherlands, ³Erasmus MC University Medical Center, Pathology, Rotterdam, Netherlands, ⁴Erasmus MC University Medical Center, Clinical Chemistry, Rotterdam, Netherlands, ⁵AMC, Gastroenterology & Hepatology, Amsterdam, Netherlands, ⁶Radboud University Nijmegen Medical Center Dept. of Pathology, Radboud University Nijmegen Medical Center, Nijmegen, Netherlands, ⁷Netherlands Cancer Institute, Dept. of Gastroenterology, Amstelveen, Netherlands

Contact E-Mail Address: e.toes-zoutendijk@erasmusmc.nl

Introduction: In 2014, a national population-based colorectal cancer (CRC) screening program was implemented in the Netherlands, using biennial fecal immunochemical testing (FIT) at a cut-off of 47 µg haemoglobin (Hb)/g feces. The CRC screening program has been successful; high participation rates and yield of screening resulting in a decrease in overall and advanced-stage CRC incidence (1-3).

However, the vast majority of people screened will never develop cancer and thus will not benefit from CRC screening. Now that the program has reached its steady state, there is potential to further optimize the program. Previous studies showed that prior fecal Hb concentration just below the FIT cut-off (<47 µg Hb/g feces) is associated with a higher risk for detection of CRC or advanced adenomas (AA) at subsequent screening rounds (2). Therefore, individuals with a prior negative FIT, but with higher prior fecal Hb concentrations below the FIT cut-off, may benefit from a shorter invitation interval, whereas individuals with unmeasurable fecal Hb concentrations could benefit from longer invitation intervals. In this study, we aim to improve the yield and effectiveness of the Dutch CRC screening program by using a personalized screening strategy based on prior fecal Hb concentrations.

Aims & Methods: This mixed-method study will consist of three parts: 1) a randomized controlled trial (RCT), 2) decision modelling, 3) and focus groups. The RCT will be conducted within the national CRC screening program among individuals with a negative FIT in the previous screening round.

Individuals in the intervention arm will receive a new invitation after one, two, or three years after their last invitation, depending on their prior fecal Hb concentration. Individuals in the control arm will receive an invitation after 2 years according to current practice.

The fecal Hb concentration thresholds for the intervention arm are >15-47 µg Hb/g feces (one-year interval), >0-15 µg Hb/g feces (two-year interval), and 0 µg Hb/g feces (three-year interval), respectively. Primary study outcome is the yield of CRC and AA per screened individual in the intervention arm compared to the control arm. Secondary study outcomes are acceptability of and adherence to personalized screening.

Results of the RCT will be incorporated into the MISCAN-Colon decision model to determine long-term benefits, harms, and costs of personalized versus uniform screening. Focus group will be organized to gain insight in the information need about personalized screening and to evaluate experiences with receiving an adjusted screening interval based on personal risk.

Results: We anticipate that with a personalized screening strategy with adjusted intervals based on prior fecal Hb concentration of individuals with a negative FIT, will result in higher yield of CRC and AA detection per screened individual, anticipating on an increase in detection rate from 1.5% to 2.0%. In the long-term, personalized screening will require fewer FITs and colonoscopies than uniform screening for the same level of benefit for the total target population.

Conclusion: In the proposed study, we aim to prove superiority of a personalized CRC screening strategy in terms of harms-benefits ratio, by using an already registered risk factor, for which no additional resources are required.

Furthermore, we aim to prove the feasibility and acceptability of personalized screening within a national population-based CRC screening program making use of the current screening infrastructure.

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P0667

DIAGNOSTIC VALUE OF BIOPSY FOR LESIONS FOUND IN THE TERMINAL ILEUM DURING COLONOSCOPY

D.S. Kim¹, H.S. Koo¹, K.-C. Huh¹

¹Konyang University College of Medicine, Gastroenterology and Hepatology, Daejeon, Korea (Republic of)

Contact E-Mail Address: hornkim0404@gmail.com

Introduction: Despite the development of enteroscopy, it is not easy to diagnose small bowel diseases. In many cases, it is possible to obtain clues about small bowel diseases by observing the terminal ileum during colonoscopy.

However, in many cases, even if a lesion is found, it is more likely to be a nonspecific finding rather than to help diagnose a specific disease. The diagnostic value of ileoscopy is not well established and the routine practice of ileal intubation is controversial.

Aims & Methods: This study was performed retrospectively in patients who had biopsy on abnormal lesions in the terminal ileum during colonoscopy from 2000 to 2019. Positive diagnosis for significant disease was defined as a case in which a specific disease was suspected or confirmed in the biopsy results, requiring additional examination or treatment for the disease. These included inflammatory bowel diseases (IBD) such as Crohn's disease, intestinal tuberculosis, infectious diseases, neoplastic diseases, and Behcet's disease.

Results: 854 biopsies were obtained from macroscopically abnormal lesions of the terminal ileum. The number of positive diagnosis for significant diseases were 75(8.8%). The rate of positive diagnosis was statistically significant in patients with anemia, clinically suspected IBD, right lower quadrant (RLQ) pain or abnormal radiologic finding on the terminal ileum. The incidence of specific diseases was higher when the lesion found in the

terminal ileum was an ulcer or when there were accompanying abnormalities in the ileocecal valve (ICV), in that case, the rate of Crohn's disease was particularly high.

	Number of cases	Positive diagnosis, n (%)	OR (95% CI)	P
Colonoscopy Indications				
Suspected IBD	28	13 (46.4)	10.680 (4.864–23.449)	<0.01
Anemia	21	7 (33.3)	5.625 (2.196–14.408)	<0.01
RLQ pain	16	4 (25)	3.601 (1.132–11.457)	0.03
Radiologic abnormality in the terminal ileum	50	15 (30)	5.314 (2.748–10.278)	<0.01
Macroscopic findings				
Ulcer	243	40 (16.5)	3.243 (2.005–5.246)	<0.01
Abnormal finding in ICV	107	15 (14)	1.867 (1.018–3.423)	0.04
Mass or polyp	63	20 (31.7)	6.224 (3.426–11.308)	<0.01

OR, Odds ratio; IBD, inflammatory bowel disease; RLQ, right lower quadrant; ICV, ileocecal valve

Table. The diagnostic yield of terminal ileum biopsy according to the indication of endoscopy and the macroscopic finding of the terminal ileum

Conclusion: Terminal ileum intubation is required if the patient has anemia, clinically suspected IBD, or has radiological abnormalities in the terminal ileum. If the lesion observed in the terminal ileum is an ulcer, polyp, or mass, and if there are accompanying abnormal findings in the ICV, a biopsy should also be performed. Crohn's disease should be considered, especially in cases of anemia, suspected IBD patients, gross ulcers on the terminal ileum, or abnormal findings in the ICV.

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P0668

EVALUATION OF 2 DIFFERENT REGIMENS OF COLON PREPARATION FOR AN ADVANCED CLEENING USING A 2LT PEG-CS WITH SIMETHICONE: A RANDOMIZED, CONTROLLED STUDY – THE ERACLES STUDY

L. Pasquale¹, G. Grande², R.M. Zagari³, A. Pisani⁴, P. Da Massa Carrara⁵, B. Germanà⁶, E. Ciliberto⁷, G. Cengia⁸, A. Lamazza⁹, L. Laterza³, C. Stillitano⁷, D. Picascia¹, M.V. Carati⁹, E. Dal Pont⁶, G. Pontillo², R. Conigliaro², G. Galloro¹⁰
¹Frangipane Hospital, Gastroenterology Unit, Ariano Irpino, Italy, ²Azienda Ospedaliero Universitaria of Modena, Gastroenterology and Digestive Endoscopy Unit, Modena, Italy, ³University Alma Mater of Bologna, Medical and Surgical Sciences, Gastroenterology Unit, Bologna, Italy, ⁴S. De Bellis Hospital of Castellana Grotte, Gastroenterology and Digestive Endoscopy Unit, Castellana Grotte, Italy, ⁵S. Jacopo Hospital of Pistoia, Gastroenterology and Digestive Endoscopy Unit, Pistoia, Italy, ⁶S. Martino Hospital, Gastroenterology Unit, Belluno, Italy, ⁷S. Giovanni di Dio Hospital, Gastroenterology Unit, Crotone, Italy, ⁸Manerbio Hospital, Digestive Endoscopy Unit, Manerbio, Italy, ⁹University La Sapienza, Surgery P. Valdoni, Digestive Endoscopy Unit, Roma, Italy, ¹⁰University Federico II of Naples, Clinical Medicine and Surgery, Surgical Endoscopy Unit, Napoli, Italy

Contact E-Mail Address: grande.giuseppe@aou.mo.it

Introduction: Although the split dose regimen is recommended as bowel preparation in patients underwent to morning colonoscopy, its use in daily practice remains limited. Conversely, the classic day before regimen account for up to 35% of inadequate bowel cleansing.

Aims & Methods: On this context, the Italian Society of Digestive Endoscopy (SIED) promoted a prospective multicentric randomised non inferiority study to compare two different regimen of low volume (PEG/citrate/symeticone) bowel preparation in patient that undergo to early morning colonoscopy

Tree hundred and twenty patients (mean 58 years old, 165 female) were equally randomised in group A to assume both dose of preparation from 8pm to midnight (*the day before late group*) and group B in which the second dose was taken 4 hours before the examination (*split dose group*).

The primary endpoint was to evaluate bowel cleansing adopting Boston Bowel Preparation Score. Secondary endpoints were the evaluation of compliance and tolerability, safety, Intraluminal boubles score, polyp detection rate.

Results: Efficacy measured using Chi-square test showed 86,1% (CI 95%, 79,7-90,7) good or optimal bowel cleansing for patients in group A and 96,8% (CI 95% 92,5-98,7) in group B (p-value <0,001). Propensity to repeat the same regimen at the next colonoscopy was significantly in favour of the *day before late group* (89,5% vs 80.8% - p value 0.034). Twenty-two patients in the group A and 40 in the group B referred fear of incontinence during the journey to the hospital (p value=0.01). Compliance and tolerability didn't show differences among the two groups.

Conclusion: Although the split dose regimen remains the standard, in some specific settings, the use of the *day before late regimen* represents an acceptable alternative that guarantees an adequate intestinal cleansing and better patients acceptability for early morning colonoscopy.

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Disclosure: Nothing to disclose.

Poster presentations

Liver and biliary

Liver and biliary

P0669

SZN-043 INDUCED QUICK AND ROBUST HEPATOCYTE PROLIFERATION IN A 14-DAY DAILY DOSING EDU-LABELING STUDY IN SCID MICE

C. Lu¹, R. Fletcher¹, J. Phipps¹, D. Shah¹, S. Deshmukh¹, T. Fisher¹, H. Baribault¹, W.-C. Yeh¹, Y. Li¹

¹Surrozen, Inc., South San Francisco, United States

Contact E-Mail Address: chenggang@surrozen.com

Introduction: Wnt/ β -catenin signaling plays a key role in hepatocyte regeneration in homeostasis and after liver injury. R-spondins (RSPO) amplify the signal of Wnt ligands by stabilizing and increasing the amount of Wnt receptors on the cell surface.

We previously showed that our hepatocyte-targeted RSPO mimetic, SZN-043, specifically induced Wnt target gene expression in the liver and promoted hepatocyte proliferation in mice. This study aims to evaluate the kinetics and the overall effects of SZN-043 induced hepatocyte proliferation in a 2-week daily SZN-043 dosing schedule.

Aims & Methods: In a 14-day period, SZN-043 treatments were administered intraperitoneally daily to NOD.CB17-Prkdcscid (SCID) mice. The control anti-GFP was administered intraperitoneally twice weekly. The nucleoside analog 5-ethynyl-2'-deoxyuridine (EdU), which labels DNA during S phase of proliferation, was included in the drinking water at 1 mg/mL throughout the 14 days of the study. Livers were collected daily of the first week and every other day of the second week. Liver sections were co-stained for EdU, Ki67, HNF4A and DAPI. At each time point, the hepatocyte proliferation index (number of Ki67+HNF4A+DAPI+ nuclei) and the accumulated number of hepatocytes that had gone through at least one round of proliferation (EdU+HNF4A+DAPI+ nuclei) were quantified with an ImageJ macro.

Results: Significant hepatocyte proliferation was observed 48 hours after the first dose of SZN-043, as shown by quantifying the Ki67+HNF4A+DAPI+ co-labeled nuclei, reaching a peak at Day 4, followed by a rapid decline to near baseline level at Day 6. This observation was supported by quantification of the EdU-labeled hepatocytes (EdU+HNF4A+DAPI+) in the study.

The percent of hepatocyte nuclei that were EdU-positive reached a plateau after Day 5, suggesting most hepatocytes stopped proliferating or incorporating EdU after this timepoint, with close to 60% of all hepatocytes in the SZN-043-treated group being EDU+ from day 6 to the end of the study.

Liver mRNA expression of *Axin2* was significantly increased with SZN-043 treatment compared to anti-GFP throughout the 14-day study, indicating that continuous daily dosing of SZN-043 maintained β -catenin signaling induction despite the much-reduced level of hepatocyte proliferation after day 5.

Significant non-hepatocyte (HNF4A-negative) cell proliferation was also observed with SZN-043 treatment. Histological evaluation suggested the Ki67-positive non-hepatocytes consisted mostly of Kupffer cells/macrophages and some endothelial cells.

Conclusion: Hepatocytes responded quickly to SZN-043 treatments and underwent a limited number of proliferation cycles, despite the continued exposure to SZN-043 and β -catenin signaling induction for up to 14 days. The proliferation observed in the HNF4A-negative cells in this study was

likely due to the tissue responding to the large number of proliferating hepatocytes, as we have previously shown that SZN-043 has no direct impact on cells other than hepatocytes (Surrozen data presented previously).

Disclosure: All authors are current employees of Surrozen, Inc. and shareholders of Surrozen stock.

P0670

INHIBITION OF BCL-2 AND MCL-1 EFFECTIVELY INDUCES CELL DEATH IN HEPATOCELLULAR CARCINOMA (HCC) CELL LINES

F. Walz¹, M. Michalski¹, M. Bauer¹, M. Müller-Schilling¹, K. Gülow¹

¹University Hospital Regensburg, Internal Medicine I, Regensburg, Germany

Contact E-Mail Address: franziska1.walz@stud.uni-regensburg.de

Introduction: Hepatocellular carcinoma (HCC) is the sixth most common cancer type and the third most common cancer related cause of death worldwide. Especially in advanced stages, prognosis is still poor. Therefore, HCC is a major health issue with urgent need of new therapeutical options.

BH3-mimetics have become an emerging class of drugs during the last years. These small molecules inhibit anti-apoptotic Bcl-2 molecules, which are frequently overexpressed in cancer, including HCC. Intrinsic apoptosis can be induced by pro-apoptotic proteins Bax and Bak, which form pores in the outer mitochondrial membrane, resulting in the release of cytochrome c and the activation of caspases. Anti-apoptotic Bcl-2 proteins such as Bcl-2 and Mcl-1 exert their function by inhibiting this apoptotic process via blockage of Bax and Bak. Thus, inhibition of anti-apoptotic Bcl-2 proteins might restore apoptosis susceptibility of cancer cells.

ABT-199, a specific inhibitor of Bcl-2, is already approved for hematologic malignancies including CLL (chronic lymphocytic leukemia). MIK665 inhibits Mcl-1 and is currently in clinical trials for hematologic malignancies. BH3-mimetics have also proven preclinical efficacy in solid tumors.

Aims & Methods: We investigated whether the two described drugs could be repurposed for the treatment of HCC.

The three HCC cell lines Hep3B, HepG2 and Huh7 were treated with up to 5 μ M ABT and up to 6 μ M MIK, either alone or in combination. After 24 and 48h, cell death was assessed using flow cytometry after staining with DAPI and Annexin V. To characterize the underlying cell death mechanism, we measured the activity of caspases 3/7 in a luminescence based assay after 4 to 24h. Cleavage of caspase 3 and its substrate PARP was assessed by Western Blot after 4h.

Results: Single application of both drugs had only minor effects on cell death of all three cell lines. 5 μ M ABT induced up to 13%, 6 μ M MIK up to 20% cell death after 48h. In contrast, the combination of both drugs in these concentrations resulted in strong effects of up to 85% cell death after 48h, suggesting a synergistic effect. The most pronounced effect was observed in HepG2. Next, we analyzed the underlying cell death mechanism in more detail.

We detected a strong time and dose dependent increase in activity of caspases 3/7 after 4 to 24h treatment with the combination of ABT and MIK. Cleavage of caspase 3 and PARP was detected in Western Blot 4h after treatment with 5 μ M ABT and 6 μ M MIK. This indicates apoptosis as underlying cell death mechanism.

Conclusion: BH3-mimetics directly target resistance to apoptosis as one of the hallmarks of cancer. They have already proven beneficial in hematologic and some solid cancers. We now provide evidence that a combination of the BH3-mimetics ABT-199 and MIK665 effectively induces cell death in HCC cell lines. Drug combinations such as the ABT199/MIK665 presented here will therefore expand the therapeutic repertoire in the management of HCC and other tumor diseases in the future.

Disclosure: Nothing to disclose.

P0671

THEROLE AND MECHANISM OF IRBITIN HYPOXIA INDUCED ACTIVATION OF HEPATIC STELLATE CELLS

Z. Jin¹, J. Xu¹, R. Xie¹

¹Affiliated Hospital of Zunyi Medical University, Department of Gastroenterology, Zunyi, China

Contact E-Mail Address: jinzhe8725@163.com

Introduction: Studies have found that that hypoxia stress and hypoxia effector molecule.

HIF-1α are involved in the whole process of activation of hepatic stellate cells (HSCs) and development of hepatic fibrosis, inhibition of HIF-1α can effectively block the continuous activation of HSCs, but the regulatory mechanism of HIF-1α in the process of liver fibrosis is not clear.

In our previous experiments, we found that the increase of intracellular calcium concentration was accompanied by the stimulation of hypoxia inducer CoCl₂, suggesting that calcium signal may participate in its regulation mechanism. IRBIT, as a binding protein of IP3 receptor, can regulate the activities of many calcium channels on the membrane and affect the calcium transport inside and outside the membrane.

The purpose of this study is to explore the role and mechanism of IRBIT and its coupled calcium channels in hypoxia induced activation of hepatic stellate cells, so as to seek new drug targets for the treatment of liver cancer.

Aims & Methods: The expression of IRBIT was detected by Western blot and immunohistochemistry. CCK8 proliferation assay was used to detect the proliferation of hepatic

stellate cells stimulated by silencing IRBIT and CoCl₂. The expression of IRBIT, α-SMA, HIF-1α and related signal pathway proteins were detected by Western blot. The changes of intracellular calcium in hepatic stellate cells

stimulated by CoCl₂ were detected by Ca²⁺ imaging. The intracellular calcium channels regulated by IRBIT were screened by agonists and blockers, and

ShRNA lentiviral vector was constructed and transfected into the cells to silence the expression of IRBIT.

Results:

1. Immunohistochemistry showed that the expression of IRBIT, α-SMA and HIF-1α in liver fibrosis group was higher than that in normal liver tissue.
2. Western blot showed that TGF-β1 could induce the expression of α-SMA in HSC-T6 and LX-2 cells, but the expression of IRBIT was increased, which had statistical significance ($P < 0.05$).
3. Western blot showed that IRBIT, HIF-1α and α-SMA were increased after CoCl₂ stimulated hepatic stellate cells. ($P < 0.05$).
4. After silencing IRBIT in hepatic stellate cells LX2, the expression of HIF-1α and α-SMA induced by CoCl₂ was significantly reversed, suggesting that IRBIT may affect the occurrence and development of hepatic fibrosis by affecting hypoxia response pathway.
5. High speed calcium imaging showed that the intracellular Ca²⁺ concentration of LX-2 cells was significantly increased after CoCl₂ stimulation. When IRBIT expression of LX-2 cells was silenced by lentivirus, the increase

of intracellular Ca²⁺ induced by CoCl₂ was significantly blocked, which proved that IRBIT may promote the occurrence and development of liver fibrosis by regulating intracellular Ca²⁺ level under hypoxia stress.

Conclusion: Hypoxia stress can stimulate the up regulation of IRBIT expression in hepatic stellate cells, increase IRBIT movement to open corresponding calcium channels on the cell membrane, mediate the intracellular Ca²⁺ remodeling, promote the continuous activation of HSCs cells and the development of liver fibrosis. The results of this study have found a new way to affect the activation mechanism of HSC, which provides theoretical basis for targeted treatment of liver fibrosis targeting IRBIT.

Disclosure: The authors declare that they have no conflict of interest.

P0672

CASR AS AN IMPORTANT PROTECTIVE FACTOR COMBINED TO THE REGULATION OF HEPATIC STELLATE CELL ACTIVATION

J. Lou¹, X. Jingyu², R. Xie², XR-TEAM Study Group

¹Affiliated Hospital of Zunyi Medical University, Zunyi, China,

²Affiliated Hospital of Zunyi Medical University, Department of Gastroenterology, Zunyi, China

Contact E-Mail Address: lj29860431@126.com

Introduction: Clinical literature shows that patients from chronic hepatitis to cirrhosis show a gradual decrease in blood calcium concentration as the disease worsens. Therefore, calcium-sensitive receptors (CASR), which can sense changes in calcium in the blood, are particularly critical in liver fibrosis. Our previous experiments showed that as the index of liver fibrosis (α-SMA) was up-regulated in liver fibrotic tissue, the expression of CASR was down-regulated. Apoptosis increased significantly during the activation of HSCs stimulated by CaCl₂. CASR may be a new protective factor to inhibit the occurrence of liver fibrosis.

Aims & Methods: Immunohistochemistry, Western blot, high-speed calcium imaging and CCK8 were used to reveal the role of CaSR in liver fibrosis

Results: 1) In clinical data, the blood calcium concentration of patients with liver cirrhosis is significantly lower than normal.

2) In human tissue specimens, with the up-regulation of liver fibrosis index (α-SMA) in liver fibrosis tissue, the expression of CASR is down-regulated, and the two are negatively correlated.

3) Before and after the activated HSCs, pre-treatment with the CASR agonist CaCl₂, it was found that the protein expression of α-SMA decreased.

4) After adding CaCl₂ stimulation to activated HSCs, it was found that the proliferation ability of activated HSCs was significantly reversed.

5) Before and after the activation of HSCs, CaCl₂ and spermine stimulation can significantly induce changes in intracellular calcium.

6) CaCl₂ can significantly promote the apoptosis of activated HSCs.

7) In the activation of HSCs by high calcium stimulation, the expression of BAX increased and the expression of Bcl2 decreased significantly.

Conclusion: The calcium signal mediated by CaSR plays an important role in regulating the activation of hepatic stellate cells. CaSR may be used as a new target therapeutic mechanism, providing a novel and effective treatment for liver fibrosis.

Disclosure: Nothing to disclose.

P0673

RELATIONSHIP BETWEEN THE RATIO OF THE MAIN PHYLOTYPES OF THE GUT MICROBIOTA AND BODY COMPOSITION IN PATIENTS WITH NON-ALCOHOLIC FATTY LIVER DISEASE

G. Fadieienko¹, O. Gridnyev¹, N. Chereliuk¹

¹Government Institution „L.T.Malaya Therapy National Institute of the National Academy of Medical Sciences of Ukraine“; Division for the Study of the Digestive Diseases and its Comorbidity with Noncommunicable Diseases, Kharkiv, Ukraine

Contact E-Mail Address: nat.chereliyk@gmail.com

Introduction: Non-alcoholic fatty liver disease (NAFLD) is one of the most common liver diseases worldwide and its development are closely related to the lifestyle of the population (especially nutrition and physical activity), especially in developed countries.

Aims & Methods: To analyse the relationship between the main phylotypes of gut microbiota (GM) and body composition in patients with NAFLD. 120 patients with NAFLD were examined: among them were 59 men (49.2%) and 61 (50.8%) women, the average age of patients was 47 years. All patients were divided into groups according to body mass index (BMI). The first group included 85 patients with NAFLD with BMI - 36.50 [32.00; 40.60] kg / m² (i.e. with obesity), and the second group included 35 patients with NAFLD with BMI - 28.00 (27.10; 29.35] kg / m² (i.e. with overweight). The control group consisted of 20 healthy volunteers: 8 men (40%) and 12 women (60%), whose average age was 43 years and BMI of 23.50 [21, 35; 24.78] kg / m². The study of GM composition at the level of basic phylotypes was performed by identifying total bacterial DNA and DNA of *Bacteroidetes* (*B*), *Firmicutes* (*F*), as well as the ratio of *F* / *B* by quantitative polymerase chain reaction in real time using universal primers for 16S rRNA and taxon specific primers. Determination of body composition was performed using bioimpedancemetry. Interpretation of the results of measuring the content of adipose tissue (AT) in the body, the percentage of visceral fat (VF) and skeletal muscle (SM) was performed according to the tables of the OMRON device. Statistical processing was performed using the Statistica 13.1 package. Data are given in the form of Me [LQ; UQ], where Me is the median, LQ and UQ are the lower and upper quartiles, respectively.

Results: In patients of the first group the relative content of *F* was - 52.12 [39, 94; 67.03]%, in patients of the second group - 51.49 [39.26; 62.88]%, which is almost 2 times higher than the corresponding indicator of the control group. The opposite dynamics was observed with respect to the relative content of *B* - in patients of the first group it acquired minimal values - 15.97 [8,10; 27.52]%, and was slightly higher in patients of the second group - 18.83 [7.96; 32.35]%, but in the control group it was probably higher. The *F* / *B* ratio in patients of the first group exceeded that of the control group by 5.7 times, and in patients of the second group by 4.3 times. Perhaps the resulting changes in the composition of GM may be associated with excessive development of AT: increase in the relative content of *F* in patients of both groups correlated with % of VF (*r* = + 0.74, *p* = 0.01 and *r* = + 0.70, *p* = 0, 01, respectively) and accordingly % SM (in patients from the second subgroup *r* = -0.47, *p* = 0.03); in turn, the decrease in the relative content of *B* in patients of both groups had reverse connection with % of VF (I- *r* = -0.48, *p* = 0.01 and II- *r* = -0.49, *p* = 0.003, respectively).

Conclusion: In patients of both groups there was an increase in the relative amount of *F* and the ratio of *F* / *B* against the background of the decrease in the relative content of *B*. These changes were statistically significantly more pronounced in patients with NAFLD in the presence of obesity. This allowed us to suggest the relationship between GM and the presence of NAFLD in patients of both groups, but this requires additional verification on the larger number of observations and is important for deepening the

understanding of the pathophysiological mechanisms of the development of ectopic fat depots, in particular in the liver.

Disclosure: Nothing to disclose

P0674

DOPAMINE REGULATES AUTOPHAGY DURING TGF- β 1-INDUCED ACTIVATION OF HEPATIC STELLATE CELLS

X. Yang¹, X. Jingyu², R. Xie²

¹Affiliated Hospital of Zunyi Medical University, Zunyi, China,

²Affiliated Hospital of Zunyi Medical University, Department of Gastroenterology, Zunyi, China

Contact E-Mail Address: yangxiaoxu90@126.com

Introduction: The activation of hepatic stellate cells (HSCs) is the key factor in the pathogenesis of liver fibrosis. Studies have confirmed that autophagy is involved in the activation of HSCs, but the regulatory mechanism of autophagy is unclear. With the development of brain gut axis and neurotransmitters in the study of digestive system diseases, our preliminary results show that neurotransmitter dopamine (DA) can significantly inhibit the expression of autophagy gene and liver fibrosis marker α -SMA during the activation of HSCs.

Further studies suggest that DA stimulates the activation of TRPV1 calcium channel on the cell membrane of HSCs, which leads to intracellular calcium remodeling, and then inhibits autophagy and activation of HSCs, and finally plays an anti-fibrosis role.

This project aims to clarify the role and mechanism of DA in the autophagy of HSCs activation from animal experiments in vivo and cell experiments in vitro, that provides a theoretical basis for the targeted therapy of autophagy during the process of liver fibrosis.

Aims & Methods: The expression of α -SMA, autophagy gene and TRPV1 in human and liver fibrosis model mice were detected by immunohistochemistry. The effect of DA on the expression of α - SMA and autophagy gene before and after activation of HSCs was detected by Western-blot. The inhibition and construction of TRPV1 interference and overexpression plasmids were transfected into HSCs to observe the effect of DA on the expression of autophagy gene Flux variation. Calcium imaging was used to detect the changes of intracellular Ca²⁺ during DA stimulation on HSCs.

Results:

1. Compared with normal liver tissue, the expression of α -SMA and autophagy gene LC3 in liver fibrosis tissue increased, while the expression of TRPV1 decreased. Compared with the normal group, the expression of α - SMA increased and TRPV1 decreased in the liver fibrosis model group, which was reversed after DA treatment
2. Compared with activated HSCs, DA can significantly reduce the proliferation of HSCs (stimulated by TGF- β 1). Flow cytometry showed that DA had no significant effect on the apoptosis of HSCs.
3. Western-blot showed that DA and capsaicin could significantly reduce the expression of α - SMA, autophagy gene LC3 protein and autophagy flow in activated HSCs, which were eliminated by TRPV1 inhibitor sb-705498 or by interfering with the function of TRPV1. Overexpression of TRPV1 could enhance the effect of DA. It is suggested that DA may play a protective role by activating TRPV1.
4. Through calcium imaging experiments, it was found that DA stimulation was accompanied by the increase of intracellular Ca²⁺ in HSCs. At the same time, the intracellular Ca²⁺ in HSCs stimulated by capsaicin was increased, while using the intracellular Ca²⁺ chelators BAPTA-AM, sb-705498 and calcium free environment could not induce the change of Ca²⁺ in HSCs.
5. Mechanism studies confirmed that DA significantly inhibited the expression of p-smad3 protein in activated HSCs, and this effect disappeared after inhibition and interference of TRPV1.

Conclusion: Dopamine may act as a protective factor in the process of liver fibrosis. Dopamine may activate TRPV1 calcium channel on cell membrane to mediate extracellular calcium influx, leading to intracellular calcium remodeling, and then inhibit the autophagy and activation of HSCs mediated by TGF- β 1/Smad3 signaling pathway, and finally play an anti-fibrosis role.

Disclosure: no conflict interest.

P0675

STERILE FECAL FILTRATE TRANSFER FOR THE TREATMENT OF PATIENTS WITH HEPATIC ENCEPHALOPATHY

R. Gedgaudas^{1,2}, J. Skieceviciene², E. Kreivenaite^{2,1}, I. Valantiene^{1,2}, S. Schreiber³, A. Franke³, J.S. Bajaj⁴, J. Kupcinskas^{1,2}

¹Lithuanian University Of Health Sciences, Gastroenterology, Kaunas, Lithuania, ²Lithuanian University of Health Sciences, Institute for Digestive Research, Kaunas, Lithuania, ³Kiel University, Institute of Clinical Molecular Biology, Kiel, Germany, ⁴Virginia Commonwealth University and McGuire Veterans Affairs Medical Center, Division of Gastroenterology, Hepatology and Nutrition, Richmond, United States

Contact E-Mail Address: R.gedgaudas@gmail.com

Introduction: Hepatic encephalopathy (HE) remains one of the most debilitating complications of liver cirrhosis. Changes in gut microbiome composition have been linked to liver diseases and its complications including HE, while direct or indirect gut microbiome modulation remains standard of care treatment in HE. Fecal microbiota transplantation (FMT) has shown great success in the treatment of recurrent *Cl. Difficile* infection which led to further studies assessing FMT's efficacy in other diseases associated with dysbiosis including cirrhosis.

Recent randomized controlled trial showed FMT to be safe and effective in HE treatment, however transferring unidentified live bacteria could cause various complications, including infections, especially in immunocompromised patients. In 2017 a pilot study developed a special device with bacterial filters to produce sterile fecal filtrate (FFT), which maintained efficacy in treating *Cl. Difficile* infection while avoiding potential risks associated with bacterial transfer.

Aims & Methods: **Aims:** We have aimed to investigate safety and efficacy of sterile fecal filtrate in the treatment of hepatic encephalopathy

Methods: The study was conducted in Lithuanian University of Health Sciences, Kaunas Clinics, Department of Gastroenterology. Sterile fecal filtrate from a healthy tested donor stools was prepared following the methods described by Ott SJ¹. Seven patients with hepatitis C virus or alcohol induced cirrhosis and HE have been enrolled in the study and received sterile fecal filtrate through the nasojejunal tube. Patients were monitored for a month after a procedure. Standard blood tests reflecting liver function in addition to stool samples were collected prior to the procedure, a week and a month after the procedure.

Psychometric HE score tests were used to monitor hepatic encephalopathy during the control visits. Micorbial DNA was isolated from stool samples and 16S rRNA sequencing was performed using V1-V2 primers to determine fecal microbiome composition.

Results: Sterile fecal filtrate transfer was well tolerated, no adverse events were registered. Cirrhosis patients showed reduced alpha diversity prior to the procedure as compared to the donor. Significant shifts in stool microbiome composition were observed in 3/7 patients, as there was an increase in Shannon alpha diversity index, reduction in abundance of *Proteobacteria* phylum and a shift towards donors' microbial composition as assessed by Bray-Curtis dissimilarity analysis. Despite compositional changes - we have not observed any significant clinical effects of the pro-

cedure. Liver function biochemical tests, psychometric HE score tests did not reveal any significant improvement over the observational period. One of the patients who received FFT died shortly after the observational period. The death was unrelated to the FFT procedure. The patient did not show significant shifts in microbiome composition after the FFT procedure, on the contrast - there was a gradual reduction in alpha diversity metrics during the control visits.

Conclusion: Sterile fecal filtrate transfer resulted in significant shifts in stool microbiota composition for a portion of the patients. Despite the effect on the microbiota composition, we have not witnessed any additional clinical benefits for these patients.

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P0676

POINT SHEARWAVE ELASTOGRAPHY TECHNIQUES FOR THE ASSESSMENT OF LIVER STIFFNESS

A. Popescu¹, C.G. Foncea¹, R. Lupusoru¹, R. Cotrau¹, F. Bende¹, R. Sirli¹, I. Sporea²

¹Victor Babes University of Medicine, Department of Gastroenterology and Hepatology, Timisoara, Romania,

²University of Medicine and Pharmacy Victor Babes Timisoara, Department of Gastroenterology and Hepatology, Timisoara, Romania

Contact E-Mail Address: alinamircea.popescu@gmail.com

Introduction: Non-invasive ultrasound-based techniques for liver stiffness assessment (LSM) were developed as an alternative to liver biopsy. Transient Elastography (TE) is the first method validated by several guidelines and recently other new methods were developed. The aim of this study was to evaluate the performance of two point Shear Waves Elastography (pSWE) techniques implemented in the same ultrasound system for liver stiffness assessment, using TE as reference.

Aims & Methods: A prospective study was conducted, in which 271 consecutive patients with or without previously diagnosed liver disease were included.

LSM was evaluated by point Shear Wave Elastography (pSWE and Auto pSWE) implemented on a Siemens ACUSON Sequoia system (Deep Abdominal Transducer-DAX) and by TE, using a FibroScan Compact M 530 system (M and XL probes).

For Auto pSWE, 15 measurements/values are automatically obtained in a single evaluation and the median and IQR are displayed. For p-SWE and TE, reliable measurements were defined as the median value of 10 measurements and IQR/M<0.3 for all probes. For significant fibrosis, a cut-off value by TE of 7 kPa was used, and for liver cirrhosis 12 kPa [1].

Results: Valid LSM were obtained in all 271 (100%) patients using both elastographic methods. A very good positive correlation was found between the LS values obtained by TE and both Auto pSWE and pSWE: $r=0.78$, $p<0.0001$; and between Auto pSWE and pSWE: $r=0.92$, $p<0.0001$.

The best pSWE and Auto pSWE cut-off value for significant fibrosis ($F\geq 2$) was 5.1 kPa (p-SWE: AUC- 0.81; Se-58.3%; Sp-94.6%; PPV-83.1%; NPV-83.5%; Auto pSWE: AUC- 0.82; Se-63.1%; Sp-90.4%; PPV-76.8%; NPV-84.4%) and for liver cirrhosis (F4) was 6.7 kPa (p-SWE: AUC- 0.92; Se-73.8%; Sp-94.3%; PPV-83.8%; NPV-95.3%; Auto pSWE: AUC- 0.93; Se-78.5%; Sp-97.8%; PPV-86.8%; NPV-96.1%).

Conclusion: The two techniques, *pSWE* and *Auto pSWE* have very good correlations with TE and similar performance for predicting significant fibrosis and liver cirrhosis in a mixed cohort of patients.

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P0677

PROGNOSTIC IMPACT OF NEUTROPHIL-TO-LYMPHOCYTE RATIO IN CIRRHOSIS

A. neji¹, S. Mrabet², L. khayat³, R. Harbi⁴, I. Akkari⁵, E. Ben Jazia³

¹Farhat Hached University Hospital, Sfax, Tunisia, ²Farhat Hached University Hospital, Gastroenterology, Sousse, Tunisia, ³Farhat Hached University Hospital, Sousse, Tunisia, ⁴Faculté de Medecine Ibn Al Jazzar de Sousse, Sousse, Tunisia, ⁵Farhat Hached Hospital, Gastroenterology, Sousse, Tunisia

Contact E-Mail Address: amanyneji7@gmail.com

Introduction: The neutrophil-to-lymphocyte (NLR) ratio is a marker of systemic inflammatory response, which has been studied as an interesting prognostic biomarker in various tumor types. This ratio incorporates two immune systems: neutrophils which exemplify the continual inflammation and lymphocytes which exemplify the regulatory pathway.

Aims & Methods: The aim of our study was to establish the correlation between NLR, the severity of cirrhosis and the occurrence of complications. This is a retrospective descriptive study including all patients followed for cirrhosis between January 2015 and January 2021.

Results: 60 patients were collected during the study period. The mean age at the time of diagnosis was 52 ± 14.88 (26-87) years. Fifty-three patients (53.3%) were female. Etiologies found for cirrhosis were: hepatitis B virus infection in 30% of cases, primary biliary cholangitis in 16.7%, non-alcoholic steatohepatitis in 11.7%, hepatitis C virus infection in 8.3 % of cases and alcohol intake in 1.7% of cases.

The aetiological assessment was negative in 28.3% of cases. The average MELD score at admission was 42 points (9-80). Cirrhosis was classified as CHILD A in 19 cases, CHILD B in 31 cases and CHILD C in 10 cases. Endoscopic signs of portal hypertension were present in 95% of cases at the time of diagnosis, of which 33% were represented by grade 1 esophageal varices, 35% by grade 2 esophageal varices and 3.3% by grade 3 esophageal varices. 11.7% of the patients had gastric varices and 48% of the patients had hypertensive gastropathy.

Ascites was the main complication present in 66.7%. The other complications of cirrhosis were upper gastrointestinal bleeding by rupture of esophageal varices in 28.3% of cases, hepatic encephalopathy in 16.7% of cases and hepatocellular carcinoma in 11.7% of cases. The average NLR score was 4.4 (0.82-22.7).

The analytical study had shown that the RNL ratio was positively correlated with the MELD score with ($p = 0.03$); as well as with the occurrence of cirrhosis complications ($p=0.05$). However, there was no correlation between NLR and CHILD score ($p=0.29$).

Conclusion: In our study, the neutrophil-to-lymphocyte (NLR) ratio was significantly correlated with the MELD score and the occurrence of complications and can thus be used to assess the prognosis of cirrhotic patients.

Disclosure: Nothing to disclose.

P0678

THE POSITIVE EFFECTS OF SYMBIOTICS ON LIVER STEATOSIS BY IMPROVING GUT MICROBIOLOGY- RANDOMIZED CONTROLLED TRIAL

M. Mitrović¹, M. Pantelic¹, D. Zlatković¹, P. Svorcan^{2,1}

¹Kbc Zvezdara, Gastroenterology and Hepatology, Belgrade, Serbia, ²School of Medicine Belgrade, Belgrade, Serbia

Contact E-Mail Address: miloskbcz18@gmail.com

Introduction: Treatment options for non-alcoholic fatty liver disease (NAFLD) are currently limited. No pharmaceutical intervention is approved, and the focus is on lifestyle modification. Altering dysbiotic gut flora through synbiotic supplementation has recently been recognized as a potential treatment strategy to reduce the production of microbial endotoxins, decrease local and systemic inflammation, and liver steatosis. Assessing the efficacy and safety of this potential strategy has been the main goal of our randomized, double-blind, placebo-controlled trial.

Aims & Methods: A total of 21 NAFLD patients aged 18-80 years with the ability to provide informed consent, were included in the study. NAFLD was defined by a baseline attenuation (ATT) coefficient score measured by shear-wave (SW) elastography of 0.63 dB/cm/MHz or higher and a baseline ALT of more than 40 IU/L for males and 35 IU/L for females.

The exclusion criteria were alcohol use (consuming > 40 g alcohol/day for men and > 20 g/day for women in the preceding 12 months), chronic viral hepatitis, the presence of hepatic carcinoma, biliary disease, drug use, and hypothyroidism associated with fatty liver.

Patients were randomized either to an intervention group ($n = 11$) receiving synbiotics (*Lactobacillus acidophilus*, *Lactobacillus casei*, and *Bifidobacterium lactis*, 32 billion colony forming units per day plus 3.2 g of inulin) or control group ($n = 10$) receiving placebo for 3 months.

The impact of treatment on the dynamic of ALT and SW elastography parameters was defined as the primary outcome of the study. Secondary outcomes included changes in the stool microbiome, serum interleukin-6 levels, high sensitivity C-reactive protein (hsCRP), diet, and safety. A correlation substudy between microbiome composition and clinical parameters was also performed. Stool microbiome analysis was performed through 16S rRNA gene sequencing.

Results: Synbiotic treatment significantly modified the gut microbiome with *Bifidobacteria* ($p = 0.11$) and *Faecalibacterium* ($p = 0.016$) genera enrichment and consequently significantly reduced serum ALT levels (Δ ALT -4.2 vs 0.6 IU/L, $p = 0.024$). The effect of synbiotics on SW elastography parameters was less pronounced.

Although both groups of patients showed a tendency towards ATT decrease, the effect of synbiotics was of larger magnitude, but fell short of statistical significance (Δ ATT -0.062 vs -0.058, $p=0.063$). An inverted correlation between *Bifidobacterium* abundance and hsCRP levels was noted ($\rho = -0.446$, $p = 0.033$). No safety issues were noted.

Conclusion: Synbiotics could be available, safe, and an effective therapeutic strategy that we could use in daily practice as a complementary treatment for NAFLD patients. Further studies on the subject are needed.

Disclosure: Nothing to disclose.

P0679

METABOLIC-ASSOCIATED FATTY LIVER DISEASE INVOLVES DEVIATIONS IN CYTOKERATINS AND GOLGI PROTEIN 73

A. Michalak¹, M. Guz², J. Kozicka¹, M. Cybulski², W. Jeleniewicz², A. Stepulak², B. Kasztelan-Szczerbinska¹, A. Rzyck¹, H. Cichoz-Lach¹

¹Medical University of Lublin, Department of Gastroenterology with Endoscopy Unit, Lublin, Poland, ²Medical University of Lublin, Department of Biochemistry and Molecular Biology, Lublin, Poland

Contact E-Mail Address: lady.agatamichalak@gmail.com

Introduction: Metabolic-associated fatty liver disease (MAFLD) is related to deviations in various serological and hematological markers. Nevertheless, looking for new laboratory parameters with a good diagnostic accuracy in its course constitutes an essential direction in hepatology all the time.

Aims & Methods: The purpose of our survey was to evaluate a diagnostic accuracy of cytokeratins [apoptosis-associated caspase-cleaved keratin 18 (CCK18) and keratin 18 (K18)] and Golgi protein 73 (GP73) together with relationships between them and selected hematological indices [red cell distribution width-to-platelet ratio (RPR), neutrophil-to-lymphocyte ratio (NLR) and red cell distribution width-to-lymphocyte ratio (RLR)], direct and indirect markers of liver fibrosis and microRNAs (miRNAs), in the course of MAFLD.

One hundred ninety six persons were enrolled to the study: 96 with MAFLD and 100 healthy volunteers in control group. Serological expression of cytokeratins (CCK18 and K18), GP73, procollagen I carboxyterminal propeptide (PICP), procollagen III aminoterminal propeptide (PIIINP), platelet-derived growth factor AB (PDGF-AB), transforming growth factor- α (TGF- α), laminin, miR-126-3p, miR-197-3p and miR-1-3p was evaluated in all examined patients. We measured AAR, APRI, FIB-4 and GPR in examined patients, too. RPR, NLR and RLR were obtained, as well. Then we looked for correlations between investigated cytokeratins, GP73 and the rest of assessed parameters.

Additionally, a diagnostic value of cytokeratins (CCK18 and K18) and GP73 together with proposed cut-off in research group were measured with area under the curve (AUC).

Results: The concentration of CCK18 and K18 together with GP73 was significantly greater in MAFLD group compared to controls ($p < 0.0001$). Moreover, MAFLD patients with BARD score ≥ 2 had significantly higher results of CCK18 and GP73 ($p < 0.05$) in comparison to persons with BARD score < 2 . K18 correlated positively with PICP, miR-126-3p, GPR, APRI and RLR ($p < 0.05$).

We did not find any dependences between cytokeratins, GP73, indirect markers of liver fibrosis and hematological scales. AUC and the cut-offs for CCK18, K18 and GP73 in MAFLD group were: 0.780, >74.56 U/L $p < 0.001$; 0.764, >64.13 U/L, $p < 0.001$ and 0.767, >323.32 ng/ml, $p < 0.001$, respectively.

Conclusion: Presented relationships seem to be the kind of novelty in the group of MAFLD patients. Noticed dependences between cytokeratins and miRNAs together with serological markers of liver fibrosis and hematological indices, should be explored as a potential new diagnostic pathway in the course of MAFLD.

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Disclosure: Nothing to disclose.

P0680

BACTERIOPHAGES TO TREAT LIVER DISEASE ELIMINATING HARMFUL BACTERIA (BATTLE) - STUDY PROTOCOL

E. Cold^{1,2,3}, J.E. Heintz⁴, A.M. Petersen^{1,4}, P.A. Stenbø², A.B. Carstens³, L.H. Hansen³, F. Bendtsen¹, H. Lambert¹

¹Copenhagen University Hospital Hvidovre, Gastrounit, Medical Division, Hvidovre, Denmark, ²Copenhagen University Hospital Herlev, Department of Gastroenterology, Medical Section, Herlev, Denmark, ³Copenhagen University, Faculty of Sciences, Department of Plant and Environmental Sciences, Frederiksberg C, Denmark, ⁴Copenhagen University Hospital Hvidovre, Department of Clinical Microbiology, Hvidovre, Denmark

Contact E-Mail Address: frederikcold422@hotmail.com

Introduction: In Nature Duan et al. recently reported how the mortality rate in patients hospitalized with alcoholic hepatitis is highly correlated with the presence of cytolysin-producing *Enterococcus (E) faecalis*.¹

The mortality 180 days after diagnosis of alcoholic hepatitis was 89% in patients hosting this bacteria in their gut microbiome compared to only 3.8% in patients without this bacteria.

Further, transfer of the bacteria to mice reproduced the liver damage and treatment with bacteriophages targeting cytolysin-producing *E. faecalis* was able to counteract this liver damage.

Aims & Methods: The first aim of the BATTLE project is to: Confirm the correlation between cytolysin-positive *E. faecalis* in the gut microbiota and poor disease outcome in patients with alcoholic hepatitis. The second aim of the BATTLE project is to: Find, test, purify and produce phages targeting cytolysin-producing *E. faecalis*.

The BATTLE-study has been approved by the regional scientific committee and will begin recruiting participants May 2022. Thirty patients with alcoholic hepatitis hospitalized at Copenhagen University Hospital Hvidovre or Herlev will be followed for one year following hospital admission. Within the first seven days following hospital admission faecal samples are collected and analysed for the presence and quantity of cytolysin producing *E. faecalis* through 16S rRNA gene sequencing using primers targeting cytolysin-producing *E. faecalis*.

Lytic bacteriophages with the potential to eliminate cytolysin-producing *E. faecalis* will be isolated from sewage water and characterised.² Bacteriophages with the ability to eliminate the disease-causing *E. faecalis* will be produced, stored, and tested according to current international standards, so they are ready for potential application in human trials or as a last-resort treatment.

Results: Primary outcome: Survival 180 days after hospital admission with alcoholic hepatitis in patients with and without cytolysin-positive *E. faecalis* in their faecal samples.

Secondary outcomes: 1) Survival 30-, 90- and 365-days following hospital admission with alcoholic hepatitis in patients with and without cytolysin producing *E. faecalis* in their faecal samples. 2) Correlation between quantity of cytolysin producing *E. faecalis* in faecal samples and survival 180 days following hospital admission. 3) Correlation between faecal bacterial alpha-diversity and survival 180 days following hospital admission.

Conclusion: The goal of the BATTLE project is to improve the prognosis for patients with alcoholic hepatitis by offering an innovative antimicrobial targeted-treatment that seeks to directly address a possibly major contributing factor leading to liver damage.

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P0681

INDICATORS OF THE MAIN PHYLOTYPES OF THE INTESTINAL MICROBIOTA AND VISCERAL OBESITY IN PATIENTS WITH NON-ALCOHOLIC FATTY LIVER DISEASE

Y. Nikiforova¹, G. Fadieienco¹, I. Kushnir¹, V. Chernova¹, T. Solomentseva¹, O. Kurinna¹, V. Galchynska¹, T. Bondar¹

¹Government Institution L.T. Malaya Therapy National Institute of the National Academy of Medical S, Department of the Study of Diseases of the Digestive System and their Comorbidity with the Noncommunicable Diseases, Kharkov, Ukraine

Contact E-Mail Address: dr.jana@email.ua

Introduction: There is evidence of a strong association between non-alcoholic fatty liver disease (NAFLD) and obesity and intestinal dysbiosis (ID) in a number of clinical studies. However, there are still many open questions.

Aims & Methods: The study of the state of the intestinal microbiota (IM) in patients with NAFLD and the determination of changes in its composition at the level of the main phylotypes, depending on the amount and activity of visceral adipose tissue (VAT).

108 patients with NAFLD with metabolic disorders and 30 people in the control group were examined. The mean age of the examined NAFLD patients was (56.46 ± 10.4) years. The assessment of anthropometric parameters included the calculation of body mass index (BMI), the percentage of visceral adipose tissue (VAT).

To determine the dysfunction of the VAT, the visceral obesity index (VOI) was calculated according to the method of Amato M.S. The composition of IMs at the level of the main phylotypes was determined by detecting total bacterial DNA and DNA of Bacteroidetes, Firmicutes, and Actinobacteria by real-time quantitative polymerase chain reaction (PCR) using universal primers for the 16S rRNA gene and the App taxon system.

Results: In patients with NAFLD, there was a probable increase in the content of Firmicutes bacteria with a simultaneous decrease in the number of Bacteroidetes and a slight increase in the content of Actinobacteria. In addition, significant changes were observed in the value of the Firmicutes: Bacteroidetes index. In patients with NAFLD, this indicator was significantly higher than in the control group ($p < 0.05$) and amounted to 6.48 and 1.28, respectively.

The study of the relative quantitative composition of IM in the study groups revealed significant differences in NAFLD patients with overweight and varying degrees of obesity compared with the control group and the group of NAFLD patients with normal BMI. In patients with varying degrees of obesity, there was a significant decrease in Bacteroidetes to 16.8 [8.7; 24.2]%, with moderate obesity and up to 11.2 [6.2; 19.8]% in morbid obesity with a simultaneous increase in the Firmicutes/Bacteroidetes ratio to 3.7 [1.8; 6.7] and 5.2 [2.9; 7.5] respectively.

It has been established that as the weight increases, deeper changes in the ratio of the main bacterial phyla of IM occur. Later, we studied the dependence of changes in MI on the amount and activity of VAT. In patients with NAFLD, as the percentage of VAT increased, the content of IM was redistributed towards an increase in Firmicutes compared with the control group and patients with NAFLD with a normal amount of VAT.

At the same time, in the NAFLD group with visceral obesity, the number of Bacteroidetes decreased, while the content of Actinobacteria did not change significantly. A similar relationship was obtained between the distribution of the main IM filets and the activity of VAT.

Thus, in patients with high VOI, an increase in the content of Firmicutes bacteria is likely; on the contrary, in these patients, the number of Bacteroidetes has decreased. In the group of NAFLD patients with a low level of VOI, a high variability in the composition of Firmicutes bacteria was revealed, although in the whole group there was a tendency to an increase in the content of bacteria of this class.

Conclusion: Changes in the composition of IM indicate the likely involvement of bacteria of the genus Firmicutes in the formation of VOI, an increase in the activity of VAT, and in the further development and progression of NAFLD.

Disclosure: No Conflict of Interest.

P0682

GUT MICROBIOTA DYSBIOSIS AND FUNCTIONAL BACTERIA IN PATIENTS WITH NONALCOHOLIC FATTY LIVER DISEASE AND CHRONIC KIDNEY DISEASE

D. Georgescu¹, A. Lascu², O.-E. Ancusa¹, M. Muntean¹, N. Basa¹, I. Suceava¹, D.-F. Lighezan¹

¹V Babes' University of Medicine and Pharmacy, Internal Medicine, Timisoara, Romania, ²V Babes' University of Medicine and Pharmacy, Functional Sciences, Timisoara, Romania

Contact E-Mail Address: dgeorgescu@hotmail.com

Introduction: Nonalcoholic fatty liver disease (NAFLD) is currently known as a risk factor for chronic kidney disease (CKD and gut microbiota dysbiosis could be a driver for both entities.

Aims & Methods: Aim of this study was to assess whether gut microbiota dysbiosis (DB) may associate more severe forms of both NAFLD and CKD.

Patients and Methods: 80 patients with NAFLD, 40% women, 60% men, average age 42 to 85 years joined this observational study.

Patients were divided in two groups based on the presence or absence of CKD: 40 patients without CKD and 40 patients with early stages of CKD (stage 1=13 patients and stage 2=27 patients). Renal obstructive pathology, lithiasis, cirrhosis and other etiologies of liver diseases were ruled out.

Biochemistry of blood and urine and microbiology of urine and stool, fatty liver index (FLI), estimated glomerular filtration rate (e-GFR) as well as abdominal Duplex/ computer tomography examination, liver point shear wave elastography were performed in all research participants.

Next generation sequencing of stool's samples from dysbiotic patients was also performed. NAFLD was classified as mild, moderate, severe and consecutively scored between 1 to 3 points.

Results: Significant differences were noted between severity of NAFLD in group without CKD :1.3±0.48 vs. group with CKD: 2.13±0.76($p=0.002$). DB range was significantly higher in patients with CKD 1.69± 0.9vs.0.7±0.67 in patients without CKD($p=0.0019$.) Decrease of H index of biodiversity of gut microbiota was observed in 20% in patients with no CKD vs.62.5% in those with CKD($p=0.0001$).

Stool's functional bacteria assessment showed significant differences related to increase of lipopolysaccharide (LPS) positive bacteria and decrease of Akkermansia muciniphila spp. in favor of patients with CKD ($p<0.001$). Good positive correlations were observed between DB range, microproteinuria, NAFLD score and FLI in patients with CKD.

Conclusion: Higher range of gut DB and particular fingerprint of functional stool's bacteria were associated to more severe forms of NAFLD and CKD.

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P0683

COMPREHENSIVE MRNA EXPRESSION PROFILE AND IDENTIFICATION OF CRUCIAL GENES IN LIVER REGENERATION

Y. Liu¹, J. Kong², T. Wang², J. Liu¹

¹Shandong University, Department of Liver Transplantation and Hepatobiliary Surgery, Shandong Provincial Hospital, Jinan, China, ²Shandong Provincial Hospital Affiliated to Shandong First Medical University, Department of Liver Transplantation and Hepatobiliary Surgery, Jinan, China

Contact E-Mail Address: dr1027188507@163.com

Introduction: The liver is a unique organ that has an extraordinary regenerative capacity. Liver regeneration (LR) is a complex process involving different molecules, signaling pathways and cellular responses.

However, genome-wide expression changes during LR have not been investigated thoroughly; thus, it is urgent to elucidate the underlying molecular mechanisms associated with LR.

Aims & Methods: RNA sequencing was performed to investigate temporal changes in transcription after partial hepatectomy (PH) in male C57BL/6 mice. Differentially expressed genes (DEGs) were identified using DESeq2. Gene Ontology (GO) and Kyoto Encyclopedia of Genes and Genomes (KEGG) enrichment analyses were performed to explore the functions of DEGs. The protein-protein interaction (PPI) network of DEGs was established, and hub genes were screened by Cytoscape.

Results: In total, 2348 and 3534 DEGs were found at 4 h and 12 h after PH, respectively. Enrichment analysis showed that these DEGs were significantly related to LR-associated pathways, such transcription factor activity, the MAPK signaling pathway, cytokine-cytokine receptor interactions, and ribosome biogenesis. Then, the protein-protein interaction network and key modules were constructed by Cytoscape, and four hub genes were identified, including ATF3, GNL3, CEBPA, and DDIT3.

Conclusion: This study presented a comprehensive transcriptomic profiling of LR and investigated the temporal variations in gene expression patterns. Furthermore, the hub genes identified by us may become key regulators of LR. Our study may provide further insights into the comprehension of LR.

Disclosure: Nothing to disclose.

P0684

THE DIAGNOSTIC ROLE OF CYTOKERATIN 8/18 IMMUNOHISTOCHEMICAL MARKER FOR LEAN NON-ALCOHOLIC FATTY LIVER DISEASE

P. Telli¹, M. Buyuk², N.B. Öztürk³, Z. İstemihan⁴, K. Nuriyev⁴, A. Atasoy⁵, B. Çavuş⁴, A. Çifcibaşı Örmeci⁴, U. Akyuz⁶, K. Demir⁴, F. Besisik⁴, S. Kaymakoglu⁴, M. Güllüoğlu², E. Akyuz⁷

¹Istanbul University Istanbul Faculty of Medicine, Internal Medicine, Istanbul, Turkey, ²Istanbul University Istanbul Faculty of Medicine, Clinical Pathology, Istanbul, Turkey, ³Mayo Clinic, Minnesota, United States, ⁴Istanbul University Istanbul Faculty of Medicine, Gastroenterology, Istanbul, Turkey, ⁵Istanbul Aydin University Faculty of Medicine, Gastroenterology, Istanbul, Turkey, ⁶Istanbul Health Sciences University Fatih Sultan Mehmet Training and Research Hospital, Dept. of Gastroenterology, Istanbul, Turkey, ⁷Istanbul University Istanbul Faculty of Medicine, Gastroenterohepatology, Istanbul, Turkey

Contact E-Mail Address: filizakyuz@hotmail.com

Introduction: Non-alcoholic fatty liver disease (NAFLD) is one of the leading causes of chronic liver diseases. NAFLD spectrum begins from simple steatosis to non-alcoholic steatohepatitis (NASH), progressive fibrosis, cirrhosis, and even hepatocellular carcinoma. Although most NAFLD patients are overweight and obese, 30% are lean. We analyzed lean and non-lean NAFLD patients' liver biopsies for cytokeratin 8/18 immunohistochemical staining differences.

Aims & Methods: Thirty biopsy-proven NAFLD patients (15 patients with BMI ≤ 25 kg/m², 15 patients with BMI > 25 kg/m²) were included in the study. Demographic, biochemical, and histologic features of the patients were recorded. Biopsy specimens from our archive were re-stained with cytokeratin 8/18 marker and were re-evaluated by a single expert hepatopathologist according to Brunt's classification, the NASH Clinical Research Network (NASH-CRN) scoring system, and fatty liver inhibition of progression (FLIP) algorithm.

Results: The presence of pathological granular staining with cytokeratin 8/18 marker in hepatocytes positively correlated with ballooning degeneration (r=0.461, p=0.027), the grade of lobular inflammation according to the FLIP algorithm (r=0.461, p=0.027), the grade of lobular inflammation according to the NAFLD activity score (r=0.545, p=0.007), presence of portal inflammation (r=0.525, p=0.010), age (r=0.534, p=0.009), gender (r=0.464, p=0.026), serum glucose value (r=0.537, p=0.008), direct bilirubin (r=0.523, p=0.022) and HbA1c (r=0.758, p=0.029) levels, and negatively correlated with hemoglobin (r=-0.473, p=0.030) and hematocrit (r=-0.437, p=0.047) levels.

	Lean (n:15)	Non-Lean (n:15)	p value
Age (Years, mean±SD)	38.27±13.6	50.73±12.8	0.016
BMI (kg.m ⁻² , mean±SD)	23.4±1.8	34.7±4.9	0.001
Presence of hepatic steatosis (%)	24.1	33.6	0.217
Hepatic cytokeratin 8/18 staining positivity (%)	75.0	93.3	0.427
Hepatic pathological granular cytokeratin 8/18 staining positivity (%)	33.3	35.7	0.926
Presence of ballooning degeneration (%)	66.7	100.0	0.028
AST (U/L, mean±SD)	52.5±45.9	39.8±22.4	0.482
ALT (U/L, mean±SD)	101.0±118.4	47.6±32.4	0.031
Triglycerides (mg/dL, mean±SD)	131.7±129.9	171.9±56.2	0.003*

BMI: Body mass index, AST: Aspartate aminotransferase, ALT: Alanine aminotransferase

Table: Characteristics of the patient groups.

There was no significant difference in the presence or staining pattern of cytokeratin 8/18 marker between the two groups. In the lean NAFLD group, liver damage was milder, serum triglyceride levels were lower ($p=0.003$) and ALT values were higher ($p=0.031$) compared to the non-lean group.

Conclusion: Although the presence of cytokeratin 8/18 immune marker staining has no role in the differential diagnosis of lean and non-lean NAFLD, the presence of granular staining may be an indicator of progression.

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P0685

THE INFLUENCE OF SUPERIMPOSED SEVERE ACUTE RESPIRATORY SYNDROME CORONAVIRUS-2 (SARS-COV-2) LIFESTYLE CHANGES ON METABOLIC DYSFUNCTION ASSOCIATED FATTY LIVER DISEASE (MAFLD) EVOLUTION: A MATTER OF BODY COMPOSITION

M. Romeo¹, M. Dallio¹, M. Cipullo¹, S. Olivieri¹, G. Iadanza¹, M. Sangineto², L. Ventriglia¹, F. Scognamiglio¹, G. Serviddio², A. Federico¹

¹University of Campania "Luigi Vanvitelli", Department of Precision Medicine, Hepatogastroenterology Division, Naples, Italy,

²University of Foggia, University Center for Liver Disease Research and Treatment (CURE), Liver Unit, Bari, Italy

Contact E-Mail Address: marioromeo@virgilio.it

Introduction: In the last decades, the Metabolic-(dysfunction)-Associated-Fatty-Liver-Disease (MAFLD) has rapidly become the most common cause of chronic liver damage and hepatocellular carcinoma (HCC) worldwide. An unhealthy lifestyle has been identified as a key element fueling its genesis and worsening.

Given the scant evidence existing, we aimed to evaluate the effects of related-confinement lifestyle changes experienced during the Severe Acute Respiratory Syndrome Coronavirus-2 (SARS-CoV-2) pandemic on MAFLD evolution.

Aims & Methods: A cohort of 122 MAFLD patients, including individuals with simple steatosis (SS), histological steatohepatitis (NASH), and liver cirrhosis (LC), was enrolled and followed during the last four years: two

years pre- and two years during the pandemic. For each patient, biochemical, fibrosis non-invasive, nutritional, and body composition data were collected, before and during the pandemic.

Results: The cohort (SS:28, NASH:45, LC:49) showed a relevant worsening in the insulin levels, liver-stiffness, controlled-attenuation-parameter (CAP), and NAFLD-fibrosis-score (NFS) during the pandemic period (Pre vs during, insulin levels: 22.01 ± 11.44 vs 24.39 ± 12.64 U/ml, $p:0.0003$; stiffness: 9.965 ± 4.816 vs 11.77 ± 5.837 kPa, $p<0.0001$; CAP: 290.9 ± 32.89 vs 335.9 ± 39.49 dB/m, $p<0.0001$; NFS: -0.75 ± 0.97 vs -0.2312 ± 1.05 , $p<0.0001$). A significant increase in daily calorie intake and a specular decrease in physical activity was also observed (Pre vs during, daily calorie intake: 2307 ± 411.5 vs 3056 ± 521.3 Kcal, $p<0.0001$; physical activity: 6.1 ± 1.3 vs 4.2 ± 1.4 hours/week, $p<0.0001$).

Body composition analysis highlighted a reduction of Free-Fat-Mass (FFM), Body-Cell-Mass (BCM), and an increase in Fat Mass (FM) (Pre vs during, FFM%: 79.6 ± 4.10 vs 73.31 ± 5.625 , $p<0.0001$ BCM%: 40.3 ± 3.1 vs 37.4 ± 3.4 , $p<0.0001$; FM%: 20.4 ± 4.1 vs 26.69 ± 5.6 , $p<0.0001$).

The Kaplan-Meier Log-Rank Test analysis on overall HCC occurrence and HCC Milan-out criteria occurrence revealed HR:2.29, 95% CI:1.1-4.6, $p:0.02$ and HR:7.7, 95% CI:2.6-22.7, $p:0.02$ respectively. The logistic regression for HCC occurrence revealed the event's independence from the stiffness threshold of 10 kPa (RR:5.06, 95% CI:7.14-3.16, $p:0.08$) and the significant impact of body composition modifications (Δ =pre-during) on the first [Δ FM (kg)= $p<0.0001$, RR 1.878, C.I. 95% 1.322-2.668; Δ FM (%) = $p<0.0001$, RR 1.704, C.I. 95% 1.248-2.327] and second [Δ FM (kg)= $p:0.007$, RR 1.478, C.I. 95% 1.111-1.967; Δ FM (%) = $p:0.006$, RR 1.469, C.I. 95% 1.114-1.937] outcome.

Variables	Pre-SARS-CoV-2 % (M±SD)	During SARS-CoV-2 % (M±SD)	p-value (Pre vs during)	Pre-SARS-CoV-2 Kg (M±SD)	During SARS-CoV-2 Kg (M±SD)	p-value (Pre vs during)
FM	20.40±4.104	26.69±5.625	<0.0001	16.23±3.726	23.12±5.900	<0.0001
FFM	79.60±4.104	73.31±5.625	<0.0001	63.37±8.139	63.51±10.04	0.9848
BCM	40.33±3.088	37.41±3.995	<0.0001	32.03±3.848	32.37±5.565	0.7994

FM: Fat mass; FFM: Free fat mass; BCM: Body cellular mass; M: mean; SD: standard deviation

Table 1. Body composition data before vs during SARS-CoV2-Pandemic.

Conclusion: The lifestyle changes imposed by the pandemic restrictions impacted MAFLD evolution promoting body compositions modifications negatively influencing the overall HCC and HCC Milan-out criteria occurrence.

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P0686

IMPACT OF RENAMING NAFLD TO MAFLD IN A SINGLE ITALIAN CENTER

V. Cossiga¹, M.R. Attanasio¹, M. Capasso¹, L. Pignata¹, F.M. Cutolo¹, R. Lieto¹, M. Guarino¹, F. Morisco¹

¹University of Naples Federico II, Department of Clinical Medicine and Surgery, Gastroenterology and Hepatology Unit, Napoli, Italy

Contact E-Mail Address: valentina.cossiga@gmail.com

Introduction: Metabolic Associated Fatty Liver Disease (MAFLD) is the novel definition and the new paradigm of NAFLD introduced in 2020, but its clinical and health public implications remain under evaluation.

Aims & Methods: The aims of this study are to analyze the prevalence of MAFLD and NAFLD and compare them in a well-defined cohort of patients with liver steatosis.

A cross-sectional study was conducted in a single Liver Unit in Italy. Clinical, laboratory and imaging data were collected. NAFLD and MAFLD were defined according to international expert consensus.

Results: A total of 404 patients with ultrasound steatosis were included. The mean age was 61.6±13.4 years (61.8% male). The mean body mass index (BMI) was 29.2±5.2 kg/m². Most of them (84.1%) were overweight/obese, 216 (53.4%) had arterial hypertension, 86 (21.2%) had type 2 diabetes and 178 (44%) had dyslipidemia. MAFLD was present in 340 (84.1%) patients, while NAFLD in 138 (34.1%) of them. The increased prevalence of MAFLD in this cohort was driven by dual etiology of liver disease (29.1% of previous HCV infection; 30.2% of virologically suppressed HBV patients). All participants classified as NAFLD met the new definition of MAFLD. Compared with NAFLD subjects, MAFLD patients had higher ALT (p=0.01), AST (p=0.009), GGT (0.0038) and FIB-4 (p=0.02) values.

No significant differences in the others non-invasive markers of fibrosis or steatosis (liver stiffness, NAFLD score, Controlled Attenuation Parameter) were observed.

Conclusion: Metabolic-associated fatty liver disease is a highly prevalent condition in this well-defined cohort. Application of these new criteria for MAFLD definition will increase the prevalence of fatty liver due to the inclusion of patients with dual etiology of liver disease.

Disclosure: Nothing to disclose.

P0687

WILSON'S DISEASE DIAGNOSIS IN PAEDIATRIC AGE

D. Araújo¹, H. Antunes^{1,2,3}

¹Hospital de Braga, Paediatric Gastroenterology Hepatology and Nutrition Unit, Braga, Portugal, ²Hospital de Braga, Academic Clinical Centre (2CA Braga), Braga, Portugal, ³Universidade do Minho, Life Sciences and Health Institute (ICVS), ICVS/3B's Associated Laboratory and School of Medicine, Braga, Portugal

Contact E-Mail Address: da.nielamatos@hotmail.com

Introduction: Wilson's Disease (WD) is a rare autosomal recessive disease. The prevalence of DW in Minho's region in Portugal is 1:37 000. In children, presentation is usually of hepatic involvement.

Aims & Methods: Our aim is to characterize the patients diagnosed with WD in a Paediatric Gastroenterology, Hepatology and Nutrition Unit of a central hospital in Portugal.

Methods: A descriptive retrospective observational study of the patients diagnosed with WD in this Unit between 1996 and 2021 was performed. Data related to the diagnosis and treatment were analysed.

Results: Twelve patients were diagnosed with WD, the majority being male (n=8). Median age at diagnosis was 8 years (IQR 5-13,8 years; minimum 3 and maximum 17 years). Four patients were diagnosed before the age of 5. The majority of patients (n=11) was referred to the Unit for

hepatic enzymes' elevation; one had neurological symptoms and Kaiser-Fletcher rings. At the time of diagnosis, renal involvement was present in one patient.

All patients had high urinary copper levels. Mutations in the ATP7B gene were found in all patients. One patient had normal levels of ceruloplasmin levels. The median time between the first observation and hepatic biopsy was 7 days (IQR 3-17 days; minimum 2 and maximum 82 days).

At the time of diagnosis, all patients initiated penicillamine and pyridoxine. During follow-up, therapy was changed to trientine and zinc sulfate in 4 patients, the majority for adverse events.

Clinical evolution was favourable in 10 of the patients.

Conclusion: We present 12 cases of WD diagnosed in children by the same paediatric gastroenterologist.

Four out of 12 patients presented symptoms before the age of 5 years, reinforcing the need to consider WD in children aged over 12 months with suggestive symptoms and/or analytic abnormalities.

As expected, hepatic involvement was the predominant form of presentation. As WD is a treatable cause of elevated liver enzymes, it is important to consider this diagnosis in the presence of elevated liver enzymes. In the presence of high clinical suspicion, normal levels of ceruloplasmin should not preclude considering WD in the differential diagnosis.

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P0688

RESISTANT STARCH SUPPRESSES HIGH-FAT DIET-INDUCED STEATOSIS

R. Yoshida¹, Y. Yano¹, N. Hoshi¹, N. Asaji¹, A. Yamamoto¹, E. Yasutomi¹, A. Minami¹, Y. Ueda¹, Y. Kodama¹

¹Kobe University, Kobe, Japan

Contact E-Mail Address: acoustic3220@yahoo.co.jp

Introduction: Obesity and related diseases, such as type 2 diabetes and hypertension, have been common problems worldwide. And non-alcoholic fatty liver disease (NAFLD) is the liver's expression of an obesity-related disease.

It has been reported that the gut microbiota in patients with obesity and NAFLD is altered from that of healthy individuals, and the changes in the gut microbiota can cause various obesity-related diseases and make steatosis worse.

Resistant starch (RS) is a type of starch that is not easily digested or absorbed in the small intestine. RS is a starch, but like dietary fiber, it is decomposed by the gut microflora into short chain fatty acids (SCFA). Many studies have reported inhibitory effect of RS on obesity and steatosis, but most of studies evaluating the effects of RS on suppressing fatty liver are using type 2 resistant starch (RS2). Therefore, in this study, we examined the inhibitory effects of type 4 resistant starch (RS4) on fatty liver using a murine high-fat-diet (HFD) induced fatty liver model.

Aims & Methods: We evaluated the effect of RS4 on fatty liver inhibition using HFD-fed mice. The changes in gut microbiota and SCFA after feeding RS were also investigated.

We prepared HFD, HFD+RS (high-fat-diet with resistant starch), and control diets. Seven-week-old male B6 mice were divided into three groups, and each group was fed HFD, HFD+RS, and control. Body weight changes were monitored weekly until 22 weeks of age. We also measured body weight, white adipose tissue weight, and liver weight, and collected plasma, liver tissue, and cecal feces for analysis.

Results: The HFD group showed marked weight gain, while the HFD+RS group showed less weight gain than the HFD group. In addition, body weight, liver weight, and white fat cell weight were all suppressed in the HFD+RS group compared to the HFD group. Furthermore, fatty liver, which was observed in the HFD group, was not observed in the HFD+RS and Control groups.

When we evaluated the liver tissue, there was no difference in the expression of fatty acid synthesis-related genes and fat accumulation-related genes between the HFD and HFD+RS groups.

Interestingly, *Bifidobacterium* and *Lactobacillus* in the feces were significantly increased in the HFD+RS group compared to the HFD group. In addition, the SCFA, acetic acid and propionic acid, were significantly increased in the HFD+RS group compared to the HFD group.

Conclusion: Our data suggests that dietary RS4 improved the gut environment in terms of the components of gut microbiota and levels of SCFA; which might have played a role to prevent weight gain and development of fatty liver in our setting. In general, SCFA receptors, such as GPR41 and GPR43, are involved for SCFA to function in the host, further studies using SCFA receptor deficient animals will be required to confirm the mechanisms.

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P0689

FEATURES OF ERYTHROCYTE AND SERUM MEMBRANE FATTY ACID SPECTRA ASSOCIATED WITH ALCOHOLIC AND NON-ALCOHOLIC GENESIS OF FATTY LIVER DISEASE

M.V. Kruchinina^{1,2}, M.V. Parulikova¹, A.A. Gromov¹, N.E. Ponomareva¹, M.V. Shashkov³, A.S. Sokolova⁴

¹Research Institute of Internal and Preventive Medicine - Branch of the Institute of Cytology and Gen, Siberian Branch of the Russian Academy of Sciences, Novosibirsk, Russian Federation, ²Novosibirsk State Medical University, Novosibirsk, Russian Federation, ³Boreskov Institute of Catalysis, Siberian Branch of the Russian Academy of Sciences, Novosibirsk, Russian Federation, ⁴Vorozhtsov Institute of Organic Chemistry, Siberian Branch of the Russian Academy of Sciences, Novosibirsk, Russian Federation

Contact E-Mail Address: kruchmargo@yandex.ru

Introduction: Fatty liver disease (FLD) is a heterogeneous group of diseases, differing significantly in a set of etiopathogenetic factors, progression rate and prognosis [1].

An important criterion for distinguishing non-alcoholic fatty liver disease (NAFLD) from alcoholic fatty liver disease (AFLD) is that patients do not drink alcohol at hepatotoxic doses. Primary NAFLD is associated with metabolic syndrome (MS) in most patients [2].

In the pathogenesis of AFLD and NAFLD with metabolic syndrome, a coincidence of most of the metabolic pathways has been noted, which creates difficulties in diagnosis [3, 4].

Aims & Methods: The aim was to investigate the fatty acid composition of erythrocyte (Er) membranes and blood serum (BS) in patients with fatty liver disease of alcoholic and non-alcoholic genesis for possible use in differential diagnosis.

Materials and methods. 45 men (51,8±3,9 years old) with WBC (F0-1) of alcoholic (n=14), non-alcoholic (n=16), mixed genesis (alcohol + metabolic factors) (n=15) and 16 conditionally healthy subjects have been screened. The study of the composition of fatty acids (FAs) of Er and BS has been performed using a gas chromatography-mass spectrometry (GC/MS) system based on the Agilent 7000B Triple Quadrupole (USA).

Results: The serum and erythrocyte membranes of patients with FLD have been dominated by saturated FAs (p<0.02), especially C16:0 (p<0.02), C18:0 (p<0.01), saturated/unsaturated FAs ratio (p<0.02) with a significant decrease in unsaturated (p<0.02), especially C18:2 n6 (p<0.01) and polyunsaturated (p<0.05) compared to healthy subjects.

AFLD is associated with decreases in linolenic, arachidonic acid (p<0.01), omega-6/omega-3 polyunsaturated FAs (p<0.001) in erythrocytes, which is probably due to chronic exposure to a universal membranotropic factor - ethanol. With NAFLD, an increase of C20:0 has been detected (p<0.01) and a decrease in C20:3 n6 (p<0.02) associated with shifts in metabolic syndrome compared to healthy controls.

In the group with fatty liver disease of mixed genesis at the background of an increase in the level of saturated FAs (p<0.04), the contents of monounsaturated (p<0.03), especially C18:1 and unsaturated (p<0.04) have been reduced both in erythrocytes and in blood serum.

A panel consisting of serum fatty acids (C14:0, 15:0, 20:0, 20:4 n6, sum of monounsaturated fatty acids, sum of PUFAs, sum of omega-6 PUFAs) and a list of red cell membrane FAs (C18:0, 22:6 n3, saturated/unsaturated FAs, saturated/polyunsaturated FAs) it allowed to differentiate patients with AFLD from NAFLD with AUC 0.790, sensitivity 0.73, specificity 0.78.

Correlations of FAs' levels in erythrocyte membranes and blood serum with manifestations of metabolic syndrome in patients with NAFLD, alcohol consumption in patients with AFLD have been revealed. In patients with NAFLD, waist circumference correlated with the amount of PUFAs in erythrocyte membranes (r=-0.48, p<0.001), HOMA-IR index - with C22:6/C20:5 n6 (r=-0.44, p<0.001). Patients with AFLD have showed associations of frequency of alcohol consumption with C20:5 n3 in erythrocyte membranes (r=-0.42, p<0.01), weekly dose of ethanol consumed with erythrocyte membrane ethyl esters level (r=0.46, p=0.002) and GGT activity with C18:2 n6 level (r=-0.43, p=0.003).

Conclusion: Peculiarities of fatty acid composition of Er and BS membranes in fatty liver disease of alcoholic, non-alcoholic and mixed genesis seem to be promising for the purposes of differential diagnosis.

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P0690

PREVALENCE AND ASSOCIATED FACTORS OF METABOLIC-ASSOCIATED FATTY LIVER DISEASE IN OVERWEIGHT AND OBESE FINNISH CHILDREN AND ADOLESCENTS

H. Riekkilä¹, L. Äärelä², L. Kivelä³, S. Lahti¹, P. Hiltunen⁴, N. Vuorela⁵, H. Huhtala⁶, T. Lakka⁷, K. Kurppa⁸

¹Tampere University, Tampere Center for Child, Adolescent and Maternal Health Research, Tampere, Finland, ²Tampere University, Tampere Center for Child, Adolescent and Maternal Health Research, Celiac Disease Research Center, Tampere, Finland, ³Celiac Disease Research Center and Tampere Center for Child, Adolescent and Maternal Health Research, Children's Hospital and Pediatric Research Center, University of Helsinki and Helsinki University Hospital, Helsinki, Finland, ⁴Tampere University Hospital, Department of Pediatrics, Tampere University Hospital, Tampere, Finland, ⁵Tampere University, Tampere Center for Child, Adolescent and Maternal Health Research, Department of Pediatrics, Tampere University Hospital, Tampere, Finland, ⁶Tampere University, Faculty of Social Sciences, Tampere, Finland, ⁷University of Eastern Finland, Institute of Biomedicine, School of Medicine, University of Eastern Finland, Research Institute of Exercise Medicine, and Department of Clinical Physiology and Nuclear Medicine, Kuopio University Hospital, Kuopio, Finland, ⁸Tampere University Hospital, Tampere Center for Child, Adolescent and Maternal Health Research, Tampere University, Celiac Disease Research Center, Tampere University, Department of Pediatrics, Tampere University Hospital, The University Consortium of Seinäjoki, Tampere, Finland

Contact E-Mail Address: hanna.riekki@tuni.fi

Introduction: Due to invasive diagnostics used, the prevalence of pediatric fatty liver disease is scarcely studied. A recently introduced concept of metabolic-associated fatty liver disease (MAFLD) enables to establish the diagnosis in children with excess adiposity and alanine aminotransferase (ALT) twice the upper limit of normal.

Aims & Methods: We investigated the prevalence, risk factors and metabolic co-morbidities of MAFLD in overweight and obese Finnish children and adolescents. Comprehensive medical data of 703 consecutive children and adolescents aged 2-16 years examined due to overweight in primary and tertiary healthcare in 2002-2020 was collected. Patients with and without MAFLD were compared, and subgroup analyses were conducted among boys and girls.

Results: The median age of the participants was 11.5 years, and 43% were girls. All were overweight, 89% obese and 47% severely obese, and the median body mass index (BMI) Z-score was 2.5. The prevalence of MAFLD was 15% (boys 18%, girls 11%, $p=0.018$). The prevalence increased in boys by age and during puberty, whereas in girls it peaked at early puberty. There was no significant change in the prevalence during the study period. Risk factors for MAFLD in boys were type 2 diabetes (T2D) (OR 7.55, 95% CI 1.23-46.2), a postpubertal stage (5.39, 2.26-12.8), hyperinsulinemia (3.20, 1.44-7.10), hypertriglyceridemia (2.97, 1.67-5.30), hyperglycemia (2.88, 1.64-5.07), low high-density lipoprotein cholesterol (HDL) (2.16, 1.18-3.99) and higher BMI (1.01, 1.05-1.15), and in girls T2D (18.1, 3.16-103), hypertriglyceridemia (4.28, 1.99-9.21), low HDL (4.06, 1.87-8.79). Overall, dyslipidemia were present in 51%, hypertension in 48%, signs of abnormal glucose metabolism in 44% and T2D in 2%.

Conclusion: The prevalence of MAFLD in overweight and obese children and adolescents was 15%, with no significant increase in the 2000s. The condition was associated with male sex, higher age in boys, puberty stage and disturbances in glucose and lipid metabolism.

Disclosure: No Conflict of Interest.

P0691

RARE DISEASES MIMICKING BILIARY ATRESIA: GENETIC ANALYSIS IS THE KEY

P.R. Tripathi¹, S. Oruganty^{2,2}, V.V. Ramaswamy²

¹Ankura Hospital for Women and Children, Pediatric Gastroenterology, Hyderabad, India, ²Ankura Hospital for Women and Children, Neonatology, Hyderabad, India

Contact E-Mail Address: parijattripathi1986@gmail.com

Introduction: A timely confirmative diagnosis of Neonatal cholestasis (NC) is vital for its management as well as prognostication. We are presenting a series of four infants with NC with classical symptoms and histo-biochemical features of extrahepatic biliary atresia (EHBA), but with few atypical signs.

Aims & Methods: Clinical, biochemical-histological and genetic data were prospectively collected.

Results: Two infants had a diagnosis of Niemann-Pick type C (NPC, C1 and C2) and the other two mitochondrial DNA depletion syndrome type-3 (MDDS-3) with clinical exome sequencing. While all four had jaundice with high colored urine in early infancy, three had pale stools and all of them were clinically suspected to have EHBA. NPC infants had splenohepatomegaly, an uncommon finding in EHBA. Of the MDDS-3 infants, one had failure to thrive (FTT) alone and the other had horizontal nystagmus along with FTT, both of which are uncommon with EHBA. Liver biopsy indicated EHBA features and GGT levels were high in all infants. (Table 1)

In view of these atypical clinical features, an earlier genetic test was done. While three infants died with progressive liver disease and coagulopathy, one with NPC2 survived with normalization of liver functions and neurological parameters till last follow-up.

Clinical presentation	Case 1: Conjugated hyperbilirubinemia with splenohepatomegaly since day 10 of life	Case 2: Conjugated hyperbilirubinemia with pale stool, splenohepatomegaly since day 30 of life	Case 3: Conjugated hyperbilirubinemia with pale stool since birth, failure to thrive, horizontal nystagmus hepatomegaly	Case 4: Conjugated hyperbilirubinemia since day 45 with pale stool, failure to thrive, ascites and hepatomegaly
Age at 1 st presentation	63 days	70 days	5 months	3 months
consanguinity	No	Yes (3rd degree consanguinity)	No	No
TB/DB (mg/dl)	17/12	11.9/9.7	8.7/6.2	16.8/14.3
AST/ALT (0-35 IU/L)	551/107	221/50	307/139	388/208
ALP (150-300 IU/L)/ GGT(0-30IU/L)	718/198	662/293	252/86	720/247
INR	1.2	1.02	1.35	2.9 (increased to 6.2)
Other test	S.GALT-normal,, AFP-168900IU/ml, HIDA -Excretory	S.GALT-Normal,, AFP-36,300 IU/ml, HIDA-Excretory	HIDA-Excretory	AFP >1000 IU/mL, HIDA -Excretory
Liver biopsy	Mild bile ductular proliferation with focal bridging fibrosis with early nodule formation	Mild bile ductular proliferation, periportal inflammation and mild portal fibrosis with extensive hepatocyte ballooning.	Bile ductular proliferation with with fibrosis with gaint cells and nodule formation	Not done (due to ascites and coagulopathy)
Genetic diagnosis And follow-up	NPC type C1 (NPC1 gene mutation) Died at 7 months of age with sepsis and GI/pulmonary bleed	NPC type C2(NPC2 gene mutation) Jaundice resolved over 8 month age, after that lost to follow-up	Hepatocerebral type of MDDS-3(DGUOK gene mutation) Died with bleeding manifestation at 10 month age (pulmonary)	MDDS-3(DGUOK gene mutation) Died at 4 month of age with bleeding manifestation (Pulmonary)

Table 1: Characteristics of the included infants.

Conclusion: Genetic analysis should be performed early in cases of NC with a suspicion of EHBA where atypical clinical features are present. Even if the prognosis in most of the aforementioned cases is poor, a confirmed genetic diagnosis could prevent futile surgical exploration and liver transplantation as well as future recurrence with genetic counselling and antenatal surveillance.

Disclosure: Nothing to disclose.

P0692

THE ROLE AND MECHANISM OF S100A6 IN PROMOTING NON-ALCOHOLIC FATTY LIVER DISEASE BY NEGATIVELY REGULATING LIPOPHAGY SIGNALING PATHWAY

Q. Du¹, J. Xu², R. Xie², B. Tuo², X. Ma³

¹Shanghai Jiao Tong University School of Medicine Affiliated Renji Hospital, Shanghai, China, ²Affiliated Hospital of Zunyi Medical University, Department of Gastroenterology, Zunyi, China, ³Shanghai Jiao Tong University School of Medicine Affiliated Renji Hospital, Division of Gastroenterology and Hepatology, Shanghai, China

Contact E-Mail Address: duqianL5@163.com

Introduction: Non-alcoholic fatty liver disease (NAFLD) has become a major chronic metabolic disease that seriously threatens human health, but the exact pathogenesis of NAFLD has not been fully clarified. We previously screened that the expression of S100A6 was up-regulated in NAFLD through animal models, cell models and transcriptomics, but its role in NAFLD was unclear.

Therefore, this study will explore the mechanism of S100A6 in the development of NAFLD from the clinical, animal and cellular levels, so as to provide new ideas and strategies for the diagnosis and treatment of NAFLD.

Aims & Methods: Overexpression/knockdown of S100A6 cell models constructed by lentivirus, overexpression/knockout of S100A6 mice models by adeno-associated virus (AAV), RFP-GFP-LC3 adenovirus, BODIPY 493/503 staining, autophagy activator and inhibition, HE, immunohistochemistry, Western Blot, qPCR and other methods gradually confirmed the regulation of S100A6 on lipid metabolism, autophagy pathway, lipid droplets, and lipophagy pathway in hepatocytes, and finally confirmed that S100A6 promotes hepatic lipid metabolism disorder by inducing lipophagy injury in hepatocytes.

Results: 1. The GEO database analysis showed that S100A6 was highly expressed in each NAFLD model. Consistent with the GEO data, the S100A6 expression was significantly increased in the two NAFLD models we established, high-fat high-cholesterol (HFHC) and high-fat-diet (HFD) induced. On the other hand, the expression of S100A6 showed a concentration-dependent up-regulation in Liver-02 cells and HepLi5 cells after stimulation with different concentrations of palmitic acid (PA)/Oleic acid (OA). These results suggest that S100A6 is highly expressed in NAFLD, which may act as a novel key factor promoting lipid metabolism disorders.

2. In the NAFLD cell models, compared with normal Liver-02/HepLi5 hepatocytes, overexpression of S100A6 aggravated the accumulation of PA/OA-stimulated intracellular lipids and induced lipid metabolism-related gene expression. After knockdown of S100A6, the lipid accumulation induced by PA/OA stimulation was alleviated, and lipid metabolism-related genes expression was reversed. The above results suggest that S100A6 may promote lipid accumulation in hepatocytes in vitro by regulating the expression of lipid metabolism-related genes.

3. In the NAFLD animal models, the tail vein injection of adenovirus-associated virus was used to overexpress/knock down the hepatic S100A6 expression in vivo, and it was found that overexpression of S100A6 could significantly increase the fat accumulation, glucose tolerance and insulin

resistance induced by HFHC. Knockdown of hepatic S100A6 expression can significantly reverse this process, reduce liver weight and serum triglyceride and low-density lipoprotein levels.

4. In the mechanistic study, we found that PA/OA stimulation significantly decreased the expression of LC3II and up-regulated the expression of P62, and inhibited autophagic flux in S100A6-overexpressing cells. Autophagy-related genes ATG5, ATG7, and ATG12 mRNA and ATG2, which is involved in lipid transport to promote autophagosome formation were significantly downregulated than those in the PA/OA-stimulated control group. At the same time, CD36 mRNA was also up-regulated and PPARα mRNA was down-regulated. All of which were reversed by knockdown of S100A6.

Conclusion: S100A6 may be a key target to promote the development of NAFLD. HFHC-induced S100A6 to negatively regulate the process of lipophagy, resulting in autophagy damage, which leads to lipid accumulation in the liver and ultimately promotes the development of NAFLD.

Disclosure: The authors declare that they have no conflict of interest.

P0693

SHORT-CHAIN FATTY ACIDS AND INSULIN RESISTANCE PROGRESSION IN OBESE CHILDREN WITH NONALCOHOLIC FATTY LIVER DISEASE

N. Zavhorodnia¹, O. Tatarchuk², I. Klenina², O. Hrabovska²

¹SI "Institute Gastroenterology of NAMS of Ukraine", Pediatric Gastroenterology Department, Dnipro, Ukraine, ²SI "Institute Gastroenterology of NAMS of Ukraine", Research Department, Dnipro, Ukraine

Contact E-Mail Address: nzavgorodni75@gmail.com

Introduction: Intestinal microbiota alteration, microbial diversity reduction, and intestinal permeability impairment which promote inflammation and insulin resistance are the cutting edges of the non-alcoholic fatty liver (NAFLD) pathophysiology.

Aims & Methods: The aim of our study was to investigate insulin resistance markers and their association with fecal short-chain fatty acids (SCFA) content in obese children with NAFLD.

104 obese NAFLD children aged from 10 to 17 years (average age was 12.15±2.51 years) were included in the study. The presence of NAFLD was determined by transient elastometry (Fibroscan®502touch, Echosence, France) with controlled attenuation parameter measurement.

Patients were divided into 3 groups according to the Homeostasis Model Assessment of Insulin Resistance (HOMA-IR) level: the I group included 23 children with the normal HOMA-IR level (up to 75 percentile according to age and sex), II group included 46 children with a moderate increase (HOMA-IR up to 6.0) and III group included 35 children with a significant increase (HOMA-IR greater than 6.0). The control group consisted of 10 children with normal weight, and normal HOMA-IR levels without liver steatosis.

Serum insulin levels were determined by enzyme immunoassay (DRG International, Inc., Germany). Assessment of insulin resistance was carried out with HOMA-IR calculation. Glycosylated hemoglobin was determined by a Lachema kit (Czech Republic). Chromatography of fecal SCFA was performed by gas chromatograph Chromatec-Crystal 5000.

Results: Children of the III group had significantly higher liver stiffness (6.6±0.9 kPa, p<0.05) compared to other groups. An increase in the HOMA-IR level in children of the studied groups was accompanied by an increase in the glycosylated hemoglobin level.

The highest content of glycosylated hemoglobin reached 4.09 (3.32; 4.91) μM fructose/gHb was observed in the III group of children. The median level of fecal acetic acid was increased in the I, II, and III groups, while the median level of fecal butyric acid was decreased. Children of the III group

had a 2-fold lower propionic acid level ($p < 0.05$), and a 1.5-fold lower total SCFA level ($p < 0.05$) compared to patients of the II group. A negative correlation was found between fecal butyric acid content, insulin levels ($r = -0.228$; $p = 0.02$), and the HOMA-IR ($r = -0.229$; $p = 0.019$), positive correlation between HOMA-IR and liver stiffness ($r = 0.37$, $p < 0.05$).

Conclusion: Progression of insulin resistance in obese NAFLD children is accompanied by an increase in glycosylated hemoglobin level, an increase in fecal acetic acid content, and a significant decrease in total SCFA content due to propionic and butyric acids reduction, which may contribute to NAFLD progression in obese children.

Disclosure: Nothing to disclose.

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INSULIN RESISTANCE IN THE LIVER FIBROSIS FORMATION IN OBESE CHILDREN WITH NON-ALCOHOLIC FATTY LIVER DISEASE

N. Zavhorodnia¹, O. Tatarchuk², I. Klenina², O. Petishko²

¹SI "Institute Gastroenterology of NAMS of Ukraine", Pediatric Gastroenterology Department, Dnipro, Ukraine, ²SI "Institute Gastroenterology of NAMS of Ukraine", Research Department, Dnipro, Ukraine

Contact E-Mail Address: nzavgorodni75@gmail.com

Introduction: The global epidemic of nonalcoholic fatty liver disease (NAFLD) occurs in parallel with other dysmetabolic diseases such as obesity and type 2 diabetes, which is reflected in the introduction of a new term «diabesity». Insulin resistance markers are promising markers for noninvasive assessment of hepatocyte damage and metabolic risk in NAFLD children so can be used to select pediatric patients at risk of disease progression.

Aims & Methods: The aim of our study was to investigate the association of insulin resistance markers with liver fibrosis in obese children with NAFLD. 40 obese children with NAFLD aged from 10 to 17 years (average age was 12.15 ± 2.51 years) were examined. Obesity was established by body mass index (BMI) calculation and comparison with the sigma deviations of BMI values according to age and sex. The presence of liver fibrosis and steatosis was established by transient elastography (Fibroscan[®]502touch, France). Children were divided into 4 groups according to transient elastography and BMI: I group - 13 children with NAFLD and liver fibrosis, II group - 13 children with NAFLD without fibrosis, and group III - 14 obese children without NAFLD and fibrosis. The control group consisted of 10 children with normal weight without NAFLD and fibrosis.

Serum insulin levels were determined by enzyme immunoassay (DRG International, Inc., Germany). Assessment of insulin resistance was carried out with a homeostasis model with the calculation of the HOMA-IR.

Results: A significant increase in median insulin level (3.1 times, $p < 0.05$) and HOMA-IR level (3.3 times, $p < 0.05$) in children of the I group was observed compared to the control group.

Moreover, the median insulin and HOMA-IR levels in children of the I group also differed significantly from children of the II group (1.5 times, $p < 0.05$ and 1.6 times, $p < 0.05$, respectively) as well as from children of the III group (2.0 times, $p < 0.05$ and 2.4 times, $p < 0.05$, respectively).

Children of the II group had 2.1 times higher median insulin and HOMA-IR levels ($p < 0.05$), and children of the III group had 1.5 times ($p < 0.05$) and 1.4 times ($p < 0.05$), respectively, higher levels compared to the control group. It was found a positive correlation between HOMA-IR and the liver fibrosis degree ($r = 0.373$; $p = 0.019$).

Conclusion: The development of liver fibrosis in NAFLD children is accompanied by a significant increase in insulin and HOMA-IR levels, indicating insulin resistance progression in these patients.

Disclosure: Nothing to disclose.

P0695

HEART RATE VARIABILITY IN CHILDREN WITH NON-ALCOHOLIC FATTY LIVER DISEASE DEPENDING ON INTESTINAL MICROBIOTA COMPOSITION

N. Zavhorodnia¹, E. Zygalo², N. Zhigir¹, O. Petishko³

¹SI "Institute Gastroenterology of NAMS of Ukraine", Pediatric Gastroenterology Department, Dnipro, Ukraine, ²SI "Institute Gastroenterology of NAMS of Ukraine", Mini-Invasive Endoscopic Interventions and Instrumental Diagnostics Department, Dnipro, Ukraine, ³SI "Institute Gastroenterology of NAMS of Ukraine", Research Department, Dnipro, Ukraine

Contact E-Mail Address: nzavgorodni75@gmail.com

Introduction: Heart rate variability (HRV) provides information about the adaptive potential of the patients and has an important prognostic and diagnostic value in non-alcoholic fatty liver disease (NAFLD).

Aims & Methods: The aim of our study was to investigate HRV in NAFLD children depending on the presence of small intestine bacterial overgrowth (SIBO).

64 obese patients with NAFLD aged from 10 to 17 years (average age was 12.15 ± 2.51 years) were included in the study. Obesity was established by body mass index (BMI) calculation and comparison with the sigma deviations of BMI values according to age and sex. The presence of liver steatosis was evaluated by transient elastography (Fibroscan[®]502touch, France). The presence of SIBO was determined with the hydrogen breath test (HBT) with glucose loading using a Gastrolyzer from Bedfont Scientific Ltd (UK). HRV assessment was performed based on the cloud technology of automated interpretation on the AMAZON web service with calculation ratio of low-frequency to high-frequency bands (HF/LF), root mean square of successive RR interval differences (RMSSD).

Children were divided into 3 groups according to transient elastography, HBT, and BMI data: 1 group - 28 NAFLD children with SIBO, 2 group - 36 NAFLD children without SIBO, 3 group (control) - 10 normal-weight children without NAFLD and SIBO.

Results: In 42.9% of NAFLD children with SIBO 2.5-fold increase ($p < 0.05$) in LF / HF ratio was found compared to the NAFLD patients without SIBO which reflects an increase in sympathetic nervous system influences. Moreover, in 60.7% of NAFLD patients with SIBO a decrease of RMSSD 4.59 times ($p < 0.05$) compared to the control group was observed while in NAFLD patients without SIBO only 38.9% of patients demonstrated a decrease of RMSSD in 1.5 times ($p < 0.05$).

Also, positive correlation between presence of SIBO and LF/HF ratio ($r = + 0.492$, $p < 0.05$) as well as negative correlation with RMSSD ($r = -0.65$, $p < 0.05$) were found.

Conclusion: The presence of SIBO in NAFLD children is accompanied by adaptive mechanisms impairment and changes in autonomic balance towards sympathicotonia.

Disclosure: Nothing to disclose.

P0696

PREDICTIVE VALUE OF SERUM ADIPONECTIN AND CHERMERIN LEVELS IN PATIENTS WITH NON-ALCOHOLIC FATTY LIVER DISEASE

A.M. El-lehlah¹, O.L. El Abd², E.A. Badr³, E.F. El Mezein⁴,
M. Abdel-Samiee⁵, A.A.A. Teima¹

¹Menoufia University, Tropical medicine, Shebin El-Kom, Egypt,
²National Liver Institute, Menoufia University, Radiology, Shebeen El Kom, Egypt, ³Menoufia University, Shebeen El Kom, Egypt,
⁴Damanhour Fever Hospital, Beheira, Egypt, ⁵National Liver Institute-Menoufia University, Hepatology and Gastroenterology, Shebin El-Kom, Egypt

Contact E-Mail Address: drmohammed100@yahoo.com

Introduction: Nonalcoholic fatty liver disease (NAFLD) is the most common cause of chronic liver disorder, which is a major cause of illness and mortality. Liver biopsy remains the best tool for its diagnosis, but it is an invasive procedure. Adiponectin and chemerin can be noninvasive diagnostic tools.

Aims & Methods: We aimed to study the levels of serum adiponectin and chemerin in patients with NAFLD and their diagnostic role.

Methods: This prospective study was carried out from March 2020 to October 2021 on 90 subjects including 60 patients with NAFLD and 30 age and gender-matched healthy individuals as control group. History was taken from all subjects, complete medical examination, thorough laboratory and radiological data were collected. Serum adiponectin and chemerin were assessed by enzyme linked immunosorbent assay (ELISA) technique and liver stiffness (LS) was assessed by point shear wave elastography (pSWE).

Results: There was a high statistically significant elevation of serum chemerin values and pSWE measurements in NAFLD patients than control. High statistically significant decrease of serum adiponectin values in patients with NAFLD than control. At cutoff point more than 280 ng/ml, serum chemerin value can predict NAFLD with 97% sensitivity, 90% specificity, while, at cutoff point less than 9 ug/ml, adiponectin level can predict NAFLD at 95% sensitivity, 97% specificity and at cutoff point more than 6.10 kpa and pSWE can predict NAFLD at 80% sensitivity, 100% specificity.

Studied variables	Group Ia (N=20)	Group Ib (N=20)	Group Ic (N=20)	Group II (N=30)	Test of sig	P value
BMI(kg/m²)						
Mean±SD	32.8±2.90	39.4±2.84	44.2±2.88	23.0±1.52	F	0.001**
Range	27.5 - 37	34.5 - 45	38 - 49	20 - 26	335.1	
WC(cm)						
Mean±SD	102.6±4.03	108.1±4.85	112.6±4.66	81.1±4.27	F	0.001**
Range	95 - 109	100 - 118	103.5 - 120	72.5 - 90	257.2	
Total cholesterol (mg/dl) (125-200)						
Mean±SD	248.5±23.6	261.0±20.8	288.9±27.7	153.1±14.4	F	0.001**
Range	205 - 300	214 - 307	252 - 357	125 - 175	197.8	
HDL-C(mg/dl)						
Mean±SD	54.0±6.09	50.5±5.86	40.9±4.48	72.9±10.9	F	0.001**
Range	44 - 65	41 - 60	33 - 49	50 - 95	75.6	
LDL-C(mg/dl)						
Mean±SD	157.5±7.55	168.2±6.32	196.2±4.54	85.2±7.44	K	0.001**
Range	147 - 170	156 - 179	189 - 204	69 - 97	79.8	
TG(mg/dl)						
Mean±SD	186.1±19.8	212.1±33.3	253.7±36.9	106.1±17.4	K	0.001**
Range	150 - 220	160 - 265	165 - 322	83 - 135	71.0	

F: ANOVA test; K: Kruskal Wallis test**High significant; BMI; body mass index
WC; waist circumference; HDL-C; high density lipoprotein cholesterol
LDL-C; low density lipoprotein cholesterol; TG; triglycerides.

Table 1. Anthropometric measurements and lipid profile of the studied patients (N=90):

Conclusion: Serum chemerin, adiponectin and point shear wave elastography, can be used as non-invasive parameters for diagnosis of NAFLD.

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P0697

VALIDATION OF SEMI-AUTOMATIC SEGMENTATION METHOD TO DETERMINE TOTAL LIVER VOLUME ON CT SCANS IN POLYCYSTIC LIVER DISEASE

T. Barten¹, S.E. Aapkes², J.P.H. Drenth¹, R.T. Gansevoort²,
W. Coudyzer³, F. Nevens⁴, M.D.A. van Gastel²

¹Radboud University Medical Centre, Gastroenterology and Hepatology, Nijmegen, Netherlands, ²University Medical Center Groningen, Nephrology, Groningen, Netherlands, ³University Hospital Leuven, Radiology, Leuven, Belgium, ⁴KU Leuven, Division of hepatology, Clinical trials, Leuven, Belgium

Contact E-Mail Address: trmbarten@gmail.com

Introduction: Polycystic liver disease (PLD) is a rare heritable disease characterized by growth of hepatic cysts and can lead to hepatomegaly. It is diagnosed in the presence of > 10 hepatic cysts and can occur as an isolated disease (autosomal dominant polycystic liver disease, ADPLD) or in combination with renal cysts (autosomal dominant polycystic kidney disease, ADPKD). Disease severity is determined using total liver volume (TLV) which is measured from computed tomography (CT) or magnetic resonant imaging (MRI) scans.

The current gold standard, manual segmentation, is time-consuming, labor-intensive and requires expert knowledge of the anatomy. This warrants the need for novel fast and reliable TLV measurement tools.

Aims & Methods: This study aims to validate a semi-automatic liver segmentation technique for CT scans of patients with PLD. Adult PLD patients were recruited from two tertiary referral centers.

We used two CT scans from each included patient. Manual contouring was performed with software programs called Pinnacle and Analyze. Both measure liver volume by manually delineating liver contours on axial CT slices.

Manual contouring was compared with a semi-automatic segmentation technique (Volume), in which the liver is contoured on every 4th axial CT slice. The program interpolates between contours and removes non-cystic and non-liver tissue based on their Hounsfield unit density.

We assessed the correlation between the two techniques using intraclass correlation coefficients (ICC) and Bland-Altman analyses. We determined the performance of the semi-automatic segmentation technique cross-

sectionally and longitudinally. Bias was defined as the mean difference between manual and semi-automatic measurements; precision as the corresponding standard deviation.

Results: We included 60 patients in this study of which 85.0% (n=51) were female, the median age was 51.3 years (interquartile range (IQR) 44.7–59.2) and median TLV was 5293 ml (IQR 3141–7840 ml). The underlying diagnosis was ADPKD with PLD for 35 patients, ADPKD without PLD in 2 patients and ADPLD in 23 patients.

Manual segmentation lasted 73.2 (standard deviation SD 45.3) minutes per scan, whereas automatic segmentation lasted only 22.2 (SD 8.4) minutes (p=0.001). Cross-sectional analysis of the first CT scan showed that manual and semi-automatic measurements correlated highly with an ICC of 0.996, and a bias and precision of 1.9% and 3.4% respectively.

Comparable results were observed in sensitivity analyses consisting of 1) CT scans without contrast (n=28, bias 1.7%, precision 4.6%), 2) ADPKD patients with PLD (n=35, bias 1.2%, precision 2.4%), and 3) patients that underwent invasive treatment before the cross-sectional CT (n=18, bias 2.2 %, precision 4.6%).

The longitudinal analysis including data from 45 patients with two CTs obtained at least 1 year apart demonstrated that percentual liver growth can be accurately determined using the semi-automatic approach with a bias of 0.0% and precision of 4.8%. Results were robust across various subgroups defined by patient characteristics.

Conclusion: Semi-automatic liver segmentation is a fast and accurate method to determine TLV in PLD patients, and has sufficient accuracy and precision to be used in clinical care as well as trials to determine change in TLV.

Disclosure: Nothing to disclose.

P0698

IMPAIRED QUALITY OF LIFE MAY HINDER THE ACHIEVEMENT OF THERAPY GOALS IN PATIENTS WITH NONALCOHOLIC FATTY LIVER DISEASE

Y. Golubeva¹, A. Sheptulina¹, A. Yafarova¹, E. Mamutova¹, O. Drapkina¹

¹National Medical Research Center for Therapy and Preventive Medicine, Moscow, Russian Federation

Contact E-Mail Address: yu_golubeva@mail.ru

Introduction: Nonalcoholic fatty liver disease (NAFLD) is often considered to be clinically asymptomatic. However, a large number of NAFLD patients complain of fatigue and decreased mood, which may affect their quality of life (QoL). This, in turn, may become a barrier to weight loss and, therefore, hinder the achievement of NAFLD therapy goals.

Aims & Methods: Present study aimed to evaluate the QoL in patients with NAFLD vs. healthy volunteers and to determine possible influencing factors. In total, 95 outpatients with NAFLD and 37 healthy volunteers were recruited. Fatty liver was diagnosed based on ultrasonographic findings. 36-Item Short Form Survey (SF-36) was used to assess the QoL.

Anxiety and depression were evaluated by the Hospital Anxiety and Depression Scale (HADS), to measure fatigue, we used the Fatigue Assessment Score (FAS).

Results: Median age was 50 years (interquartile range (IQR)=43-58) in NAFLD patients and 45.5 (IQR=36-51) for healthy volunteers; the majority of patients in this study were women: 62.1% and 78.4% in NAFLD and control groups respectively; 60.6% of NAFLD patients and 2.6% of controls had body mass index >30 kg/m².

Physical component summary score was significantly lower in NAFLD patients compared to the healthy volunteers (Mann-Whitney U-criteria, p<0.001). Fatigue was more common in NAFLD patients (χ², p<0.045), and

there was a trend towards an increased prevalence in depression in NAFLD group (U-criteria, p<0.014), compared to controls. Impaired QoL was significantly associated with fatigue (FAS score ≥22, p<0.001) and depression (HADS-D ≥8, p<0.001).

Conclusion: Adults with NAFLD had a significantly poorer QoL compared to healthy volunteers, in particular with regard to the physical component of health. Impaired QoL seems to be associated with fatigue and depression, and together they may militate against the increased physical activity and lifestyle modifications in NAFLD patients.

Disclosure: Nothing to disclose.

P0699

METABOLIC ASSOCIATED FATTY LIVER DISEASE (MAFLD) AND COVID-19: AN INTERPLAY LEADING TO POOR PATIENT OUTCOME?

V. Milivojević¹, I. Babić², J. Bogdanović³, I. Ranković¹, A. Pavlovic Marković¹, M. Krstić¹, T. Milosavljević⁴

¹University Clinical Centre of Serbia, University of Belgrade, Clinic for Gastroenterology and Hepatology, Belgrade, Serbia, ²University Clinical Centre of Serbia, Clinic for Endocrinology, Diabetes and Metabolic Diseases, Belgrade, Serbia, ³University Clinical Centre of Serbia, University of Belgrade, Clinic for Endocrinology, Diabetes and Metabolic Diseases, Belgrade, Serbia, ⁴Euromedic, General Hospital, Gastroenterology, Belgrade, Serbia

Contact E-Mail Address: dotorevlada@gmail.com

Introduction: Metabolic associated fatty liver disease (MAFLD) is a novel term that represents a spectrum of chronic liver disease phenotypes with systemic metabolic dysfunction. The SARS-CoV2 virus has been proven to cause innate and adaptive immunity impairment leading to abrupt systemic metabolic alterations. The question arises as to what extent does the bidirectional MAFLD/COVID-19 relationship affect patient outcome.

Aims & Methods: Our aim was to assess the influence of MAFLD on COVID-19 severity and its outcome. A retrospective study was conducted, including 130 patients, divided into two groups, group A (MAFLD) and group B (non-MAFLD). MAFLD diagnosis was made using criteria set by an International Consensus Panel.

Detailed demographic, anthropometric, biochemical analysis, comorbidities, and vital parameters were recorded. COVID-19 severity and liver fibrosis were assessed using NEWS2 and FIB-4 score (respectively). COVID-19 outcome was regarded as discharged patients, mechanical ventilation (MV) need and non-survivors.

Results: MAFLD prevalence was 42%, mortality rate was 14%, 67% of patients were discharged, and 19% needed MV. MAFLD patients were significantly younger (53.5±4.5ys vs 62.3±4.2yr, p<0.001), had higher body mass index (BMI, 28.5 kg/m²±2.8 vs 24.8±3.1 kg/m², p<0.05), respiratory rate (RR, 19.2±1.9 vs 16.0±1.4, p<0.05) and higher systolic blood pressure (SBP, 142.5±10.1mmHg vs 130.4±7.9mmHg, p<0.05) than nonMAFLD patients. When it came to metabolic syndrome and inflammatory parameters: group A had significantly higher glycemia at admission (8.4±1.2mmol/l vs 7.1±2.6mmol/l, p=0.008), lower HDL-c (0.7±0.1mmol/l vs 1.0±0.4mmol/l, p<0.01), higher triglycerides (Tg, 3.4±0.9mmol/l vs 2.8±1.0mmol/l, p<0.01), higher CRP (29.5±11.0mg/l vs 21.2±7.9mg/l, p<0.001), IL-6 (56.5±5.1pg/ml vs 54.2±4.1pg/ml, p<0.05) and ferritin (331.2±31.0µg/l vs 256.2±28.5µg/l, p<0.05) than group B.

MAFLD was associated with more prevalent type 2 diabetes (p=0.035) and hypertension (p<0.05). NEWS2 score was significantly higher among MAFLD patients (6.5±0.5 vs 3±1.0, p<0.05). MAFLD presence was associated with lower patient discharge (p<0.01), increased need for MV (p=0.024) and presence of advanced liver fibrosis (p<0.05). Multiple regression analysis showed that BMI (OR 2.3 (95% CI) 1.7-3.1, p=0.045), IL-6 (OR 2.1 (95% CI)

1.2-2.0, $p=0.03$), and MAFLD (OR 3.4 (95% (CI) 3.0-6.3, $p<0.05$)) are independent risk factors for poor COVID-19 infection outcome. MAFLD patients are at increased risk for poor outcome (RR 2.1 95% (CI) 1.2-3.8, $p<0.001$) as compared to nonMAFLD patients.

Conclusion: Our results imply that MAFLD poses a risk for poor COVID-19 infection outcome. In that sense, it is important to put an emphasis on MAFLD as one of the modifiable risk factors for severe COVID-19 infection in order to ameliorate MAFLD-related inflammatory state that contributes to poor COVID-19 outcome.

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P0700

NOVEL MAFLD CLASSIFICATION: A MORE REALISTIC CONCEPT OF FATTY LIVER DISEASE

J. Serrazina¹, A. Craciun¹, R. Rios Crespo^{1,2}, S. Policarpo³, S. Carvalhana¹, H. Cortez-Pinto^{1,2}

¹Hospital de Santa Maria, Centro Hospitalar Universitário Lisboa Norte, Gastroenterology and Hepatology, Lisboa, Portugal,

²Faculdade de Medicina, Universidade de Lisboa, Clínica Universitária de Gastroenterologia, Lisboa, Portugal, ³Hospital de Santa Maria, Centro Hospitalar Universitário Lisboa Norte, Dietetics & Nutrition, Lisboa, Portugal

Contact E-Mail Address: julianaserrazina@gmail.com

Introduction: A terminology-change from nonalcoholic fatty liver disease (NAFLD) to metabolic associated fatty liver disease (MAFLD) has recently been proposed. MAFLD is a novel concept based on “positive criteria” that accurately reflects metabolic dysfunction, regardless of alcohol consumption or concomitant diseases. We aim to evaluate the importance of the novel MAFLD classification, by reclassifying our study cohort according to MAFLD and NAFLD definition.

Aims & Methods: This study was conducted at the outpatient Hepatology Clinic of a tertiary University hospital, where patients were followed due to fatty liver disease, by a multidisciplinary team.

Results: Amongst overall population ($n=157$), there were 92 males (58.6%), with a mean age of 54.2 $\pm$ 14.4 years at diagnosis. Mean body mass index (BMI) was 32.25 $\pm$ 6.49 Kg/m². 101 patients met diagnostic criteria for NAFLD (64.3%) while 154 (98.1%) fulfil MAFLD criteria. Only 3/157 were non-MAFLD patients. Analysing MAFLD-patients who were excluded from NAFLD definition ($n=56$), 51 (91.1%) had significant alcohol consumption (20 g/per day in women and 30 g in men), and 5/56 (8.9%) had another aetiology for liver disease. We further analyse non-NAFLD patients ($n=56$) according to metabolic risk factors and we did not find any significant difference in prevalence of arterial hypertension ($p=0.517$), dyslipidemia ($p=0.516$), diabetes mellitus ($p=0.741$) and overweight (BMI > 25 kg/m²) ($p=0.833$). From our total cohort, 17.3% had advanced fibrosis, from which 55.6% were non-NAFLD patients. The non-NAFLD group more frequently had advanced fibrosis ($F4 > 10.4$ kPa), (26.8 vs 12%, $p=0.019$). Evaluating the degree of hepatic steatosis with controlled attenuation parameter (CAP), no statistical difference between the groups was found ($p=0.989$).

Conclusion: Patients with fatty liver disease frequently fulfil MAFLD criteria, with is a substantial overlap between NAFLD and MAFLD. A significant proportion of MAFLD patients not fulfilling NAFLD criteria, had advanced fibrosis, thus emphasising the importance of MAFLD concept.

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P0701

PREDICTIVE SCORES IN PATIENTS WITH TYPE 2 DIABETES

R.G. Mare¹, R. Lupusoru¹, I. Sporea¹, A. Popescu¹, R. Sirli¹

¹Victor Babes University of Medicine and Pharmacy, Internal Medicine II, Division of Gastroenterology and Hepatology, Center for Advanced Research in Gastroenterology and Hepatology, Timisoara, Romania

Contact E-Mail Address: ruxi2323@yahoo.com

Introduction: The prevalence of non-alcoholic fatty liver disease (NAFLD) is increasing in patients with type 2 diabetes (T2D), as a result, a systematic screening in this population should be performed.

Aims & Methods: The aim of this study was to identify risk factors associated with moderate steatosis and advanced fibrosis and to develop a score that could be used in daily practice.

A prospective study on 534 patients with T2D was conducted using Vibration Controlled Transient Elastography (VCTE). We stratified our cohort into study cohort (348 patients) and validation cohort (186 patients). We aimed for 10 valid Controlled Attenuation Parameter (CAP) and liver stiffness measurements (LSM) with an IQR/Median $<30\%$. A cut-off value of 290 dB/m was used to define moderate steatosis (S2) while for advanced fibrosis ($F\geq 3$) a cut-off of 9.7 kPa [1]. For developing a score for stratifying the risk of moderate steatosis, and of advanced fibrosis, we used univariate and multivariate logistic regression analysis.

Results: Out of 534 patients, 62.7% had at least moderate steatosis and 19.2% had at least advanced fibrosis by VCTE. In univariate analysis, BMI ($p<0.0001$), waist circumference -WC ($p<0.0001$), elevated levels of ALT ($p=0.001$), total cholesterol ($p=0.03$), triglycerides ($p=0.01$), blood glucose ($p=0.004$) and presence of hypertension ($p=0.04$) were associated with at least moderate steatosis. The steatosis score is composed of: 0.5 points for high BMI (>32.1 kg/m²), cholesterol (> 235 mg/dl), triglycerides (> 165 mg/dl), glycemia (> 200 mg/dl), ALT (> 40 U/L) and WC (> 100 cm) and 1 point for the presence of hypertension. The maximum score can be 4 points. In univariate analysis, BMI ($p<0.0001$), WC ($p<0.0001$), elevated levels of AST ($p=0.001$), liver steatosis ($p=0.03$) were associated with at least advanced fibrosis. The fibrosis score is composed of: 0.5 points for high BMI (>32.4 kg/m²), AST (> 42 U/L), WC (> 110 cm) and for the presence of steatosis. The maximum score can be 2 points. The derived steatosis and fibrosis cut-offs for identifying patients with T2D were for steatosis $\geq S2$ (2 points) with an AUROC of 0.72 (42.4% Se, 96.7% Sp, 45.2% PPV, 90.9% NPV) and for fibrosis $\geq F3$ (1 point) with an AUROC of 0.68 (77.3% Se, 56.4% Sp, 37.8% PPV, 90.1% NPV). When we validate both scores, we obtained an accuracy of 83.9% for identifying at least moderate steatosis and 84.1% for advanced fibrosis.

Conclusion: Both steatosis and fibrosis score can be used in clinical setting for identifying patients with T2D at risk for developing at least moderate and advanced fibrosis.

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P0702

ESTIMATION OF THE PREVALENCE OF NON-ALCOHOLIC FATTY LIVER DISEASE DURING OBSTRUCTIVE SLEEP APNEA SYNDROME

A. Ben Mohamed¹, M. Yakoubi¹, A. Khsiba¹, M. Mahmoudi¹, M. Medhioub¹, M.L. Hamzaoui¹, M.M. Azzouz¹

¹Department of Gastroenterology, Mohame Taher Maamouri Hospital, Gastroenterology, Nabeul, Tunisia

Contact E-Mail Address: asmabenmed2014@gmail.com

Introduction: The non-alcoholic fatty liver disease (NAFLD) is emerging as an important public health problem across the globe due to the increase of the prevalence of obesity and metabolic syndrome. Recent data have shown a frequent association between this liver disease and obstructive sleep apnea syndrome (OSAS).

Aims & Methods: The aim of our study was to estimate the prevalence of non-alcoholic fatty liver disease in patients with confirmed OSAS with daily alcohol consumption <20 g / day in women and <30 g / day in men. **Methods:** This is a prospective, comparative study over a period of 6 months, through which we tried to compare the prevalence of NAFLD between two groups of patients: the first comprising patients with confirmed OSAS and followed up in the department of pneumology, the second was a control group of patients followed for irritable bowel syndrome (IBS) at the outpatient clinic. The two groups were comparable for age, sex and co-morbidities.

Results: We collected 60 patients followed for OSAS. The mean age was 55.25 ± 11.14 years [23-75]. The sex ratio (M / F) was 0.5. Obesity, defined by a body mass index (BMI) > 30 kg / m², was noted in 76.6% and overweight (25 < BMI < 30 kg / m²) was present in 26.6% of the population. The average waist circumference was 112.34 ± 14.61 cm [90-150] and the average neck circumference was 37.17 ± 5.58 cm [28-58]. Type 2 diabetes was present in 25% of cases and high blood pressure in 41.6% of cases. An abdominal ultrasound, performed in all patients, showed a steatotic liver in 51.66% of cases (31/60) whereas this prevalence was lower in the control group (8% (4/50) with a statistically significant difference (p < 0.001). In univariate analysis, waist circumference > 115 cm was associated with hepatic steatosis (p < 0.001) which is the same for type 2 diabetes (p = 0.003). In multivariate analysis, the only independent variable associated with hepatic steatosis was a waist circumference > 115 cm.

Conclusion: The prevalence of non-alcoholic fatty liver disease is higher in patients with obstructive sleep apnea syndrome. Screening for this pathology in these patients would help in managing them and monitoring of the liver complications.

Disclosure: Nothing to disclose.

P0703

EFFECTIVENESS OF THE FIBROSCAN-ASAT (FAST) SCORE IN IDENTIFYING NON-ALCOHOLIC STEATOHEPATITIS (NASH) PATIENTS WITH SIGNIFICANT ACTIVITY AND FIBROSIS: A PROSPECTIVE STUDY

K. Amalou¹, R. Rekab¹, F. Belghane¹

¹HCA, Gastroenterology, Algiers, Algeria

Contact E-Mail Address: amalou_kh@yahoo.fr

Introduction: The prevalence of non-alcoholic fatty liver disease (NAFLD) is increasing worldwide. A major priority is to identify patients with non-alcoholic steatohepatitis (NASH) who are at higher risk of progression to cirrhosis, and who will be candidates for clinical trials and new emerging drug therapies.

Aims & Methods: We sought to investigate the effectiveness of the FAST score in identifying patients with NASH, high NAFLD activity score (NAS ≥ 4) and advanced fibrosis (fibrosis stage ≥ 2).

This prospective study included a cohort of patients aged 18 years or older, scheduled to undergo liver biopsy for suspected NAFLD at a tertiary care centre in Algeria. The measurement of liver elasticity (LSM) by transient vibration-controlled elastography and the controlled attenuation parameter (CAP) measured by the FibroScan device were combined with aspartate aminotransferase (ASAT), alanine aminotransferase (ALAT) or AST/ALT ratio. To identify patients with NASH, elevated NAS and significant fibrosis. **Results:** Between March 1, 2019 and January 21, 2019, 220 patients suspected of having NAFLD. The most predictive model combined LSM, CAP and AST, and was designated FAST (FibroScan-AST). The performance was satisfactory in the derivation data set (C-statistic 0-80, 95% CI 0.78-0.87) and was well calibrated. The cut-off was 0-38 for a sensitivity of 0-90 or greater and 0.67 for a specificity of 0.90 or greater in the derivation cohort, leading to a positive predictive value (PPV) of 0.85 (86/101) and a negative predictive value (NPV) of 0.88 (94/110).

Conclusion: The FAST score offers an effective means of non-invasively identifying patients at risk of progressive NASH for clinical trials or treatments when they become available, and thus reducing unnecessary liver biopsies in patients unlikely to have significant disease

Disclosure: Nothing to disclose

P0704

ALCOHOL BIOMARKERS AS PREDICTORS OF READMISSION AND FATAL OUTCOME IN PATIENTS WITH ALCOHOL-RELATED LIVER CIRRHOSIS

K. Ikonnikova¹, N. Eroshhenko², V.N. Drozdov³

¹Federal State Autonomous Educational Institution of Higher Education, I.M. Sechenov First Moscow State Medical University, Ministry of Health of the Russian Federation (Sechenov University), Department of Clinical Pharmacology and Propaedeutics of Internal Diseases, Moscow, Russian Federation, ²Federal State Autonomous Educational Institution of Higher Education, I.M. Sechenov First Moscow State Medical University, Ministry of Health of the Russian Federation (Sechenov University), Center of Bioanalytical Research and Molecular Design, Moscow, Russian Federation, ³Sechenov University, Chair of Clinical Pharmacology and Introduction to Internal Medicine, Moscow, Russian Federation

Contact E-Mail Address: karolin.ikonnikova@yandex.ru

Introduction: Alcohol biomarkers are divided into direct ones, which are formed only during the ethanol metabolism (e.g. phosphatidylethanol, Peth), and indirect ones – enzymes that can change in response to alcohol consumption (e.g. alanine transaminase, ALT; aspartate aminotransferase, AST; gamma-glutamyltransferase, GGT). A direct alcohol biomarker Peth is formed only in the presence of alcohol, while liver enzymes can be elevated due to a number of causes. To protect against false positives, Peth is considered to be an indicator of purposeful alcohol consumption at values >20 ng/mL. The detection time of Peth can be maintained up to 2-3 weeks. Indirect markers have found the most widespread use in clinical practice, they are used to determine the etiology, severity and prognosis of liver cirrhosis. While direct markers are considered mainly only as a means of establishing the fact and nature of alcohol consumption. In our study, we evaluated alcohol biomarkers as a prognostic factor in patients with alcohol-related liver cirrhosis (ARC).

Aims & Methods: We aimed to assess the risk of readmission and fatal outcome in patients with ARC based on the alcohol biomarkers level. We performed a prospective observational cohort study involved 112 patients with history of ARC. All patients underwent clinical and laboratory examination on the first day of hospitalization, including quantitative LC/MS/MS determination of the Peth level and the liver cirrhosis severity on the Child-Pugh scale. Repeated contact to determine the outcomes (the pres-

ence of re-admission or fatal outcome) was appointed a year after the initial examination. Depending on the outcome, the patients were divided into groups: favorable outcome (n=74) - patients without re-admissions or fatal outcome; unfavorable outcome (n=38) - patients with re-admissions (n=36) and/or with fatal outcome (n=18). A ROC analysis of the relationship between the level of alcohol biomarkers and the course of liver cirrhosis was performed.

Results: The average level of Peth was higher in patients with fatal outcome and re-admission compared with patients with a favorable outcome of cirrhosis (468.7 ng/ml, 392.7 ng/ml and 249.8 ng/ml, respectively), a similar situation is typical for the GGT level (390.1 U/l, 270.7 U/l and 137.7 U/l, respectively) and alkaline phosphatase (ALP) (388.3 U/l, 331.3 U/l and 240.6 U/l, respectively).

The difference between the levels of albumin, ALT, AST, total and direct bilirubin, creatinine, INR values and the severity of liver cirrhosis on the Child-Pugh scale between the groups had no statistical significance. The indicators for which a statistically significant difference was obtained were used for ROC analysis. Re-admission was significantly associated with the level of Peth ($p=0.004$), GGT ($p=0.028$), and ALP ($p=0.05$), no significant relationship was obtained for platelet, leukocyte and Maddrey score values. The fatal outcome was significantly associated with the Peth level ($p=0.001$). Based on the ROC analysis results, the odds ratio (OR) of re-admission and fatal outcome in patients with ARC for 1 year were calculated. For lethality, a significant value of OR was observed with an increase of Peth more than 340 ng/ml (OR =3.8 (1.0-14.01); $p=0.04$). For re-admission, a significant OR value was noted with an increase in Peth > 340 ng/ml (OR 4.86 (2.0-11.8); $p=0.0005$).

Conclusion: Alcohol consumption is one of the factors influencing the prognosis of ARC. The Peth level >340 ng/ml is associated with an increased risk of re-admission and fatal outcome in patients with alcohol-related liver cirrhosis.

Disclosure: Nothing to disclose.

P0705

SZN-043, AN R-SPONDIN MIMETIC IN DEVELOPMENT FOR THE TREATMENT OF LIVER DISEASE, DEMONSTRATES A STRONG SAFETY PROFILE IN NONCLINICAL TOXICOLOGY STUDIES

J. Tibbitts¹, M. Newman¹, P. Stathis², A. Diep¹, G.F. Vanhove²

¹Surrozen Inc, Nonclinical Development, South San Francisco, United States, ²Surrozen Inc, South San Francisco, United States

Contact E-Mail Address: jtibbitts@surrozen.com

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 Lipoprotein receptor related protein co-receptors. SZN-043 is a hepatocyte-targeted antibody-based R-spondin mimetic shown to stimulate hepatocyte proliferation and improve hepatic function in preclinical models of liver injury.

Toxicology studies are essential to the development of potential therapeutic agents. For SZN-043 the mouse and cynomolgus monkey nonhuman primate (NHP) are relevant species based on their similarities in the binding and cellular function of SZN-043 to humans.

Aims & Methods: To support dosing in humans for up to one month, 4-week Good Laboratory Practice (GLP) compliant toxicology studies were conducted in mice and NHPs.

The purpose of these studies was to evaluate the toxicology and toxicokinetics (TK) of SZN-043. Normal mice (C57BL/6) or NHPs received 0, 12.5, 37.5, or 125 mg/kg SZN-043 intravenously (IV) (slow bolus) twice weekly for 28 days. A cohort of animals was terminated one day after the last dose and the remaining animals were terminated 28 days later.

Standard toxicologic analyses were included such as clinical and anatomic pathology, physical and other organ system evaluations, and toxicokinetic and antidrug antibody assessment.

Results: There were no SZN-043-related effects on body weights, food consumption, physical examinations, vital signs, ECGs, neurologic examinations, ophthalmology, hematology, coagulation, urinalysis, macroscopic examinations and histopathology.

Mice and NHPs receiving SZN-043 showed minimally to markedly increased alkaline phosphatase (ALP) levels during the dosing period which returned to baseline following cessation of dosing. The increase in serum ALP levels was not accompanied by changes in other hepatic, nor was there any evidence of hepatic injury by histopathology. This change was not considered adverse as increases in ALP are an expected pharmacologic effect of SZN-043 related to binding to the hepatocyte-specific protein ASGR1 preventing the elimination of ALP from serum. In mice but not NHP, a minimal decrease in serum albumin and total protein were observed with partial recovery following dosing.

An increase in liver weight was observed in male and female mice, and in female NHPs, receiving SZN-043 with no microscopic correlate. Liver weight returned to baseline during recovery and was not considered adverse. This is an expected pharmacologic effect of SZN-043 related to a transient increase in hepatocyte proliferation. In mice, other SZN-043-related changes in organ weights at the terminal necropsy included minimally higher adrenal and pituitary gland weights in some male animals at the higher doses; which was reversible and nonadverse, with no microscopic correlate.

Serum concentrations of SZN-043 were consistent with the dose and route of administration. Area under the curve increased greater than proportional to dose; consistent with the binding of SZN-043 to ASGR1.

Conclusion: Administration of SZN-043 was well-tolerated up to 125 mg/kg twice weekly. SZN-043-related changes were considered nonadverse and limited to clinical chemistry and organ weight changes. All observations showed evidence of recovery. There were no macroscopic or microscopic SZN-043-related observations. Serum exposure was consistent with the nature of SZN-043 and its dosing regimen. Based on the results of these studies, the no-observed-adverse-effect level was the highest dose of 125 mg/kg.

Disclosure: Nothing to disclose.

P0706

INTESTINAL ENDOTOXEMIA IS ONE OF THE FACTORS OF METABOLIC DISORDERS AND PROGRESSION OF NON-ALCOHOLIC FATTY LIVER DISEASE

G. Fadieienco¹, I. Kushnir¹, V. Chernova¹, T. Solomentseva¹, Y. Nikiforova¹, O. Kurinna¹

¹Government Institution L.T. Malaya Therapy National Institute of the National Academy of Medical S, Department of the Study of Diseases of the Digestive System and their Comorbidity with the Noncommunicable Diseases, Kharkov, Ukraine

Contact E-Mail Address: dr.jana@email.ua

Introduction: The progression of non-alcoholic fatty liver disease (NAFLD) is based on multiple parallel mechanisms that explain the complex molecular pathogenesis of NAFLD. One of the mechanisms of influence on the development of NAFLD is a violation of the intestinal microbiota (IM) and the production of endotoxin (ET) - lipopolysaccharide of the outer part of the cell membrane of gram-negative microorganisms.

Aims & Methods: To study the level of ET and evaluate the relationship between endotoxemia, metabolic parameters and the degree of hepatic steatosis in patients with NAFLD.

Materials and methods: The 86 patients with NAFLD with various metabolic disorders and 30 individuals in the control group were examined. All patients underwent an assessment of anthropometric parameters, a study of body composition with the determination of the percentage of visceral adipose tissue (VAT). VAT dysfunction was calculated by the visceral obesity index (VOI) according to the M.C. Amato method. Staging of steatosis according to the results of ultrasound CM was performed on the scale of the parameter of controlled attenuation (PCA), which corresponded to the morphological scale of fat activity NAS (Non-Alcoholic Steatosis). Serum ET concentration was determined using the LAL Chromogenic End-point Assay kit (Hycult Biotech, Netherlands).

Results: The levels of bacterial ET in the peripheral blood of the examined patients were almost three times higher than in the control group and amounted to 1.68 ± 0.19 U ET/ml and 0.43 ± 0.05 U ET/ml, respectively ($p < 0.05$). The relationship between the level of endotoxemia and the degree of nutritional status of patients with NAFLD was determined. In patients with overweight (BMI 25-30 kg/m²) and obesity (BMI >30 kg/m²), higher levels of ET were determined - 0.81 ± 0.09 U ET/ml and 1.84 ± 0.12 U ET/ml, respectively, compared with NAFLD patients with normal weight - 0.51 ± 0.05 ET units/ml ($p < 0.05$). In the examined patients, a direct correlation was determined between ET indices and parameters of abdominal obesity, namely, waist circumference (WC) ($r = +0.42$), the ratio of WC to hip circumference - ($r = +0.37$) and visceral obesity (VAT) ($r = +0.43$).

In the group of patients with high activity of VAT, the maximum levels of ET were recorded, which statistically significantly differed from those in patients with low and medium VOI ($p < 0.05$). In patients with steatosis of the 2nd and 3rd degree, the level of endotoxemia was higher, the difference in indicators in the control group and in the group with steatosis of the 1st degree was statistically significant ($p < 0.05$).

Conclusion: The data obtained suggest that bacterial metabolites of the IM, namely endotoxemia, make a significant contribution to the formation and maintenance of one of the components of the metabolic syndrome, namely visceral obesity with subsequent formation of fatty liver infiltration.

Disclosure: None

P0707 WITHDRAWN

P0708

LIVER FIBROSIS AND STEATOSIS ASSESSMENT USING ELASTOGRAPHIC TECHNIQUES: A COMPARISON BETWEEN NONALCOHOLIC FATTY LIVER DISEASE AND ALCOHOLIC LIVER DISEASE

C.G. Foncea^{1,2}, I. Sporea^{1,2}, R. Lupusoru^{1,2,3}, R. Cotrau^{1,2}, F. Bende^{1,2}, R. Sirli^{1,2}, A. Popescu^{1,2}

¹University of Medicine and Pharmacy "Victor Babes", Department of Gastroenterology and Hepatology, Department of Internal Medicine II, Center for Advanced Research in Gastroenterology and Hepatology, Timisoara, Romania, ²Center for Advanced Hepatology Research of the Academy of Medical Sciences, Timisoara, Romania, ³"Victor Babes" University of Medicine and Pharmacy, Center for Modeling Biological Systems and Data Analysis, Department of Functional Sciences, Timisoara, Romania

Contact E-Mail Address: foncea.camelia@gmail.com

Introduction: Alcoholic liver disease (ALD) and Non-alcoholic fatty liver disease (NAFLD) are becoming the most common causes of chronic liver diseases and the leading causes of liver transplantation. Developing non-invasive methods for liver fibrosis and steatosis assessment are needed in these patients.

In addition to Transient Elastography (TE), new methods were developed. The aim was to evaluate and compare the performance of two point shear wave elastography techniques (pSWE and Auto pSWE) for the assessment of fibrosis and of Ultrasound Derived Fat Fraction (UDFF) for the assessment of steatosis, in patients with NAFLD and ALD using TE with Controlled Attenuation Parameter (CAP) as a reference methods.

Aims & Methods: A prospective study was conducted in which 166 consecutive patients with previously diagnosed ALD and NAFLD were included. All were evaluated in the same session by pSWE, Auto pSWE and UDFF, implemented in a Siemens ACUSON Sequoia system, using a Deep Abdominal Transducer (DAX), and by TE with CAP, implemented in a FibroScan Compact M 530 system (M and XL probes). Reliable measurements were defined as the median value of 10 measurements with an IQR/M < 0.3. The following TE cut-off values were used: for significant fibrosis ($F \geq 2$) - 9 kPa for ALD and 8.2 kPa for NAFLD. For mild (S1) steatosis, the following CAP cut-off values were used: 268 dB/m for ALD and 294 dB/m for NAFLD [1,2,3].

Results: Fibrosis distribution was the following: in the ALD group $F \geq 2$ - 10% (5/48) patients and $F 4$ - 25% (12/48) patients; in the NAFLD group, $F \geq 2$ - 4.2% (5/118) patients and $F 4$ - 6% (7/118) patients. In the ALD group 50% (24/48) had severe steatosis and in the NAFLD 39% (46/118), with no significant differences between the two groups, p -values > 0.05.

The best cut-off values for identifying significant fibrosis ($F \geq 2$) with pSWE and Auto pSWE in ALD patients were: >7 kPa, with AUCs (0.94 and 0.90), Se (83.3% and 41.6%), Sp (83.3% and 100%); in NAFLD patients: >5.2 kPa, AUCs (0.71 and 0.75), Se (40% and 60%), Sp (100% and 96.2%); For the presence of at least mild steatosis, UDFF cut-off value in ALD patients was >5%, AUC=0.94, Se=96.6%, Sp=83.3% and in NAFLD patients was >12%, AUC=0.87, Se=78.5%, Sp=84.2%.

Conclusion: The cut-off values by pSWE and Auto pSWE for identifying significant fibrosis were >7 kPa in ALD patients and > 5.2 kPa in NAFLD patients. The cut-off values for UDFF in diagnosing at least mild steatosis were >5% in ALD patients and >12% in NAFLD patients.

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Disclosure: Nothing to disclose.

P0709

THE FREQUENCY AND IMPACT OF INFECTIONS IN PATIENTS WITH ALCOHOLIC HEPATITIS

C.G. Foncea^{1,2}, R. Fofiu^{1,2}, I. Sporea^{1,2}, G.-A. Burdan^{1,2}, T.V. Moga^{1,2}, R. Sirlu^{1,2}, A. Popescu^{1,2}

¹University of Medicine and Pharmacy Victor Babes, Gastroenterology and Hepatology, Internal Medicine II, Center for Advanced Research in Gastroenterology and Hepatology, Timisoara, Romania, ²Center for Advanced Hepatology Research of the Academy of Medical Sciences, Timisoara, Romania

Contact E-Mail Address: foncea.camelia@gmail.com

Introduction: Alcoholic hepatitis (AH) is one of the most severe forms of alcohol induced liver disease, especially severe alcoholic hepatitis (sAH), defined by a modified discriminant function (MDF) >32, being associated with 1 month mortality of 30%. Infections complicates AH and is the main cause of death in these group of patients, even in those who benefit from corticotherapy.

Aim: to evaluate the frequency of infections in patients with AH and the outcome of these patients.

Methods: A retrospective study was performed including 150 patients with AH over a period of 6 years in a tertiary Department of Gastroenterology and Hepatology. Systematic screening of infections was performed at admission, including chest x-ray, blood, urinary and ascites cultures. Severe AH was defined by a MDF score >32, response to corticotherapy was evaluated by Lille score at 7 days. Univariate regression was used to determine independent factors related to mortality.

Results: One hundred and fifty subjects were included in the final analysis, 84% male, mean age 55.5 ± 9.42. All patients were previously diagnosed with liver cirrhosis. 39.3% (59/150) presented infections at admission and 37.3% of the subjects with infections (22/59) died during admission, while only 19.7% (18/91) of those without infections, died (p=0.0283). 72.7% (109/150) of the included subjects had MDF>32 and received corticosteroid therapy and 42.2% of these (46/109) had an associated infection. In the group of those who received corticosteroid therapy, 35/109 (32.1%) deaths were recorded, 18/35 of them in patients with an associated infection (51.4%). Lille-7 was calculated in 90/109 subjects. 75.2% (82/109) of the subjects who received corticosteroid therapy were not responsive at 7 days and 31.7% of them (26/82) died, while 25% (2/8) of the responders died (p=0.9926).

In univariate regression analysis the presence of infections at admission was found to be an independent predictor for mortality (p=0.027).

Conclusion: AH is associated with a high risk of infection and infection screening is mandatory in these patients. The presence of infections at admission was found to be an independent predictor for mortality.

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Disclosure: Nothing to disclose.

P0710

ROLE OF OSTEOPONTIN AS A POTENTIAL SERUM MARKER OF HCV RELATED HEPATOCELLULAR CARCINOMA

E. Abdelatti¹, A. Ezz¹, R. Elkholy², K. Elsayed¹

¹Faculty of Medicine, Menoufia University, Gastroenterology and Hepatology, Alexandria, Egypt, ²Faculty of Medicine, Menoufia University, Clinical Pathology, Menoufia, Egypt

Contact E-Mail Address: ehab_abdelatty@hotmail.com

Introduction: Hepatocellular Carcinoma (HCC) is a major type of primary liver cancer and one of the most frequent human malignant neoplasm. Owing to the lack of reliable clinical HCC markers, fewer than 20% of patients are diagnosed at a stage where curative treatment can be performed.

The poor outcome of patients with HCC is related to the late detection with more than two-thirds of patients diagnosed at advanced stages of disease. Osteopontin is an important tumor marker. It presents as an immobilized extracellular matrix molecule in addition to present as a secreted form in body fluids involving plasma.

Aims & Methods: The aim is to evaluate the role of plasma Osteopontin (OPN) level as potential serum marker of HCC among HCV related liver cirrhosis.

The study was carried out on 80 Egyptian patients with HCV related liver disease (chronic hepatitis (CH) group: 30 patients with HCV positive chronic hepatitis, Liver cirrhosis (LC) group: 20 patients with HCV positive liver cirrhosis without HCC and HCC group: 20 patients with HCV positive liver cirrhosis and HCC) and 20 healthy volunteers as controls from Menoufia University Hospitals (Egypt).

They underwent history taking, physical examination and laboratory investigations (CBC, liver profile {ALT, AST, albumin, bilirubin, PT}, urea, creatinine, AFP, HBsAg, HCV Ab and serum Osteopontin).

Child-Pugh score was calculated for all patients. Abdominal ultrasonography was done for all patients and controls. HCC is further confirmed by triphasic CT. Patients with extrahepatic malignancy, having any bony lesions or chronic liver disease other than HCV were excluded from the study.

Results: Osteopontin level was significantly higher in HCC group (232.1±59.7) ng/ml than LC (92.9±18.5) ng/ml, CH (27.8±13.8) ng/ml and control group (33.1±16.4) ng/ml (P=0.001 for all). Also OPN level was significantly higher in LC group than CH and control group (P=0.001 for both) but there was no significant difference between CH and controls (P=0.8). AFP level was significantly higher in HCC group (639±2226.8) ng/ml than LC (24.8±25.9) ng/ml, CH (8.1±2.8) ng/ml and control group (4.6±2.4) ng/ml (P<0.05).

Also AFP level was significantly higher in LC group than CH and control group (P=0.03 for both) but there was no significant difference between CH and controls (P=0.06). In LC group, one patient (3%) was Child A, 15 patients (50%) were Child B and 14(49%) patients were Child C. In HCC group, 26 patients (86.7%) were Child A, 4 patients (13.3%) were Child B. In HCC group, size of HCC ranges from 1.4 to 9 cm. 90% of the patients (n=27) have single lesion, 2 patients (n=2) have 2 lesions and only one patient have 3 lesions.

Three patients (10%) have portal vein thrombosis. In HCC group, there was a significant positive correlation between OPN level and age (r=+0.5, P=0.001) and AFP (+0.56, P=0.001). In HCC group, there was a negative correlation between OPN and WBC (r=-0.2, P=0.03), platelet count (r=-0.54, P=0.001), PT (r=-.45, P=0.001) and albumin (r=-.45, P=0.001). In HCC group, there was no correlation between OPN level and blood urea, serum creatinine, AST, ALT, bilirubin, size of HCC and number of HCC (P>0.05). OPN at cutoff level >164.5 ng/ml have 96.7% sensitivity and 98.6% specificity for detection of HCC. AFP at cutoff level >6.5 ng/ml have 80% sensitivity and 96% specificity for detection of HCC.

Conclusion: Osteopontin has a higher sensitivity and specificity than AFP for detection of HCC. Therefore Osteopontin could be used for detection of HCC.

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Disclosure: I do not have any conflict of interest.

P0711

QUALITY OF LIFE WITH THE USE OF PERITONEAL CATHETER IN TERMINAL PATIENTS WITH REFRACTORY ASCITIS AT HOSPITAL REGIONAL LIC. ADOLFO LOPEZ MATEOS

A. Chávez Santiago¹

¹Hospital Regional Lic. Adolfo López Mateos ISSSTE, Department of Gastroenterology, Ciudad De México, Mexico

Contact E-Mail Address: alejandrogastro140517@gmail.com

Introduction: In patients with a terminal disease state who develop ascites,* intractable with medical management, require repeated evacuating paracentesis; but it must be taken into account that this treatment method causes a great psychological and economic waste, both for the patient and for their main caregiver.

The literature reports that the placement of the peritoneal catheter as a palliative procedure attracts certain anticipated complications, not only because of the discomfort that the procedure itself entails, but because of the comorbidities that these patients present. Therefore, the cost-benefit of using this procedure should be evaluated, depending on the diagnosis of each patient and the etiology.

However, this research considers that any approach that contributes to mitigating the secondary symptoms of ascites and, therefore, to a better quality of life for the patient, is worth performing as part of the treatment provided by our hospital institution, after evaluation their status and their informed consent.

However, it is necessary to carry out studies with a more representative population of patients with the aforementioned characteristics of peritoneal catheter carriers, in order to weigh the positive effects of this procedure on their quality of life and that of their main caregivers.

Aims & Methods: A total of 12 patients participated in the study who were admitted with a diagnosis of intractable ascites of any etiology to the Regional Hospital "Lic. Adolfo López Mateos" in the period from March 2019 to February 2020, which also met the inclusion criteria of the protocol. A Tenckhoff catheter was placed in 6 patients in the experimental group, while said catheter was not placed in the remaining 6 patients in the control group.

The SF-36 Questionnaire was applied twice to all the patients in the control group: the first time at the start of their hospital admission and the second time 3 months later, while in the same lapse the respective caregivers were given the Zarit abbreviated scale. Likewise, in equal time and form, the SF-36 Questionnaire was applied twice to all the patients in the

experimental group: the first time at the start of their hospital admission and the second three months after the Tenckhoff catheter was placed, while in the same lapse the Zarit abbreviated Scale was applied to their respective caregivers.

Finally, the results of the questionnaires were compared with each other, in order to have a reliable clinical parameter that would allow the hypothesis to be verified or not.

Results: No statistically significant difference was found before and after placement of the Tenckhoff catheter on the quality of life of the patient ($p = 0.29$) and the burden of the main caregiver ($p = 0.65$). On the other hand, compared to the control group of patients, there was also no statistically significant difference on the quality of life of the patients ($p = 0.67$), so the hypothesis was null.

Conclusion: The results obtained in this study do not suggest significant differences in the quality of life of the patient and the main caregiver after the placement of the Tenckhoff catheter, having made an evaluation three months after the placement of this device.

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Disclosure: Nothing to disclose.

P0712

PRELIMINARY RESULTS ON LSECTIN INDUCTION BY ANTI-INFLAMMATORY CYTOKINES IN HEPATIC ANTIGEN PRESENTING CELLS FROM CIRRHOTIC MICE

E. Angel Gomis^{1,2}, S. Martínez López^{1,2}, I. Gomez-Hurtado^{3,2}, P. Boix Navarro^{1,2}, E. Caparrós Cayuela^{2,1}, R. Francés Guarinos^{1,2,3}

¹Universidad Miguel Hernández, Departamento de Medicina Clínica, San Juan De Alicante, Spain, ²Hospital General Universitario de Alicante, IIS Isabial, Alicante, Spain, ³Instituto de Salud Carlos III, CIBERehd, Madrid, Spain

Contact E-Mail Address: enrique.angel@goumh.umh.es

Introduction: Hepatic Antigen Presenting Cells (hAPCs), mainly Liver Sinusoidal Endothelial Cells (LSECs) and Kupffer Cells (KCs), express C-type lectin receptors, like LSECTin. This protein is known for its interaction with effector T-cell ligands and its consequent role in inflammatory response control during liver damage (1).

Previous studies from our laboratory showed a negative transcriptional regulation of LSECTin in models of experimentally induced cirrhosis that resulted in a proinflammatory T-cell expansion (2).

Aims & Methods: Our aim in this study is to investigate whether LSEctin expression can be restored via an external intervention in hAPC from cirrhotic mice. For that objective, progressive liver damage was induced in mice by oral administration of carbon tetrachloride (CCl₄). Laparotomies were performed at week 12 in pools of control and treated mice (n = 6). Liver cirrhosis was assessed by qPCR and IHC staining of different proinflammatory and profibrogenic markers. LSEctin expression in whole livers was studied by qPCR, WB and IHC. FACS-isolated hAPCs were treated with and without combinations of anti-inflammatory cytokines (IL-4, IL-13, IL-10 and TGFβ1) for 48 hours. LSEctin expression was assessed in primary cultures by flow cytometry and qPCR.

Results: Livers from treated mice exhibited a strong expression of proinflammatory and profibrogenic markers indicating the onset of cirrhosis. A reduction of LSEctin expression during fibrosis progression was confirmed in our model, not only transcriptionally, but also at the protein level by IHC, WB and flow cytometry. LSEctin gene expression was induced in primary cultures of LSECS and KCs from control and fibrotic mice in the presence of anti-inflammatory cytokines (Table 1). Although IL-10 and IL-13 stood out individually, the combination of all four anti-inflammatory cytokines exhibited a synergistic upregulatory effect on LSEctin expression.

	KCs		LSECS	
IL-4	1.60	0.84	1.17	0.58
IL-10	1.53	0.99	1.68	1.18
IL-13	2.34	0.10	1.88	0.45
TGF-B	1.65	0.41	1.44	0.59
IL-4+IL-10	2.07	0.73	0.95	0.37
IL-4+TGF-B	2.11	0.33	0.94	0.15
IL-10+TGF-B	1.28	0.27	1.34	0.27
IL-4+IL-10+TGF-B	1.01	0.44	1.43	0.48
IL-4+IL-10+IL-13+TGF-B	1.93	0.12	3.05	1.72

Table 1. LSEctin Relative Expression induced by cytokine treatment (10 ng/mL). Relative expression values indicated as mean ± SD (untreated: 1.00 ± 0.00).

Conclusion: LSEctin expression can be exogenously induced in cirrhotic hAPCs by the generation of a tolerogenic microenvironment. Cytokine-induced LSEctin restoration may constitute a new tool in the control of liver inflammatory response in advanced liver disease.

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P0713 WITHDRAWN

P0714

CONTRIBUTION OF THE NEW PROGNOSTIC SCORE LIVER-RENAL-RISK (LIRER) IN PREDICTING SURVIVAL IN CIRRHOTIC PATIENTS

M. Mtir¹, D. Cherif¹, H. Garraoui¹, H. Hassine¹, H. Kechir¹, N. Maamouri¹

¹La Rabta Hospital, Department of Gastroenterology B, Tunis, Tunisia

Contact E-Mail Address: mtirmaha@gmail.com

Introduction: The Model for End stage Liver Disease (MELD) score has been widely used in the selection of cirrhotic candidates for liver transplantation (LT) by prioritising them on the waiting list. For patients with a relatively low score (below 18), the MELD may underestimate the severity of the disease. For this reason, several scores have been proposed to improve its predictive value, including the MELD-Na. More recently, the liver-renal-risk score (LIRER) has been developed to resolve this problem.

Aims & Methods: The aim of this study was to evaluate the reliability of the LIRER score in predicting survival in cirrhotic patients compared to standard scores.

We conducted a monocentric retrospective study collecting all cirrhotic patients over an 8-year period (2008-2015). Clinical, biological, morphological and evolutionary data were collected.

The LIRER score was calculated for all patients according to the formula :
LIRER= [Natremia (mEq/L) x -0.09] + [Bilirubinemia (mg/dl) x 0.27] + [Albuminemia (g/dl) x -1.16] + [GFR-MDRD (ml/min) x -0.01] + Presence of ascites (1.2 if yes; 0 if no) +30 (constant)

Moreover, the glomerular filtration rate (GFR) was calculated according to the formula :

$$\text{MDRD} = 186 \times (\text{creatinine } (\mu\text{mol/l}) / 88.4)^{-1.154} \times \text{age}^{-0.203} \times (0.742 \text{ if female}) \times (1.212 \text{ if black})$$

A cut-off of 15.9 for the LIRER score was identified as a factor in rapid disease progression.

The performance of this score was compared with that of the Child And Pugh (CP), MELD and MELD-Na for 1 year, 3 years and 5 years survival using the area under the ROC curve (AUROC) with 95% confidence.

Results: We included 120 cirrhotic patients with an M/F sex ratio equal to 0.5. The mean age was 57 years [14-85]. The most frequent aetiology of cirrhosis were viral C (49%) and viral B (31%). Eighty-eight patients were in the complication stage, and the remaining 22 were still in the compensated stage. The mean overall survival was approximately 6 years after diagnosis. The mean scores were: CP 7.6 (stage B), MELD 17.54, MELD-Na 17.47 and LIRER 14.46 [range 1.1 - 19.9].

By analysing the areas under the ROC curves, the prognostic performances for 1 year, 3 years and 5 years survival were respectively:

	AUROC survival at 1 year	AUROC survival at 3 years	AUROC survival at 5 years
Child And Pugh	0.692	0.658	0.662
MELD	0.569	0.582	0.553
MELD-Na	0.547	0.578	0.577
LIRER	0.634	0.616	0.619

Furthermore, among the 71 patients with a low MELD score (below 18), 11 patients (9.1%) had a LIRER score above 15.9 constituting the group of patients underestimated by the MELD but with a high risk of unfavourable evolution. The LIRER score allowed us to reclassify this group of cirrhotics who can thus join the waiting list as potential candidates for TH.

Conclusion: At the end of this study, our results suggest that the LIRER score is a new reliable prognostic tool, with performances comparable to the usual scores, notably CP, MELD and MELD-Na, in predicting survival in

cirrhotics. Its use as an auxiliary prognostic tool in patients with a MELD of less than 18 could broaden the criteria for inclusion in the liver transplant waiting list.

References:

Marta Freitas and others, 'LIRER Score - a Valuable Tool to Predict Medium-Long-Term Outcomes in Hepatic Cirrhosis Decompensation', *Scandinavian Journal of Gastroenterology*, 55.9 (2020), 1079–86 <<https://doi.org/10.1080/00365521.2020.1797156>>.

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P0715

LIVER-RENAL-RISK (LIRER): PERFORMANCE AND RELIABILITY IN PREDICTING THE OCCURRENCE OF HEPATORENAL SYNDROME IN CIRRHOTICS

M. Mtir¹, D. Cherif¹, H. Garraoui¹, H. Hassine¹, H. Kechir¹, N. Maamouri¹

¹La Rabta Hospital, Department of Gastroenterology B, Tunis, Tunisia

Contact E-Mail Address: mtirmaha@gmail.com

Introduction: Cirrhosis is a frequent pathology whose evolution can be marked by the occurrence of multiple complications that condition the prognosis.

Thus, the use of simple and reproducible prognostic scores could considerably improve its management. For this purpose, several scores have been developed, including the liver-renal-risk (LIRER) score, which has been proposed by certain authors in order to assess the severity of cirrhosis and thus allow the stratification of patients by order of priority for receiving a liver transplant.

Among these complications, renal dysfunction remains one of the most dreaded, namely the hepatorenal syndrome (HRS), often fatal in the absence of a liver transplant.

Therefore, we were interested in evaluating the performance of the LIRER score in predicting the occurrence of HRS and its reliability compared to the usual scores.

Aims & Methods: We conducted a monocentric retrospective study collecting all cirrhotic patients over an 8-year period (2008-2015). Clinical, biological, morphological and evolutionary data were collected.

The LIRER score was calculated for all patients according to the formula:

$$\text{LIRER} = [\text{Natreemia (mEq/L)} \times -0.09] + [\text{Bilirubinemia (mg/dl)} \times 0.27] + [\text{Albuminemia (g/dl)} \times -1.16] + [\text{GFR-MDRD (ml/min)} \times -0.01] + \text{Presence of ascites (1.2 if yes; 0 if no)} + 30 \text{ (constant)}$$

Moreover, the glomerular filtration rate (GFR) was calculated according to the formula :

$$\text{MDRD} = 186 \times (\text{creatinine } (\mu\text{mol/l}) / 88.4)^{-1.154} \times \text{age}^{-0.203} \times (0.742 \text{ if female}) \times (1.212 \text{ if black})$$

A cut-off of 15.9 for the LIRER score was identified as a factor for rapid disease progression.

The performance of this score was compared with that of the Child and Pugh (CP), MELD (Model for End stage Liver Disease), and MELD-Na regarding HRS occurrence using the area under the ROC curve (AUROC) with 95% confidence.

Results: We included 120 cirrhotic patients with an M/F sex ratio equal to 0.5. The mean age was 57 years [14 - 85]. The most frequent aetiology of cirrhosis were viral C (49%) and viral B (31%).

The mean serum creatinine was 10.23 mg/l [5 - 52], and the GFR calculated by MDRD was 85.9 ml/min/1.73m². The latter was below the threshold value in 55% of cirrhotics.

The mean scores were : CP 7.6 (stage B), MELD 17.54, MELD-Na 17.47 and LIRER 14.46 [1.1 - 19.9].

Thirty-five patients (29.1%) developed HRS and almost half of them were in refractory ascites stage (n=18). HRS was more frequent in patients classified as Child B and C by 37.1% and 51.4% respectively.

The mean LIRER score in patients who developed HRS was 16.07 [11.7 - 19.9] and that in cirrhotic patients without HRS complication was 13.78 [1.1 - 17.2].

The cut-off of the LIRER score in the occurrence of HRS in our population was 14.85 with a sensitivity of 80% and a specificity of 77,6%.

In univariate study and using the Chi-square test, the predictive factors for the occurrence of HRS were : an infectious episode apart from ascites fluid infection (AFI) with p= 0.0001, AFI (p= 0.002), ascitic decompensation (p= 0.0001), hyponatremia of less than 136 mmol/l (p= 0.005) and a CP stage C (p= 0.0001).

Furthermore, by analyzing the areas under the ROC curves, the prognostic performances regarding the occurrence of HRS of the CP, MELD, MELD-Na and LIRER scores were respectively:

	Child And Pugh	MELD	MELD-Na	LIRER
AUROC in predicting the occurrence of HRS	0.800	0.660	0.692	0.841

Conclusion: Our results suggest that the new prognostic score "LIRER" is a reliable and powerful tool in predicting the occurrence of renal dysfunction including hepatorenal syndrome.

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Disclosure: Nothing to disclose.

P0716

PREDICTION MODEL OF 30-DAY INPATIENT MORTALITY FOR ALCOHOLIC HEPATITIS

H. Ali¹, R. Pamarthy¹

¹East Carolina University, Greenville, United States

Contact E-Mail Address: alih20@ecu.edu

Introduction: Alcoholic hepatitis (AH) is associated with morbidity and mortality depending upon the disease severity. Studies estimate that 30% of chronic alcohol drinkers will develop AH. Early recognition of high-risk patients can help improve mortality outcomes during AH hospitalizations.

Aims & Methods: We aimed to devise a mortality scoring system for risk stratification for AH hospitalizations. National Inpatient Sample (NIS) database from January 1st, 2019 to December 31st, 2019 was used to identify AH hospitalizations for the derivation cohort in the United States population. A mortality scoring system was derived using multivariable cox regression and validated using receiver operating characteristic curves in the NIS database 2018.

Results: Independent predictors for 30-day all-cause mortality included anemia [Adjusted Hazard Ratio (aHR):1.45, 95% CI:1.18–1.78, p < 0.001], Age > 60 years [aHR:1.75, 95% CI:1.51–2.03, p < 0.001], Female gender [aHR:1.16, 95% CI:1.01–1.33, p < 0.001], Mechanical Ventilation [aHR:2.8, 95% CI:2.4–3.3, p < 0.001], Vasopressor [aHR:2.3, 95% CI:1.82–2.8, p < 0.001], Hepatorenal syndrome [aHR:1.73, 95% CI:1.45–2.04 p < 0.001], Spontaneous bacterial Peritonitis [aHR:1.37, 95% CI:1.1–1.72, p < 0.001] Acute Renal failure [aHR:4.9, 95% CI:4.1–6.1, p < 0.001] and Coagulopathy [aHR:1.76, 95% CI:1.51–2.1, p < 0.001]. These were used to develop the predictive scoring system for inpatient 30-day inpatient mortality (Table

1). The cut-off was 4 points using Liu index (Sensitivity 78.38%, Specificity 92.98%) for 30-day mortality based on the highest sensitivity and specificity values from the ROC curves. The Area under curve (AUC) of the derivation cohort was 0.8766 (95% CI, 0.865–0.888). The validation cohort had an AUC of 0.862 (95% CI, 0.855–0.868).

Score	30-Day Mortality Rate (%)
1	0.29%
2	8.01%
3	4.1%
4	14.7%
5	33.1%
6	51.1%
7	69.6%
≥ 8	99%

Table 1: Risk Score system for 30-day inpatient mortality for AH hospitalizations using the US population

Conclusion: This system can be used as an objective method for predicting 30-day all-cause mortality for AH hospitalizations.

Disclosure: Nothing to disclose.

P0717 WITHDRAWN

P0718

RELATION OF PROTEIN S AND PORTAL VEIN THROMBOSIS IN EGYPTIAN PATIENTS WITH HCV RELATED LIVER CIRRHOSIS

E.A. Abdelatti¹, R. Elkholy², A. Talkhan¹, A. Ezz¹

¹Faculty of Medicine, Menoufia University, Gastroenterology and Hepatology, Alexandria, Egypt, ²Faculty of Medicine, Menoufia University, Clinical Pathology, Menoufia, Egypt

Contact E-Mail Address: ehab_abdelatty@hotmail.com

Introduction: Portal vein thrombosis (PVT) is common in cirrhotic patients with a risk related to the severity of the disease. The prevalence ranges from 1%, at earlier stages to 30% in candidates for liver transplantation. PVT causes portal hypertension with development of esophageal varices, and if severe, can cause variceal hemorrhage and ischemic bowel disease. Protein S (PS) is natural anticoagulant protein produced by hepatocytes and decreased in setting of liver cirrhosis. Patients with PS deficiency are at increased risk for venous thromboembolic disease, arterial thrombosis and PVT. The pathogenesis of PVT has not been identified clearly, but it can be related to systemic causes such as protein S deficiency.

Aims & Methods: The aim was to investigate the relation of serum protein S level and pathogenesis of PVT in patients with HCV related liver cirrhosis. The study was carried out on 70 Egyptian patients with HCV related liver cirrhosis (LC) (LC group: 36 cirrhotic patient without PVT and LC+PVT group: 34 cirrhotic patient with cirrhosis and PVT) and 20 healthy volunteers as controls from Menoufia University Hospitals (Egypt). The study was conducted in the period from June 2020 and July 2021. They underwent history taking, physical examination and laboratory investigations (CBC, liver profile [ALT, AST, serum albumin, bilirubin, PT %], urea, creatinine, HBsAg, HCV Ab and PS assay). Abdominal ultrasound with Doppler of portal vein (PV) was done for all patients and controls. Triphasic CT of the liver was done for patients with PVT to exclude hepatocellular carcinoma (HCC). Child-Pugh score, AST/Platelet ratio index (APRI score) and FIB-4 were calculated for all patients. Patients on anticoagulant therapy, age less than 18 years, inflammatory or bleeding events in previous 2 months,

history of personal unprovoked thromboembolism (familial in first-degree relatives), diabetes mellitus, and HCC are excluded from the study.

Results: Protein S level was significantly lower in LC+PVT group (2.1 ± 1.9) than in LC (12.6 ± 12.9) and control group (20.8 ± 12.3) ($P=0.0001$ for both). Also PS level was significantly lower in LC group than in control group ($P=0.01$). PV diameter was significantly higher in LC+PVT group (14.3 ± 1.3) than in LC group (12.1 ± 1.3) ($P=0.001$). FIB-4 was significantly higher in LC group (6.56 ± 3.04) than in LC+PVT group (4.93 ± 1.77) ($P=0.02$).

There was no significant difference between LC+PVT group and LC group as regard, history of encephalopathy, history of gastrointestinal bleeding, presence of ascites, CBC, liver profile (ALT, AST, serum albumin, bilirubin, PT%), Child-Pugh score, APRI score, renal function (urea, creatinine), liver size and spleen size ($P>0.05$).

There was a significant positive correlation between PS level and PT%, APRI score, FIB-4, in LC+PVT group ($P=0.03$, 0.03 and 0.04 respectively). There was no correlation between PS level and age, platelet count, serum albumin, AST, ALT, serum bilirubin, blood urea, serum creatinine and spleen size ($P>0.05$). PS at cutoff level 3.2 ng/ml have 91% sensitivity and 98% specificity for prediction of PVT. In LC+PVT group, 82% have partial PVT (grade I) ($n=28$), 12% complete PVT (grade II) ($n=4$) and 6% complete PVT with superior mesenteric extension (grade III) ($n=2$).

Conclusion: Low protein S concentration is associated with pathogenesis of PVT in liver cirrhosis. Protein S concentration is potential biochemical marker in diagnostic strategy of PVT in patients with cirrhosis. Protein S below 3.2 is highly indicator of PVT in cirrhotic patients with high sensitivity and specificity.

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Disclosure: I do not have any conflict of interest.

P0719

BAVENO VII CRITERIA AS NON-INVASIVE PREDICTORS OF ESOPHAGEAL VARICES AND RISK OF DECOMPENSATION

E. Afecto¹, S. Sousa-Fernandes¹, J.P. Laranjeira Correia¹, M.M. Estevinho¹, A.P. Silva¹, T. Freitas¹

¹Centro Hospitalar de Vila Nova de Gaia/Espinho, Vila Nova de Gaia, Portugal

Contact E-Mail Address: joaopaulo_laranjeira@hotmail.com

Introduction: The presence of clinically significant portal hypertension (CSPH) is an important prognostic marker in chronic liver disease (CLD). The recent Baveno VII consensus proposes non-invasive diagnostic methods for this condition, using transient elastography (TE) and platelet count. This work aims to evaluate these criteria and their influence on long-term prognosis.

Aims & Methods: We retrospectively included patients with compensated CLD, submitted to TE between 2013 and 2015, who had an analytical study (within 3 months from TE) and upper digestive endoscopy (within 1 year from TE). Patients with decompensated CLD were excluded. CSPH was defined as liver stiffness ≥ 25 kPa and absence of CSPH as liver stiffness ≤ 15 kPa + platelets ≥ 150000 , per Baveno criteria. The prediction accuracy of the Baveno criteria for CSPH was compared with the presence of varices in endoscopy.

Results: 104 patients were included, 69.2% men, mean age 56.8 years. Hepatitis C (79.8%) and alcohol (11.5%) were the main causes of CLD in our cohort. Esophageal varices were present in 26 patients, 9 of which were considered high risk. The Baveno criteria significantly predicted the presence of esophageal varices ($p < 0.001$), with sensitivity, specificity, positive and negative predictive value of 95%, 82%, 67%, and 98%, respectively. Additionally, over a mean follow-up of 56 months, the patients classified as CSPH under Baveno criteria had increased risk of bleeding, death, or transplantation (HR 9.9).

Conclusion: This study demonstrates the ability of the Baveno criteria to non-invasively identify patients with CSPH immediately and their risk of gastrointestinal bleeding, death or transplantation over a long period of follow-up, which highlights its usefulness in clinical practice.

Disclosure: Nothing to disclose.

P0720

THE IMPACT OF COVID-19 PANDEMIC IN LIVER CIRRHOSIS HOSPITAL ADMISSIONS

V. Martins^{1,2}, R. Oliveira^{1,2}, J. Roseira^{1,2}, A.M. Vieira^{1,2}

¹Centro Hospitalar Universitário do Algarve, Portimão, Portugal,

²Algarve Biomedical Centre, Faro, Portugal

Contact E-Mail Address: viviana.s.martins@hotmail.com

Introduction: The impact of COVID-19 pandemic in cirrhotic patients' management is yet to be determined. Whether the unavoidable clinical practice modifications resulted in worse outcomes remains unanswered.

Aims & Methods: We aimed to compare hospital admissions due to cirrhosis acute decompensations or complications before and during the pandemic.

Methods: Retrospective unicentric cohort study considering all hospital admissions due to cirrhosis acute decompensations or complications between April-September 2019 (pre-pandemic), 2020 (early pandemic in Portugal) and 2021 (1 year post pandemic start).

Patients' sociodemographic, clinical and biochemistry data at admission were reviewed. Hospital 30-day readmission and mortality (at hospital; post discharge: 30, 90 days, 1 year), were the outcomes of interest.

Statistics: descriptive statistics, chi-square, Mann-Whitney and Kruskal-Wallis tests.

Results: We evaluated 127 admissions of 96 patients, mean age 60.1 $\pm$ 11.0 years, mostly male (84.4%), with alcohol related liver cirrhosis (59.4%), and no previous hepatocarcinoma diagnosis (87.5%).

Overall, patients' clinical status before and during the pandemic (including both periods) was similar, regarding causes of admission, biochemistry data, prognostic scores, and outcomes (all $p > 0.050$).

Most patients presented severe disease at admission (median Child Pugh, 10; median MELD, 22). Ascites (68.5%) and hyponatremia (53.5%) were the most common clinical features detected. As for admission causes, hydropic decompensation and hepatic encephalopathy were the main findings irrespective of the study's timepoints (before 40.0% and 17.5%, during 37.9% and 17.2%, respectively). Interestingly, patients were discharged sooner during the pandemic (median 9 vs 14 days, $p < 0.049$).

Conclusion: Unlike empirical belief, this study showed that disease severity and decompensation of cirrhotic patients admitted to the hospital during the last 3 years, were similar, irrespective of COVID-19 pandemic, suggesting the contingency plans did not negatively impact these patients. Larger studies may further confirm these results. Whether cirrhotic patients delayed discharges before pandemic were modified due to contingency plans or social causes remains unaddressed.

Disclosure: Nothing to disclose.

P0721

LIVER-SPECIFIC PROGNOSTIC SCORES ABILITY TO PREDICT MORTALITY IN CIRRHOTIC PATIENTS ADMITTED TO THE GASTROENTEROLOGY INTENSIVE CARE UNIT

K. Babbou¹, H. Jlassi², S. Meriam³, B. Nawel¹, D. Trad³, H. Elloumi³, N. Bibani⁴, D. Gargouri⁵

¹Habib Thameur Hospital, Faculty of Medicine, Gastroenterology, Tunis, Tunisia, ²Mongi Slim Hospital, Faculty of Medicine, Gastroenterology, Tunis, Tunisia, ³Habib Thameur Hospital, Gastroenterology, Tunis, Tunisia, ⁴Hopital Habib Thameur, Tunis, Tunisia, ⁵Habib Thameur Hospital, Les Berges du Lac, Tunisia

Contact E-Mail Address: khouloudabbou1@gmail.com

Introduction: End-stage liver disease is a major cause of death worldwide. It usually evolves over several years from compensated to decompensated cirrhosis, which is identified by the onset of acute decompensation (AD) with the development of hepatic encephalopathy (HE), ascites, and variceal hemorrhage (VH). Further decompensation frequently leads to the terminal stage of cirrhosis characterized by occurrence of acute-on-chronic liver failure (ACLF). Patients with either AD or ACLF usually require admission to the intensive care unit (ICU). Several ICU and liver-specific scores have been used to predict outcomes of critically ill patients with cirrhosis. The most often used ICU scores is Sequential Organ Failure Assessment (SOFA) scores.

Aims & Methods: This study was conducted to evaluate the performance of prognostic scores, including Chronic Liver Failure Consortium (CLIF-C) SOFA, CLIF-C OF and CLIF-C ACLF scores, in predicting mortality of cirrhotic patients admitted to the gastroenterology ICU.

Cirrhotic patients admitted in the Gastroenterology Department for the management of an acute decompensation of cirrhosis between January 2019 and January 2022 were retrospectively included. All prognostic scores were calculated in the first 24 hours of admission. Their ability to predict mortality was measured using the analysis of the area under the receiver operating characteristic curve (AUC).

Results: A total of 62 consecutive patients (sex-ratio M/F: 1.58, mean age 64.82 $\pm$ 13.51 years) were admitted due to AD of cirrhosis ($n=46$) or ACLF ($n=16$). At the time of the study, cirrhosis had progressed for a mean of 5.9 $\pm$ 4.56 years. Most of cirrhosis was due to viral hepatitis C (28%). The average MELD score was 16 $\pm$ 7 [range 7-31].

The AD/ ACLF occurred on average 31 [0-154] months after the diagnosis of cirrhosis. The main clinical features of those individuals were bacterial infections with or without sepsis or septic shock (30%), HE (10%) and VH (23%). Among the patients, 39 had concurrent ascites (63%).

The average (CLIF-C) SOFA, CLIF-C OF and CLIF-C ACLF scores were respectively 5.22 $\pm$ 3.47, 7.63 $\pm$ 2.17 and 51.56 $\pm$ 8.37. According to CLIF-C criteria, 16 patients (26%) had ACLF classified grade I ($n=8$), grade II ($n=7$), or grade III ($n=1$).

The mean length of hospital stay was 8 $\pm$ 6 days. Mortality was observed in 18 patients (29%). Analysis of AUC revealed that CLIF-C OF (0.880) and CLIF-SOFA (0.942) had the best ability to predict mortality in all patients. CLIF-SOFA, and CLIF-C OF had the highest AUC values in patients with ACLF, with no statistical difference ($p: 0.875$).

Conclusion: When compared to other general or liver-specific prognostic scores, CLIF-C OF, CLIF-SOFA, and CLIF-C AD have good accuracy to predict mortality in critically ill patients with cirrhosis and patients with AD. According to the clinical scenario, different scores should be used to provide prognosis to patients with cirrhosis in the ICU.

Disclosure: Nothing to disclose.

P0722

DEVELOPMENT OF A MODEL TO PREDICT 90-DAY MORTALITY AMONG PATIENTS WITH ACUTE VARICEAL BLEEDING

I.G. Garrido¹, R. Medas¹, R. Liberal¹, D. Martinho Dias², G. Macedo¹

¹Centro Hospitalar Universitário de São João, Gastroenterology, Porto, Portugal, ²ACES Tanso Tirso-Trofa+, ARS Norte, USF Ao Encontro da Saúde, Porto, Portugal

Contact E-Mail Address: isabelmng@hotmail.com

Introduction: Acute variceal bleeding is a major cause of death in patients with liver cirrhosis. The aim of this study was to investigate mortality predictors and develop a simplified prognostic model in patients with acute variceal bleeding.

Aims & Methods: We conducted a retrospective monocentric study in a cohort of cirrhotic patients with acute variceal bleeding between January 2010 and December 2021.

Results: A total of 131 patients were included, the majority male (80.2%), with a median age of 59 years old (IQR 50-65). Alcoholic liver disease was the leading cause of liver cirrhosis (77.8%). Twenty-six patients (19.8%) had concomitant hepatocellular carcinoma. Eleven (8.4%) patients were taking antiplatelet agents and six (4.6%) anticoagulants. Esophageal and gastric varices were the cause of bleeding in 123 (93.9%) and 8 (6.1%) patients, respectively. All patients received endoscopic therapy at the time of initial endoscopy. Band ligation was performed in 114 patients (87.0%), sclerotherapy in 17 (13.0%) and cyanoacrylate injection in 9 (6.9%). The 90-day overall mortality rate was 16.0%. The value of aspartate aminotransferase ($p < 0.001$), albumin ($p = 0.006$), sodium ($p = 0.001$) and rebleeding within five days of endoscopy ($p = 0.010$) were independent predictors of mortality after the acute variceal hemorrhage episode. A new logistic model using these variables was developed: $0.716 * \text{Albumin} + 1.022 * \text{aspartate aminotransferase} + 0.694 * \text{sodium} + 42.169 * \text{rebleeding within five days of endoscopy}$. This model's AUROC was 0.841 (CI 95% 0.726-0.956, $p < 0.001$), which was significantly higher than that of MELD (0.723, CI 95% 0.555-0.891, $p = 0.007$) or Child-Pugh scores (0.789 CI 95% 0.653-0.924, $p = 0.001$).

Conclusion: Our new simplified model accurately and consistently predicted 90-day mortality in patients with acute variceal bleeding. Our system can be used to identify high-risk cirrhotic patients.

Disclosure: Nothing to disclose.

P0723

SPLENIC ARTERY ANEURYSMS AND PORTAL HYPERTENSION: CAUSE OR CONSEQUENCE

S. hmimass¹, I. Khalif¹, M. Borahma¹, M. Kadiri¹, I. Benelbarhdadi¹, F.z. Ajana¹

¹University Mohammed V, Medicine C-Hepatogastroenterology, Rabat, Morocco

Contact E-Mail Address: hmimass19@gmail.com

Introduction: Splenic artery aneurysms (SAAs) are rare, asymptomatic and incidentally discovered. The majority of SAAs are medium-sized, measuring 3 cm at diagnosis. Associations with portal hypertension (PH) have been frequently reported.

Recently, attention has been drawn to chronic liver disease requiring liver transplantation as risk factors. The risk of rupture of true aneurysms appears to be negligible, below a size of 2 cm.

Aims & Methods: This was a retrospective study conducted in a hepatogastroenterology department. Splenic artery aneurysms were discovered incidentally by performing an angiography scan in our patients followed for portal hypertension. The aim of our work was to identify risk factors for the occurrence of ASA in patients with PH.

Results: We registered 5 patients with splenic artery aneurysms over a period of 2 years (2021-2022). The mean age of the patients was 44.4 years with extremes ranging from 36 to 59 years, with a male predominance (sex ratio of 1.5). The circumstances of discovery were variable, all patients presented an anemic syndrome, upper GI hemorrhage was found in 60% of cases, abdominal pain at the left upper quadrant with weight loss, homogeneous abdominal distension and chronic malabsorption diarrhea encountered in 20% of cases each.

Clinical examination revealed splenomegaly (SMG) in 80% of the patients, signs of hepatocellular insufficiency, conjunctival jaundice, and stage I hepatic encephalopathy in 2 patients each; collateral venous circulation (CVC) in both flanks and basithoracic in 20% of the patients, and in only one patient ascites grade III.

The clinical examination of the liver revealed an overloaded liver in 40%, a dysmorphic liver with a cirrhotic appearance in 20%, and hepatomegaly in only one case. Liver function tests showed chronic hepatocellular failure in 60% of the cases, cytotoxicity in 2 patients, and no patient had cholestasis, with elevated total bilirubin in 2 patients. Abdominopelvic ultrasound with Doppler examination showed an inhomogeneous dysmorphic liver in 2 patients, a normal liver in 40%, and heterogeneous hepatomegaly with irregular contours in 20% and portal cavernoma in 20% of cases.

All our patients had PH with portosystemic shunts. An abdominal angiography scan was performed as part of the monitoring and etiological work-up of our patients who were all asymptomatic; and objectified a single splenic artery aneurysm in 80%, with an aneurysm size greater than 2 cm in 50% of the patients and less than 2 cm in 2 patients; and 3 splenic artery aneurysms were found in only one patient. A partial atheromatous plaque was found in only one patient. Splenic artery aneurysms were found on angiography scan at the time of diagnosis of PH in 3 patients, after 9 years in one case and after 5 years in another case.

In terms of the etiology of PH, autoimmune hepatitis at the stage of cirrhosis was diagnosed in 2 cases, of which one case was associated with celiac disease, hepatic sarcoidosis at the F1 stage was associated with celiac disease in one case, and PH caused by portal cavernoma and Portosinusoidal vascular disease (PSVD) in one case each. Therapeutically only one patient was splenectomized with good outcomes, 2 patients needed clinical +/- radiological monitoring, one patient will be scheduled for surgical treatment and only one patient refused treatment.

Conclusion: Splenic artery aneurysm is a rare and often asymptomatic complication of portal hypertension. In our series, 3 patients had advanced PH in the setting of chronic liver disease and in 2 cases was developed after more than 5 years of evolution.

Disclosure: Nothing to disclose.

P0724

USEFULNESS OF MELD AND MELD-NA FOR PREDICTING MORTALITY IN CIRRHOTIC PATIENTS WITH SPONTANEOUS BACTERIAL PERITONITIS

C. Coxeter-Smith¹, A. Al-Adhami², L. Alrubaiy²

¹Imperial College, School of Medicine, London, United Kingdom,

²St Mark's Hospital, Gastroenterology, Harrow, United Kingdom

Contact E-Mail Address: dr.amsk82@yahoo.com

Introduction: Spontaneous bacterial peritonitis (SBP) is defined as a bacterial infection of the ascitic fluid that occurs in the absence of any surgically treatable intra-abdominal sources of infection [1]. SBP is common in patients with cirrhosis and ascites [2,3] as a result of increased bacterial translocation from the gastrointestinal tract to mesenteric lymph nodes and other extraintestinal sites [4]. Due to impaired local [5] and systemic [6] immune defences, these microorganisms, most commonly gram-negative enteric bacteria [7], may not be killed effectively and therefore can colo-

nise the ascitic fluid [4]. Presentation with SBP varies; some patients are asymptomatic and are diagnosed incidentally during large volume paracentesis [8], whereas others present with severe sepsis and multiorgan failure [9,10]. Despite vast improvements in the early diagnosis and treatment of SBP [11], the short-term prognosis is poor; in-hospital and 90-day mortality is 36% and 45% respectively [12].

The model for end-stage liver disease (MELD) is a widely used prognostic score in patients with cirrhosis. Originally designed to predict short-term survival following elective transjugular intrahepatic portosystemic shunt (TIPS) placement [13], it subsequently showed excellent ability to predict 90-day mortality in patients on the liver transplant waiting list in the United States [14,15]. Therefore, in 2002, MELD replaced Child-Turcotte-Pugh as the basis for prioritising donor livers to patients on the waiting list with the poorest short-term prognosis [16].

Outside of the context of donor liver allocation, MELD has also been validated as a prognostic score in multiple other cohorts: for example, to predict short-term mortality in cirrhotic patients undergoing elective and emergency surgery [17] and in alcoholic hepatitis [18].

Currently, the accuracy of the model for end-stage liver disease (MELD) and MELD-sodium (MELD-Na) as prognostic scores in cirrhotic patients with SBP is unclear.

Aims & Methods: This study aimed to evaluate and compare the accuracy of MELD and MELD-Na for predicting 90-day mortality and determine whether the mortality risk estimates they provide accurately reflect the poor prognosis of SBP patients. Cirrhotic patients with SBP were retrospectively identified from ascitic fluid samples sent for microscopy, culture and sensitivity analysis (1/1/18-31/12/20) and a previous audit. MELD and MELD-Na scores at diagnosis were calculated and associations with 90-day mortality were assessed using univariate analysis. Receiver operator characteristic curves were compared, and standardised mortality ratios (SMRs) were calculated by comparing the number of deaths observed to the number predicted by MELD and MELD-Na.

Results: Of the 567 patients identified, 15 cirrhotic patients with SBP were included. 90-day mortality was 66.7% (10/15). Only concurrent hyponatremia (<135mmol/L) was associated with mortality (6/10 non-survivors vs 0/5 survivors, $p=0.04$). The difference in MELD and MELD-Na's c-statistic was not significant: 0.66 (95% CI: 0.35-0.98) vs 0.74 (95% CI: 0.47-1.0) respectively ($p=0.72$). Patients with a MELD-Na >18.5 had significantly higher 90-day mortality than patients with MELD-Na ≤18.5 (88.9% (8/9) vs. 33.3% (2/6), $p=0.05$). The SMR (95% CI) for each MELD decile evaluated was 33.3 (0-79.5), 11.1 (0.2-22.0) and 3.4 (0-7.0) for scores ≤9, 10-19 and 20-29 respectively. For each MELD-Na tertile these were: 25 (0-59.6), 5.2 (0.1-10.3) and 2.7 (0.1-8.1) for scores <17, 17-26, ≥27 respectively.

Conclusion: In a small cohort of cirrhotic patients with SBP, the MELD's accuracy in predicting 90-day mortality was limited. MELD-Na's accuracy was higher but not significantly. Both scores consistently underestimated participants' mortality, therefore future studies could evaluate the accuracy of alternative prognostic scores in this patient group.

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Disclosure: Nothing to disclose.

P0725

TREATMENT AND OUTCOMES OF POST-BANDING ULCER BLEEDING AFTER PROPHYLACTIC ENDOSCOPIC BAND LIGATION

R. Medas¹, R. Liberal¹, R. Coelho¹, H. Cardoso¹, G. Macedo¹

¹Centro Hospitalar Universitário São João, Gastroenterology, Porto, Portugal

Contact E-Mail Address: renatogmedas@gmail.com

Introduction: Post-banding ulcer bleeding (PBUB) is a potential complication after endoscopic band ligation (EBL), with a reported incidence between 2-8%. Several endoscopic treatments have been described to manage PBUB, however, optimal management strategy remains undefined.

Aims & Methods: We aim to describe the management and outcome of patients presenting with PBUB after prophylactic EBL, defined as upper gastrointestinal bleeding within 30 days after EBL. All EBL procedures performed in a tertiary center, between 2015 and 2021, were analyzed retrospectively. Patients with noncirrhotic portal hypertension or submitted to EBL for treatment of acute variceal haemorrhage were excluded.

Results: 871 prophylactic EBL, performed in 281 patients, were included. PBUB occurred in 20 cases (2.3% of procedures; 18 patients) within a median time of 11 days (IQR 8-17). Most patients were male (94.4%) and median age was 58 years (IQR 50-69). 77.8% patients were Child-Pugh B.

Most PBUB occurred after primary prophylaxis (70.0%) and of those, 52.9% occurred after first EBL session. Endoscopic plus medical treatment (sucralfate plus pump proton inhibitors) was performed when high-risk stigmata were present (clot=6, visible vessel=2, active bleeding=3). Polidocanol was the preferred treatment (63.6%).

Despite a technical success of 100%, re-bleeding occurred in 5 cases (45.5%). The remaining cases received only medical therapy (clean base=9). Re-bleeding occurred in 33.3% of these patients. 4 patients (22.2%) died before home discharge for causes related to bleeding episode. 6 and 12-month mortality rate were 44.4% and 72.2%, respectively. Portal hypertensive bleeding and hepatocellular carcinoma were the main causes of death (38.9% and 22.2%, respectively).

Conclusion: Most cases of PBUB occurred in primary prophylaxis and after first EBL session. Re-bleeding was a frequent event, even after adequate endoscopic treatment, posing PBUB as a life-threatening complication. Our results reinforce the role of beta-blockers as the preferred method for variceal bleeding primary prophylaxis.

Disclosure: Nothing to disclose.

P0726

LATE-STAGE PRESENTATION OF CIRRHOSIS WITH DECOMPENSATION IS ALARMINGLY COMMON AND FAVORABLE OUTCOME IS ONLY OBSERVED WITH ETIOLOGIC THERAPY

M. Schwarz^{1,2,3}, C. Schwarz^{1,2,3}, W. Hübl⁴, M. Mandorfer^{2,3}, M. Gschwantler^{1,5}, T. Reiberger^{2,3}

¹Klinik Ottakring, Department of Internal Medicine IV, Vienna, Austria, ²Medical University of Vienna, Department of Internal Medicine III, Division of Gastroenterology and Hepatology, Vienna, Austria, ³Vienna HIV & Liver Study Group, Vienna, Austria, ⁴Klinik Ottakring, Department for Clinical Chemistry and Laboratory Medicine, Vienna, Austria, ⁵Sigmund Freud University, Vienna, Austria

Contact E-Mail Address: schwarz.medizin@gmail.com

Introduction: Advanced chronic liver disease (ACLD)/cirrhosis is often only diagnosed after the development of complications, when therapeutic options are generally limited. In our study we assessed clinical characteristics at first diagnosis of cirrhosis and its further course during etiologic and/or portal hypertension treatment.

Aims & Methods: Charts of patients presenting at a large, non-liver transplant center were reviewed for presence of esophageal varices in endoscopy, liver stiffness ≥ 15 kPa in elastography, or undergoing paracentesis for ascites to define the date of diagnosis of cirrhosis (at our center). Clinical, laboratory, and imaging data were collected at diagnosis (DG) and last follow-up (FU). The observation period was 01/2015 until 03/2020.

Results: 477 patients were included, 345 (72.3%) were male, and median age at diagnosis was 55 years. Most common etiologies were alcohol-related liver disease (ALD; n=211, 44.2%) and viral hepatitis (n=163, 34.2%). 105 patients (22.0%) presented with Child-Pugh C and 160 (33.5%) with MELD >15 ; 239 patients (50.1%) presented with at least one decompensation event (ascites, bleeding, encephalopathy) at DG. Median follow-up was 12 months (range 6-26 months).

In ALD patients, we observed an improvement in MELD (mean 17.4 to 11.6, $p<0.001$) and Child-Pugh score (CPS; mean 8.6 to 7.7, $p<0.001$), while in viral hepatitis patients overall there were no significant improvements during FU for MELD (mean 10.2 to 10.0, $p=0.26$) and for CPS (mean CPS 5.9 to 5.9, $p=0.35$). However, in patients with hepatitis C virus cirrhosis achieving virological cure (n=109/147, 74.1%), we observed significant improvements in liver stiffness (26.2 to 17.7 kPa, $p<0.001$) and in platelet count (147 to 169 G/L, $p<0.001$).

Overall, 17 patients (3.6%) were diagnosed with hepatocellular carcinoma at DG and 6 (1.3%) during FU. Eight patients received locally ablative therapy, and 3 received systemic therapies. Fourteen patients (2.9%) presented with portal vein thrombosis at DG and 7 (1.5%) developed PVT at a later date. Overall, 115 patients (24.1%) died during FU.

Conclusion: At a large non-liver transplant center, about 50% patients diagnosed with cirrhosis presented with decompensation at baseline. Liver cancer was mostly diagnosed in advanced stage without curative treatment options. This calls for action in terms of developing strategies for screening and early diagnosis of liver disease.

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P0727

FRAILITY IS INDEPENDENTLY ASSOCIATED WITH DEPRESSION AND MINIMAL HEPATIC ENCEPHALOPATHY IN CIRRHOSIS

C. El Khoueiry¹, S. Khazaka¹, B. El Khoury¹, K. Honein², R. Slim Karam¹, C. Yaghi³

¹Hotel Dieu de France University Hospital, Gastroenterology and Hepatology, Beirut, Lebanon, ²Hospital Hotel Dieu de France, Beirut, Lebanon, ³Hotel Dieu de France University Hospital, Gastroenterology, Beirut, Lebanon

Contact E-Mail Address: ber_kh712@hotmail.com

Introduction: Cirrhosis is believed to be associated with frailty and depression, and is often unrecognized. The relationship between frailty and depression in cirrhosis is poorly understood.

Quantifying disease burden for cognitive disorders and frailty is an important measure for predicting functional decline and adverse outcomes in cirrhosis.

Aims & Methods: The aim of this study is to assess the relationship between frailty and depression in cirrhotic patients, and other factors associated with the disease. This is a cross sectional study that included 57 cirrhotic patients over 18 years of age, enrolled from April 2020 to December 2021. These patients were hospitalized, seen in the endoscopy service for routine or therapeutic interventions, or seen in the clinics for follow up. Patients with neurological or psychiatric disease, severe cardiac or renal insufficiency, were excluded from the study.

The patients filled out a questionnaire containing the demographic and anthropometric characteristics (body mass index, circumference of the neck and the calf, age, sex), the etiology and complications of the cirrhosis (ascites, encephalopathy, Child Pugh score and the MELD Na), and the latest blood test (creatinine, albumin, bilirubin, Na, INR).

The presence of depression was assessed using the PHQ9 score. The frailty status was determined by using the frailty scale risk assessment score. One point was assigned for each component of the score: fatigue, resistance, ambulation, illness and loss of weight.

The presence of minimal hepatic encephalopathy was assessed using the animal naming test (ANT). Patients having a score ≥ 3 were classified as frail. All data collected from the questionnaires were introduced in a table and analyzed using statistical package for social science (SPSS) software. A level of $\alpha = 0.05$ was used to denote statistical significance. In order to establish the correlation between different variables, the Pearson correlation coefficient was used.

Results: We identified 15 (26.7%) frail patients. Compared with non-frail patients, the frail patients were older (68 in frail versus 59 in not frail, $p=0.038$), had higher neck circumference (39.7 in frail versus 35 in not frail, $p=0.025$), higher serum creatinine level (114 in frail versus 69 in not frail, $p=0.015$), and lower blood levels of sodium (134.8 in frail versus 137.1 in not frail, $p=0.032$) and albumin (31.4 in frail versus 35.8 in not frail, $p=0.038$).

Moreover, frail patients had higher MELD Na score (17.9 in frail versus 13.9 in not frail, $p=0.022$), higher Child Pugh score (66.7% of frail patients Child B or C versus 35.7% of not frail, $p=0.038$), and higher prevalence of ascites (73.3% of frail patients versus 14% of not frail, $p=0.007$).

Frailty score was strongly correlated with the PHQ9 score using the Pearson correlation ($r=0.725$, $p<0.001$), and moderately correlated with the MELD Na score ($r=0.449$, $p=0.002$). Severe depression was noted in 80% of the frail patients, versus 19.4% of the non-frail patients ($p<0.001$). Therefore, the frailty was strongly associated with the depression with an odds ratio of 16.57 (confidence interval 3.67-75).

In multivariate analysis, frailty was independently associated with the PHQ9 score ($\text{Exp}(\beta)=1.408$, $p=0.003$, confidence interval 1.125-1.763), and with the ANT ($\text{Exp}(\beta)=0.74$, $p=0.040$, confidence interval 0.555-0.987).

Conclusion: To sum up, frailty and depression are common in cirrhotic patients. Frailty in cirrhosis is independently associated with the depression and the minimal hepatic encephalopathy.

Disclosure: Nothing to disclose.

P0728

LIVER FRAILTY INDEX PREDICTS POOR OUTCOMES IN PATIENTS HOSPITALIZED FOR ACUTE DECOMPENSATION OF CIRRHOSIS

S. Incicco¹, R. Gagliardi¹, N. Zeni¹, M. Tonon¹, V. Calvino², C.G. Gambino², A. Brocca¹, P. Angeli³, S. Piano²

¹University of Padova, Department of Medicine-DIMED, Padova, Italy, ²University of Padova, Department of Medicine - DIMED, Padova, Italy, ³University-Hospital of Padova, DAIS di Medicina, Padova, Italy

Contact E-Mail Address: simone.incicco@gmail.com

Introduction: Physical frailty is highly prevalent in patients with end stage liver disease and has been associated with poor outcomes. Liver Frailty Index (LFI) is a standardized tool to assess frailty in patients with cirrhosis on liver transplant waiting list. However there is a paucity of data on the prognostic value of LFI in patients hospitalized for acute decompensation (AD) of cirrhosis.

Aims & Methods: We evaluated LFI in patients hospitalized for AD and the association of LFI with complications occurred during hospitalization and 90-day survival. We enrolled 117 consecutive patients admitted for AD of cirrhosis from 2019 to 2021. LFI was performed at the time of hospital admission. Occurrence of complications (hepatic encephalopathy [HE], sepsis, organ failures, ACLF) during hospitalization was recorded. Patients were followed up until death, liver transplant or 90 days.

Results: mean age and MELD-Na were 64 ± 10 and 20 ± 7 , respectively. The majority of patients were male (71%) and had alcohol-related cirrhosis (56%). Median LFI was 6.1 (IQR 5.0 – 6.5). LFI showed a weak, but significant, correlation with age ($r=0.202$; $p=0.029$), MELD-Na ($r=0.292$; $p=0.001$) and parameters of systemic inflammation such as C-Reactive Protein ($r=0.235$; $p=0.014$) and white blood cell (WBC) count ($r=0.207$; $p=0.025$). LFI was significantly higher in patients developing hepatic encephalopathy, sepsis, renal failure, circulatory failure, respiratory failure and ACLF than in those who did not. Patients transferred to the ICU had significantly higher LFI than those who did not.

LFI was significantly higher in patients who died than in those who survived during hospitalization (median=6.5 [IQR=6.0-6.7] vs 6.0 [IQR 4.8-6.5]; $p=0.006$) and at 90 days (6.45, IQR 6-6.64 vs 5.87, IQR 4.81-6.37; $p=0.001$). In multivariate analysis LFI was an independent risk factor of 90-day mortality (HR=1.88, 95% CI 1.07-3.32; $p=0.028$), as well as MELD-Na (HR=1.11, 95% CI 1.04-1.18; $p=0.01$) and WBC(HR=1.08, 95% CI 1.00-1.17, $p=0.046$).

Conclusion: In patients with cirrhosis hospitalized for AD, LFI identifies patients at higher risk of worse outcomes and can be used for the assessment of frailty in these patients.

Disclosure: Nothing to disclose.

P0729

DISTURBANCES IN SODIUM AND CHLORIDE HOMEOSTASIS PREDICT OUTCOMES IN STABLE AND CRITICALLY ILL PATIENTS WITH CIRRHOSIS – NOT TWO SIDES OF THE SAME COIN

G. Semmler^{1,2}, B. Scheiner^{1,2}, R. Paternostro^{1,2}, B. Simbrunner^{1,2}, L. Balcar^{1,2}, M. Pinter^{1,2}, M. Trauner¹, M. Mandorfer^{1,2}, C. Zauner¹, T. Reiberger^{1,2}, G.-C. Funk^{3,4}

¹Medical University of Vienna, Department of Internal Medicine III, Division of Gastroenterology and Hepatology, Vienna, Austria, ²Medical University of Vienna, Vienna Hepatic Hemodynamic Lab, Division of Gastroenterology and Hepatology, Department of Internal Medicine III, Vienna, Austria, ³Klinik Ottakring, Department of Internal and Respiratory Medicine, Vienna, Austria, ⁴Karl-Landsteiner-Institute for Lung Research and Pulmonary Oncology, Vienna, Austria

Contact E-Mail Address: georg.semmler@meduniwien.ac.at

Introduction: Serum electrolyte disturbances are common in cirrhosis. Hyponatremia has profound prognostic implications, and thus, has been incorporated in the 2016 update of the UNOS MELD. Changes in serum chloride (Cl) are thought to be interrelated, however, are less well studied in the context of cirrhosis.

Aims & Methods: We investigated the prognostic utility of Na- and Cl-changes on hepatic decompensation/liver-related mortality in patients with stable cirrhosis as well as on ICU mortality in critically ill patients with cirrhosis.

Therefore, 891 patients with stable cirrhosis managed at the Vienna General Hospital between 2003-2020 were included in *cohort I*. 181 critically ill patients with cirrhosis admitted to ICUs at the Vienna General Hospital between 2004-2007 were recruited for *cohort II*. Hypo-/hyper-Na (normal range: 136-145mmol/L) and hypo-/hyper-Cl (normal range: 98-107mmol/L) were assessed.

Results: *Cohort I:* 68% male patients with a median UNOS MELD of 11 (9-17) were included (Child-Pugh-stages A/B/C: 46%/38%/16%). Na and Cl levels were significantly interrelated (Pearson's $r=0.63$, $p<0.001$).

Hypo-/hyper-Na were present in 29%/0% and hypo-/hyper-Cl in 15%/9%. The median follow-up was 59.9 months during which 445 patients (50%) experienced hepatic decompensation/liver-related death. Cl showed a linear association with hepatic decompensation/liver-related mortality on multivariable Cox regression analysis adjusting for age, HVP, albumin, MELD (adjusted average hazard ratio [HR] per mmol/L: 0.972, 95% confidence interval, [95%CI]: 0.949-0.996, $p=0.022$). In line, hypo-Cl was significantly associated with hepatic decompensation/liver-related mortality (adjusted average HR: 1.553, 95%CI: 1.149-2.098, $p=0.004$).

Cohort II: 70% male patients had a median MELD of 31 (22-39) at ICU admission (92% with Child-Pugh-stage C). Again, Na and Cl levels were strongly correlated (Pearson's $r=0.82$, $p<0.001$).

Hypo-/hyper-Na was present in 47%/7% and hypo-/hyper-Cl in 30%/25%. ICU-mortality was 50% after a median of 6 (5-7) days. While the effect of Na on ICU mortality was U-shaped in restricted cubic spline analyses, it seemed to be rather linear for Cl with a worse prognosis in patients with hypo-Cl.

In univariable logistic regression analyses, patients with hypo-Cl (odds ratio [OR]: 3.039, 95%CI: 1.569-6.075, $p=0.001$), but not hypo-Na had a significantly worse ICU survival, which was confirmed after adjusting for hypo-/hyper-Na and MELD (aOR CI: 1.267-7.659, $p=0.014$).

Conclusion: Even though Na and Cl levels are strongly interrelated in cirrhosis, the presence and severity of hypochloremia provides incremental prognostic information – especially in critically ill patients with cirrhosis.

Disclosure: Nothing to disclose.

P0730

MCP1, CRP AND PROCALCITONIN AS NOVEL DIAGNOSTIC MARKERS IN CIRRHOTIC PATIENTS WITH SPONTANEOUS BACTERIAL PERITONITIS

M. Yousry¹, Y. Aboamer², S. Abd-Elsalam³, W. Salah⁴, M. Badr⁵, H. Eldeeb⁶, A. Adaroas⁶, R. Abdelmonem⁷, H. Abostate⁸, A. Ahmed⁹, G. Soliman¹

¹Faculty of Medicine for Boys, Al-Azhar University, Hepatology, Gastroenterology and Infectious Diseases, Cairo, Egypt,

²Mahala Hepatology Teaching Hospital, Hepatology, Gastroenterology and Infectious Diseases, Gharbia, Egypt,

³Faculty of Medicine, Tanta University, Tropical Medicine Department, Tanta, Egypt, ⁴National Institute of Diabetes and Endocrinology, Internal Medicine, Cairo, Egypt, ⁵Faculty of medicine, Cairo University, Internal Medicine, Cairo, Egypt, ⁶El Sahel Teaching Hospital, Clinical and Chemical Pathology, Cairo, Egypt, ⁷Faculty of Pharmacy, Cairo University, Microbiology and Immunology, Cairo, Egypt, ⁸Faculty of Pharmacy, Egyptian Russian University, Microbiology, Cairo, Egypt, ⁹National Hepatology and Tropical Medicine Research Institute, Biochemistry Department, Cairo, Egypt

Contact E-Mail Address: doctor_gemy@yahoo.com

Introduction: Early diagnosis of spontaneous bacterial peritonitis (SBP) especially in asymptomatic patients is based on a high index of suspicion and associated with a better outcome. Although the gold standard for diagnosis is based on polymorphonuclear leukocyte count $\geq 250/\text{mm}^3$ in ascitic fluid with or without positive ascitic culture, we still need rapid and reliable inflammatory markers for diagnosis of SBP.

Aims & Methods: The aim of the study was to evaluate serum c-reactive protein (CRP), ascitic procalcitonin (PCT) and monocyte chemotactic protein-1(MCP-1) in the diagnosis of spontaneous bacterial peritonitis (SBP) in cirrhotic patients. A cross-sectional analytic study that included 199 patients with decompensated cirrhosis (101 with SBP and 98 without SBP). Patients were classified according to Child-Pugh criteria. Ascitic PCT and MCP-1 were measured by enzyme-linked immunosorbent assay. Serum CRP, liver and renal functions were assessed.

Results: The three markers are significantly elevated in SBP patients than those without ascites. Using the ROC curve at AUC 0.883 and a cut-off value of $>186 \text{ ng/ml}$, the diagnostic performance of ascitic MCP-1 level was higher than CRP (AUC 0.562) and ascitic fluid procalcitonin (AUC 0.751) in the diagnosis of SBP. The sensitivity and specificity were 86.15% and 79.59 % at the cutoff of 186 ng/ml for MCP-1, 65.4 and 75.5 at $\geq 1 \text{ ng/ml}$ for PCT, and 52.5 and 64.3, at 11.2 mg/dl for CRP respectively.

Conclusion: Ascitic MCP-1 has a better diagnostic value with higher sensitivity and specificity in SBP diagnosis compared to CRP and procalcitonin which has higher diagnostic accuracy than CRP.

Further studies with a large number will be necessary to evaluate the usefulness of these markers in diagnosis, follow-up and relation to morbidity and mortality of SBP patients.

Disclosure: Nothing to disclose.

P0731

CLINICAL OUTCOMES OF CRYPTOGENIC COMPARED WITH VIRAL CIRRHOSIS

Z. Benzarti¹, B. Bouchabou¹, M. Kefi¹, S. Chtioui¹, A. Nakhli¹, N. Hemdani¹, R. Ennaifer¹

¹Mongi Slim Hospital, Department of Hepatology, Marsa, Tunisia

Contact E-Mail Address: zeinebbenzarti9@gmail.com

Introduction: Cryptogenic cirrhosis (CC) is the end stage of a chronic liver disease in which its underlying etiology remains unknown after extensive clinical, serological, and pathological evaluations. Since identification of non alcoholic steato-hepatitis (NASH), many CC have been reclassified to post-NASH cirrhosis.

Models of the natural history of cirrhosis are based on findings in individuals with viral or alcoholic cirrhosis and the outcome of CC is far less characterized than cirrhosis with a definite etiology.

Aims & Methods: To characterize natural history of cryptogenic cirrhosis (CC) and compare its clinical features and outcomes to those of viral related cirrhosis.

Between 2019 and 2020, we identified all patients with a diagnosis of cryptogenic or viral cirrhosis. The criteria for the exclusion of diagnosis of CC were: cases with histological clear-cut features of fatty changes and cirrhosis with definite etiology such as: excessive alcohol consumption, HCV antibody positivity, hepatitis B surface antigen positivity, autoimmune hepatitis, primary biliary cirrhosis, primary sclerosing cholangitis or genetic liver diseases.

The following outcomes were assessed: severity of liver disease at the time of first diagnosis; liver decompensation (*i.e.*, at least 1 episode of ascites, encephalopathy, or variceal bleeding either at presentation or during follow-up); HCC diagnosed according to current guidelines and death. Cardiovascular events, particularly the presence of coronary artery disease, were recorded. SPSS version 26.0 was used for the descriptive and comparative analysis.

Results: A total of 77 patients with cirrhosis were enrolled (cryptogenic $n = 35$; viral $n = 42$). Compared with viral cirrhosis, patients with CC were older (mean age 63 vs 59 years, $p = 0,04$) and had a significantly higher prevalence of overweight/obesity, hypertension, dyslipidemia and gallstone disease ($p = 0,04$; $p = 0,028$; $p = 0,004$ and $p = 0,01$ respectively). Over a median period of 19 months of follow up, hepatocellular carcinoma development was more observed in viral cirrhosis group (74 % vs 29% in CC patients, $p < 0,001$).

On the other hand, there was no significant difference in terms of liver decompensation ($p = 0,96$). Patients with CC exhibited a significantly higher prevalence of cardiovascular events ($p = 0,02$). Kaplan Meier survival analysis showed no significant differences in survival between both types of cirrhosis for all grades of severity.

Conclusion: Comparatively to viral cirrhosis, patients with CC have more frequently features of metabolic syndrome and a higher risk of developing cardiovascular events and thus a poor prognosis owing to non liver-related morbidity. Our study confirms that CC likely results from the progression of unrecognised NASH in a large proportion of cases.

Disclosure: Nothing to disclose.

P0732

MALNUTRITION IN PATIENTS WITH CHRONIC LIVER DISEASE UNDERGOING INPATIENT LIVER TRANSPLANT EVALUATION

K. Cooper¹, D. Devuni²

¹University of Massachusetts Medical School, Worcester, United States, ²University of Massachusetts Medical School, Gastroenterology and Hepatology, Worcester, United States

Contact E-Mail Address: katherine.cooper@umassmed.edu

Introduction: Malnutrition is a known complication of cirrhosis and a predictor of post-operative mortality in liver transplantation. We aimed to identify predictors of malnutrition in patients with chronic liver disease (CLD) undergoing inpatient liver transplant evaluation (LTE) and assess the effect of malnutrition on outcomes in the liver transplantation evaluation outcomes.

Aims & Methods: Medical records for all patients undergoing ILTE between 10/15/2017 and 8/3/2021 were reviewed. Those patients with CLD undergoing inpatient LTE for first transplant were included in the study; patients with a history of liver transplant or in fulminant liver failure were excluded. Demographics, past medical history, and transplant evaluation details were collected using RedCAP. Patients were categorized by nutritional status as determined by the transplant nutritionist at the time inpatient LTE (Malnutrition vs. No Malnutrition). Issues with skin integrity included pressure ulcers and moisture associated skin damage. Outcomes included: 1) Overall outcome [Dead, Transplanted and 32) Listing outcome [listed at some point vs. never listed]. Variables were compared using Fisher's exact test and student's T-tests. Predictors for malnutrition were assessed using multivariable linear regression. Significance was evaluated at $p=0.05$ given low participant number in the malnourished group.

Results: One hundred and fifty-nine patients, mean age 57.7 were included and one in three were diagnosed with malnutrition (33.9%). There were no differences in age, gender, disease etiology, or MELD-Na between groups. Patients without malnutrition tended to have ACLF grade higher than Grade 2 more often (42.9% vs. 29.6%, $p=0.10$) and had higher BMI (33.2±9.9 vs. 27.6±7.1, $p<0.001$). Overall outcome did not differ by malnutrition status, but patients with malnutrition tended to be listed for liver transplant less often than those without malnutrition (86.4% vs. 95.3%). Patients with malnourishment were more likely to have issues skin integrity (33.1% vs. 17.1%, $p=0.02$) and a recent significant weight loss (51.9% vs. 17.1%, $p<0.0001$). In a model including age, gender, disease etiology, BMI, history of low albumin and previous hepatic decompensations, the following were predictors of being diagnosed with malnutrition during inpatient LTE: BMI ($p=0.05$), a prior episode of spontaneous bacterial peritonitis ($p=0.03$), and having known varices by imaging or EGD ($p=.03$)

		Malnutrition (n=54)	No Malnutrition (n=105)
Outcomes	Dead	24.1%	34.3%
	Transplant	44.4%	35.2%
	Listed at any point	86.4%	95.3
Demographics	Gender (%Male)	63%	55.20%
	BMI	27.6	33.2
	MELD-Na (Points)	28.22	26.57
	ACLF Grade ≥ 2	70.4%	57.1%
	Alcohol associated liver disease	57.4 %	43.8 %

Table.

Conclusion: Malnutrition may impact likelihood to be listed for transplant in patients with CLD who require inpatient LT evaluation. However, once approved, malnutrition may not negatively impact transplant rate in this

population. Of the hepatic decompensations, patients with a history of spontaneous bacterial peritonitis may be at increased risk for malnutrition, which may reflect the impact that malnutrition has on immune regulation.

Disclosure: Nothing to disclose.

P0733

MIRNA 203 AS AN EARLY PREDICTIVE MARKER FOR GENOTYPE 4 HCV INDUCED HCC

M. Elzallat¹, M. Hassan¹, E. El-Ahwany¹, H. Abu-Taleb², N. Amin³, M. Zoheiry¹

¹Theodor Bilharz Research Institute, Immunology & Therapeutic Evaluation Department, Giza, Egypt, ²Theodor Bilharz Research Institute, Environmental Research Department, Giza, Egypt,

³Theodor Bilharz Research Institute, Department of Haematology, Giza, Egypt

Contact E-Mail Address: zallatzallat@gmail.com

Introduction: Hepatitis C virus (HCV) infection is a significant cause of morbidity and mortality worldwide. HCV infection inflames the liver which, if untreated, will inevitably result in fibrosis and then progress to cirrhosis which has many co-morbid complications such as hepatocellular carcinoma (HCC). Cancer stem cells (CSCs) are a small subpopulation in cancer, have been proposed to be cancer-initiating cells, and be responsible for chemotherapy resistance and cancer recurrence.

The identification of CSC subpopulations inside a tumor presents a new understanding of cancer development because it implies that tumors can only be eradicated by targeting CSCs.

Aims & Methods: This study was conducted to assess the use of miRNA 203 in circulating liver CSCs as non-invasive predictive and early diagnostic markers in genotype 4 HCV-induced HCC. 150 patients with chronic hepatitis C (CHC) were participated in this study and divided into 3 groups: 1) HCV group: 50 patients infected with HCV without cirrhosis, 2) Liver cirrhosis group: 50 patients infected with HCV with liver cirrhosis, 3) HCC group 50 patients infected with HCV and cirrhosis. 50 normal controls were also included in the current study.

Peripheral blood mononuclear cells were separated by the gradient density separation method and assessed for the presence of EpCAM/CD44 as markers for CSCs. Total RNA was extracted from these cells and miRNA 203 was relatively quantified by real-time PCR. The receiver operating characteristics curve (ROC) and confidence interval (CI) of miRNA 203 were established to discriminate HCV-induced HCC from CHC.

Results: Our results showed that the relative expression of miRNA 203 was significantly decreased ($p<0.001$) in the HCC group when compared to the liver cirrhosis group and the HCV group. miRNA 203 had a sensitivity of 100%, specificity of 97.5%, and AUC of 0.987 (95% CI: 0.88 – 1.0), suggesting that measuring miRNA 203 level could be a promising non-invasive predictive early diagnostic marker for HCC development in patients with CHC.

Conclusion: miRNA 203 could be used as a predictive marker for HCC in Egyptian people with CHC.

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Disclosure: Nothing to disclose.

P0734

HIGH SERO-PREVALENCE OF HEPATITIS E VIRUS AMONG HEALTHY ASYMPTOMATIC BLOOD DONORS IN PAKISTAN: CAN THE RISK OF TRANSFUSION DEPENDENT TRANSMISSION BE IGNORED?

A. Rahat¹, L. Kamani¹

¹Liaquat National Hospital, Gastroenterology and Hepatology Department, Karachi, Pakistan

Contact E-Mail Address: adeelrahat@gmail.com

Introduction: Hepatitis E Virus (HEV) is now recognized as a major public health issue, causing over 20 million infections every year worldwide and accounting for approximately 70,000 deaths^[1].

HEV-RNA prevalence in blood donors was reported at one per 600 to 800 donations in Germany and The Netherlands^[2,3]; and seroprevalence, documenting prior exposure, as high as 52 percent in Southwestern France^[4,5]. It has been estimated that the mortality rates for HEV infections in pregnant women and young people are about 20% and 3%, respectively^[6]. Transfusion of blood products (cellular and plasma) is a frequent, potentially life-saving medical treatment. The safety of blood products has been a concern. Subsequently, testing for HIV, HBV and HCV has been implemented in Pakistan.

There is emerging evidence that HEV can be transmitted by transfusion of different types of blood-derived products. Immunosuppressed individuals, organ transplant recipients, hemodialysis patients, and pregnant women are at a high risk of developing life-threatening diseases, including chronic hepatitis and acute liver failure, after infection with HEV^[7,8].

Chronic hepatitis E can progress to chronicity, resulting in liver failure with life-threatening complications. Till the availability of vaccine, HEV-RNA testing is the only effective mitigation to prevent transfusion-transmission. Immunosuppressed individuals and pregnant women are at higher risk of developing acute liver failure and chronic hepatitis secondary to HEV. HEV is endemic in Pakistan and routine screening of blood donors for HEV has not yet been implemented in Pakistan and other endemic South Asian countries. There is dearth of literature regarding the sero-prevalence and viremia of HEV among healthy blood donors.

Aims & Methods: A cross-sectional study was conducted at Liaquat National Hospital, Karachi, Pakistan to assess sero-prevalence and viremia of HEV among healthy blood donors in a tertiary care set-up. Blood samples were obtained for HBsAg, Anti-HCV Antibody, Anti-HIV Antibody, Syphilis, Malaria, ALT and HEV antibodies (IgG and IgM by ELISA kits (Novalisa by Novatec immundiagnostica GmbH)) after written informed consent. Positive samples for anti-HEV IgM were subjected to detect HEV-RNA by real-time reverse transcription polymerase chain reaction assay (RealStar® HEVRT-PCR Kit 2.0 by Altona Diagnostics).

Results: Total of 515 adult participants were enrolled with a mean age of 30.08 ± 7.56 years. Mean ALT levels of 43.05 ± 32.45 IU/L were observed. Anti HEV IgG was positive in 365 participants (70.9%) with ALT levels of 43.61±34.03. 31 participants (6%) were positive for Anti HEV IgM with ALT levels of 44.06±69.21. All IgM positive were subjected to PCR testing which came out negative (PCR detection limit >18 copies/mL). Patients who tested positive for HBsAg, Anti-HCV Ab, Syphilis and HIV were 11 (2.1%), 9 (1.7%), 9 (1.7%) and 0 (0%) respectively.

Serology	Results (Total number of participants : 515)
Anti HEV IgM	31 (6%)
Anti HEV IgG	365 (70.9%)
HBsAg	11 (2.1%)
Anti-HCV Ab	9 (1.7%)
Syphilis	9 (1.7%)
Anti HIV Ab	0 (0%)

Conclusion: High sero-prevalence of Anti HEV IgM among healthy blood donors emphasizes the need for further studies and robust measures of routine screening for HEV of all blood products in endemic countries to prevent transfusion dependent transmission with special consideration when the recipients are either immunocompromised or pregnant.

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P0735

OSEPHAGEAL VARICEAL RECURRENCE 4 YEARS BEYOND ENDOSCOPIC BAND LIGATION IN HEPATITIS C PATIENTS WHO ACHIEVED SUSTAINED VIROLOGICAL RESPONSE WITH ORAL DIRECT ACTING ANTIVIRAL THERAPIES

E.-S. Ibrahim¹, M. Abdel-Samiee¹, M.I. Youssef², H.M. Elshazly¹, A.-E.A. A.El-Gendy², A. Ahmed Sakr³, D. Elwazzan⁴, A.G. Badran⁵, M.R. Nassar⁶, A.A. Elshormilisy⁷, A. Madkour⁸, M. Kamal⁷, Y.M. Amrousy⁷, S.W. Elkhadry⁹, E. Abdelsameea¹

¹National Liver Institute-Menoufia University, Hepatology and Gastroenterology, Shebin El-Kom, Egypt, ²Al-Azhar University, Nasr City, Egypt, ³Kasr Al Ainy Teaching Hospital, Cairo, Egypt, ⁴Alexandria University, Alexandria, Egypt, ⁵Specialized Medical Center-Damas Liver Center, GIT and Hepatology, Mansoura, Egypt, ⁶Menoufia University, Shebeen El Kom, Egypt, ⁷Helwan University, Helwan, Egypt, ⁸Helwan University, General Administration of Medical Affairs, Cairo, Egypt, ⁹National Liver Institute-Menoufia University, Shebin El-Kom, Egypt

Contact E-Mail Address: prof_abdo1985@yahoo.com

Introduction: Oral Direct-acting antivirals (DAAs) are safe, highly effective altering disease burden and prognosis in hepatitis C patients. Sustained virologic response (SVR) is achieved nowadays in more than 90% of the treated patients and related to the improvements in functions of the liver, fibrosis plus survival. Furthermore, portal hypertension is thought to be improved with achievement of virological response, parallel to the improvements in hepatic inflammation and fibrosis.

Aims & Methods: We aimed to assess the recurrence rate of oesophageal varices by long-term follow-up in patients treated with different DAAs regimens who had achieved SVR. We studied 176 Child A cirrhotic HCV pa-

tients who achieved SVR after DAAs treatment and had a history of endoscopic oesophageal varices obliteration and were on maximum tolerated propranolol dose. They were subjected to follow-up upper gastrointestinal endoscopy repeated every 6 months for 4 years.

Results: Fifty-two patients (29.5%) had recurrence of oesophageal varices observed during the 4-years follow-up upper GIT endoscopy. On multivariate analysis, platelet count was the only significant variable, P-value = .007*. HbA1C, HOMA IR, BMI 1 and BMI 2 showed non-significant differences between the studied groups.

By ROC analysis, we identified baseline platelet count of 96 000/ μ L with 100% sensitivity (95% confidence interval [CI] [91%-100%]) and 74% specificity (95% CI [65%-81%]). Spearman correlation showed a positive correlation between AFP, age, AST, Bilirubin, creatinine, INR.

Exp (B)	P-Value	Df	Wald	S.E.	B	
1.918	0.336	1	0.924	0.678	0.651	Sex
1.000	0.007*	1	4.275	0.000	0.000	Platelet count
1.000	0.340	1	0.912	0.000	0.000	TLC
1.167	0.968	1	0.002	3.896	0.154	BILIRUBIN
0.053	0.253	1	1.305	2.576	-2.944	ALBUMIN
.9470	0.13	1	7.319	.200	-0.055	AST level
0.000	0.176	1	1.832	10.307	-21.312	CREATININE
77.405	0.450	1	0.571	5.755	4.349	INR

AST: aspartate aminotransferase TLC: Total leucocytic count
INR: International normalized ratio

Table 1. Multivariate regression analysis for predicting recurrence of esophageal varices.

Conclusion: Patients who achieved SVR post DAAs showed a significant decrease in oesophageal varices recurrence post endoscopic obliteration. Baseline platelet count was found to be a strong independent predictor for oesophageal varices recurrence.

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P0736

CLINICAL SPECTRUM AND OUTCOMES OF PATIENTS WITH SEVERE SPONTANEOUS HEPATITIS B FLARES AND REACTIVATION

A. Jindal¹

¹Institute of Liver and Biliary Sciences, Hepatology, New Delhi, India

Contact E-Mail Address: ankur.jindal3@gmail.com

Introduction: Reactivation of hepatitis B presenting as acute hepatic flare can have variable outcomes; acute hepatic insult (serum bilirubin > 5 mg/dl and INR >1.5) alone (*pre-ACLF*) or with the development of new ascites or hepatic encephalopathy (HE) within 4 weeks (*ACLF-B*), which connotes high mortality. The clinical outcome of hepatitis B flare in decompensated cirrhosis is largely unknown.

Aims & Methods: Patients with pre-ACLF, ACLF-B and hepatitis B flares in decompensated cirrhotics (DC flare) were compared for clinical, biochemical, serological and virological parameters. Patients with hepatitis B related acute liver failures were excluded. All patients received potent antivirals and standard medical therapy; none underwent liver transplantation.

Results: 827 consecutive patients (Mean age – 47.1 + 16 years; Male: Female – 4:1) with acute hepatic insult presented with pre-ACLF, ACLF-B and DC flare – 23.9%, 53.3% and 22.7% respectively.

Almost 15% patients with ACLF-B had superimposed hepatic insults [alcoholic hepatitis (n=23), drug-induced liver injury (n=31) and hepatitis E superinfection (n=14)]. Baseline mean HBV DNA (Log 5.4 IU/ml), HbsAg (Log 3.6 IU/ml) levels and positive HBeAg rates (49.5%) were comparable among the groups and did not independently predict mortality.

Patients with pre-ACLF compared to ACLF-B had higher baseline ALT (median - 850 IU/L vs. 140 IU/L; p<0.01) with higher rates of HBeAg (34.6% vs. 7.7%; p<0.01) and HbsAg seroconversion (11.6% vs. 1.1%, p<0.05) at 6 month. In comparison to DC flare, ACLF-B had higher baseline HVP (19.4 + 2.6 vs. 15.2 + 2.4 mm Hg; p<0.007) and liver related complications including HE (42.4% vs. 18.1%, p<0.01), acute kidney injury (32.9% vs. 18.6%, p<0.01) and sepsis (51.2% vs. 22.9%, p<0.01).

Mortality at 3-month was highest in ACLF-B group (45.1%) than in DC flare (18.6%) and pre-ACLF (1%), p<0.05. Presence of sepsis (HR-6.4) and HE (HR-2.7) were independent predictors of mortality.

Conclusion: More than one-half of symptomatic hepatitis B flares have ACLF. Hepatitis B DNA or HBeAg at baseline or follow-up did not predict clinical outcomes. Hepatitis B flares in decompensated cirrhosis are different from ACLF-B. Presence of ACLF-B warrants careful monitoring and need for early liver transplantation. New-onset HE and sepsis were independently associated with high mortality.

Disclosure: Nothing to disclose.

P0737

CLINICAL COURSE AND PREDICTORS OF OUTCOME OF SEVERE HEPATITIS B REACTIVATION PRESENTING WITH NEW-ONSET ASCITES

A. Jindal¹

¹Institute of Liver and Biliary Sciences, Hepatology, New Delhi, India

Contact E-Mail Address: ankur.jindal3@gmail.com

Introduction: Reactivation of hepatitis B (HBVr) presenting as acute icteric flare can have variable presentations. New-onset ascites in patients with HBVr might predispose to bacterial infections, hepatic encephalopathy (HE) and acute kidney injury (AKI). Predictors and outcomes of HBVr with ascites are largely unknown.

Aims & Methods: Icteric HBVr patients, with or without new-onset ascites were enrolled. HBVr was diagnosed based on AASLD 2018 recommendations. All patients received potent antivirals, and were followed for further complications and outcomes.

Results: Of 347 patients (mean age- 49.2±14.7 years; M: F- 4:1; mean HBV-DNA- 4.2 Log₁₀ IU/ml, 48.5% HBeAg +), 242 (69.7%) had ascites at presentation. Despite comparable baseline HBV DNA and quantitative HBsAg levels, patients with new onset ascites compared to no ascites were older and had more frequent large esophageal varices (13.3% vs. 2%; p-0.001), higher baseline HVPg (15.3 ± 5.9 mmHg vs. 9.9 ± 4.7 mmHg; p-0.001) and MELD score (27.5 ± 6.9 vs. 22.3 ± 5.2; p-0.02).

None of the patients without ascites had cirrhosis on biopsy. HVPg ≥12 mmHg alone was independently associated with ascites (area under ROC: 0.78; 95% CI: 0.66-0.89). Each 1 mmHg change in HVPg increased the probability for ascites by 30% (p-0.002; 95% CI: 1.09-1.52).

Patients with HBVr and ascites had more complications during hospital course (Hepatic encephalopathy- 37.6% vs. 6.7%, pneumonia- 11.2% vs. 1.9%, acute kidney injury- 38.4% vs.12.4% and variceal bleed- 8.7% vs. 1%; all p<0.01) as well as higher mortality (40.1% vs. 8.6%; p-0.001). Presence of HE (OR: 4.7, p-0.001), pneumonia (OR: 10.3, P-0.003), MELD ≥26.5 (OR: 1.12, p-0.01) and total leucocyte count ≥9.9x10³ per cu.mm (OR: 1.09, p-0.04) were independent predictors of mortality.

Among those who survived, 26 (7.5%) patients lost HBsAg by 12 months. Despite higher ALT flare in patients without ascites (762 U/L (227-1554) vs. 138 U/L (74-295); p<0.01), loss of HBV DNA at the end of 4 week was unrelated to presence of ascites (70.1% vs. 63.3%; p-0.2) and outcomes.

Conclusion: Acute rise in portal pressure following hepatocellular necrosis is associated with development of ascites in patients with severe reactivation of hepatitis B. Early recognition of these "high risk" patients who have underlying chronic liver disease or cirrhosis (acute-on-chronic liver failure) is important to prevent organ failure, development of complications and list them for liver transplantation.

Disclosure: Nothing to disclose.

P0738

OCCULT HEPATITIS C AFTER DIRECT ACTING ANTI VIRAL, A STUDY IN A COHORT OF EGYPTIAN PATIENTS

E. Habba¹, T. elbedewy², R. Elkholy³

¹Tanta Faculty of Medicine and Tanta University Hospitals, Tropical Medicine, Hepatology and Gastroenterology, Tanta, Egypt, ²Tanta Faculty of Medicine, Internal Medicine, Tanta, Egypt, ³Tanta Faculty of Medicine, Clinical pathology, Tanta, Egypt

Contact E-Mail Address: eah2007@yahoo.com

Introduction: Hepatitis C virus (HCV) is a common viral infection affecting over 180 million persons all over the world. DAAs (Direct acting antivirals) may improve thrombocytopenia after achieving sustained virologic re-

sponse (SVR), but some patients may be manifested with thrombocytopenia after SVR. The aim of our study was to evaluate the presence of OCI in the peripheral blood mononuclear cells (PBMCs) in thrombocytopenic patients after achieving SVR with DAAs.

Aims & Methods: This cross-sectional study included 32 thrombocytopenic patients who achieved SVR with DAAs and 32 HCV-infected patients who achieved SVR with DAAs without thrombocytopenia as a control group. All patients were investigated for HCV-ribonucleic acid (RNA) in PBMCs (peripheral blood mononuclear cells), hepatitis C virus core antigen (HCV cAg), platelet autoantibodies, and serum thrombopoietin.

Results: Among thrombocytopenic, non-thrombocytopenic, and both groups, HCV-RNA in PBMCs were detected in 40.63, 6.25, and 23.44%, respectively, although HCVcAg was detected in 31.25, 3.13, and 17.19%, respectively. The comparisons between thrombocytopenic and nonthrombocytopenic patients regarding HCV-RNA in PBMCs and HCVcAg were statistically significant.

Conclusion: Our study is the first to provide insights into the relationship between occult hepatitis C and thrombocytopenia in patients with chronic hepatitis C virus infection after achieving sustained virologic response with direct-acting antivirals. The association between occult hepatitis C and thrombocytopenia may be explained by auto-immune mechanism due to the development of platelet auto-antibodies.

A complete eradication of HCV after SVR seems to be doubtful in spite of significantly improvement in DAAs efficacy due to occult C occurrence in other body compartments. Consequently, we recommend testing for occult C infection by HCV-RNA in PBMCs and/or HCVcAg in addition to serum HCV-RNA testing at the end of DAAs therapy before confirmation of SVR.

Disclosure: Nothing to disclose.

P0739

ELIMINATE: A PCR RECORD-BASED HCV MACRO-ELIMINATION PROJECT IN AUSTRIA

D. Bauer^{1,2,3}, C. Schwarz^{1,2,3}, L. Dorn⁴, M. Jachs^{1,2}, L. Hartl^{2,1}, D. Chromy^{2,5}, L. Weseslindtner⁶, N. Pfisterer^{7,1,2}, B. Hennlich⁷, R. Strassl⁸, A. Voill-Glaninger⁹, W. Hübl¹⁰, M. Willheim¹¹, K. Köhrer¹², S. Jansen-Skoupny¹³, S. Tomez¹⁴, W. Krugluger^{14,15}, C. Mad^{16,17}, M. Schwarz^{1,2,3}, L. Brinkmann^{1,2,3}, L. Burghart^{1,2,3}, L. Antonitsch¹⁸, G. Weidinger¹⁸, F. Riedl⁴, H. Laferl¹⁹, V. Kurteva¹⁹, M. Traugott¹⁹, C. Wenisch¹⁹, A. Aburaia²⁰, C. Sebesta^{20,21}, D. Schmidt²², S. Rothweiler²³, J. Remetic²³, A. Maieron⁴, M. Gschwantler^{3,17}, T. Reiberger^{2,1}

¹Medical University of Vienna, Division of Gastroenterology and Hepatology, Department of Medicine III, Vienna, Austria, ²Medical University of Vienna, Vienna HIV & Liver Study Group, Vienna, Austria, ³Klinik Ottakring, Department of Internal Medicine IV, Vienna, Austria, ⁴University Hospital of St. Pölten, Internal Medicine 2, Gastroenterology and Hepatology and Rheumatology, Karl Landsteiner University of Health Sciences, St. Pölten, Austria, ⁵Medical University of Vienna, Department of Dermatology, Vienna, Austria, ⁶Medical University of Vienna, Center for Virology, Vienna, Austria, ⁷Klinik Landstraße, Department of Internal Medicine IV, Vienna, Austria, ⁸Medical University of Vienna, Clinical Institute for Laboratory Medicine, Vienna, Austria, ⁹Klinik Landstraße, Central Laboratory and Blood Bank, Vienna, Austria, ¹⁰Klinik Ottakring, Central Laboratory, Vienna, Austria, ¹¹University Clinic St. Pölten, Clinical Institute of Laboratory Medicine, St. Pölten, Austria, ¹²Landeskrankenhaus Wiener Neustadt, Institute of Medical-Chemical and Molecularbiological Laboratory Diagnostics with Blood Depot, Wr. Neustadt, Austria, ¹³Klinik Favoriten, Institute of Laboratory Diagnostics, Vienna, Austria, ¹⁴Klinik Donaustadt, Institute of Laboratory Medicine with Blood Depot, Vienna, Austria, ¹⁵Klinik Floridsdorf, Institute of Laboratory Medicine with Blood Depot, Vienna, Austria, ¹⁶Klinik Landstraße, Department of Internal Medicine IV, Vienna, Austria, ¹⁷Sigmund Freud University, Vienna, Austria, ¹⁸Landeskrankenhaus Wiener Neustadt, Department of Internal Medicine, Gastroenterology and Hepatology, Wiener Neustadt, Austria, ¹⁹Klinik Favoriten, Department of Internal Medicine IV, Vienna, Austria, ²⁰Klinik Floridsdorf, Department of Internal Medicine and Gastroenterology, Vienna, Austria, ²¹Klinik Donaustadt, Department of Internal Medicine II, Vienna, Austria, ²²Austrian Agency for Health and Food Safety (AGES), Vienna, Austria, ²³Gilead Sciences, Vienna, Austria

Contact E-Mail Address: david0bauer@gmail.com

Introduction: The elimination of hepatitis C virus (HCV) was declared a global public health goal by the world health organization (WHO). Here, we present an interim analysis of an Austrian macro-elimination project, aiming to link patients with a positive HCV PCR result at the last available HCV test to care and provide antiviral treatment.

Aims & Methods: Patients who were last tested positive via HCV-RNA PCR between 2010 and 2020 at one of the 8 participating HCV treatment centers in Eastern Austria (Burgenland, Lower Austria and Vienna) were identified. We describe the demographics and report the preliminary results of the systematic recall, direct-acting antiviral (DAA) treatment-uptake, as well as the sustained virological response (SVR) rates of these persons.

Results: Among 22682 persons tested during the study period, 11216 were HCV-RNA PCR positive at any time, while 6223 tested positive at the last available test (i.e. indicating potential persisting HCV viremia). At the time of abstract submission, 2252/6223 (36.2%) persons have been evaluated: Finally, 215 (9.6%) could be linked to hepatological care, active viremia

was confirmed in 82 (38.1%), and 56 (26.0%) initiated DAA treatment, of which 38 (67.9%) already achieved SVR. The major obstacles in linking patients to care through this project were the lack of valid contact data in n=687 (30.5%) or pre-treatment death in n=429 (19.0%), while n=497 (22.1%) had already reached SVR before contact through this project.

Conclusion: 6223 persons with potential persisting HCV viremia could be identified through the ELIMINATE project so far. Among the 2252 persons evaluated, lack of valid contact data (30.5%) and pre-treatment mortality (19.0%) were the most common obstacles in linkage to care through the ELIMINATE project. Nevertheless, 215 persons were already linked to hepatological care and 56 started DAA therapy.

Disclosure: This project is financially supported by Gilead.

P0740

EFFECT OF DIRECT ACTING ANTIVIRAL DRUGS ON THE OCCURRENCE AND RECURRENCE OF INTRA- AND EXTRA-HEPATIC MALIGNANCIES IN PATIENTS WITH CHRONIC HEPATITIS C

P.-I. Radu¹, C. Becchetti¹, J. Schropp¹, P. Schmidt², P. Künzler-Heule³, J. Mertens⁴, D. Moradpour⁵, B. Müllaupt⁶, D. Semela³, F. Negro⁷, M. Heim⁸, O. Clerc⁹, M. Roelens¹⁰, O. Keiser¹⁰, A. Berzigotti¹

¹Inselspital, University Hospital of Bern, Department of Visceral Surgery and Medicine, Berne, Switzerland, ²Cantonal Hospital St. Gallen, Division of Infectious Diseases and Hospital Epidemiology, St. Gallen, Switzerland, ³Cantonal Hospital St. Gallen, Division of Gastroenterology and Hepatology, St. Gallen, Switzerland, ⁴University Hospital of Zürich, Department of Gastroenterology and Hepatology, Zürich, Switzerland, ⁵Centre Hospitalier Universitaire Vaudois, Service de Gastro-entérologie et d'Hépatologie, Lausanne, Switzerland, ⁶University Hospital of Zürich, Swiss Hepato-Pancreato-Biliary Center and Department of Gastroenterology and Hepatology, Zürich, Switzerland, ⁷University Hospital of Geneva, Services de Gastroentérologie et d'Hépatologie et de Pathologie Clinique, Geneva, Switzerland, ⁸University Hospital Basel, Gastroenterology and Hepatology, Basel, Switzerland, ⁹Pourtalès Hospital, Department of Internal Medicine and Infectious Diseases, Neuchâtel, Switzerland, ¹⁰Institute of Global Health, University of Geneva, Geneva, Switzerland

Contact E-Mail Address: iuliana-pompilia.radu@insel.ch

Introduction: Direct-acting antivirals (DAAs) have improved the treatment of chronic hepatitis C allowing high rates of sustained virological response (SVR) and better outcomes. However, data concerning the risk of de novo intrahepatic (IHT) and extrahepatic tumors (EHT) following DAAs remains controversial (1-3).

Aims & Methods: We aimed at assessing whether the exposure to DAAs as compared to IFN-based therapy, taking into account SVR, is associated with the occurrence and recurrence of intrahepatic- (IHT), and extrahepatic tumors (EHT) in Switzerland. We performed a retrospective analysis of patients prospectively included in the Swiss Hepatitis C cohort, from September 2000 to September 2018 in 7 centers in Switzerland.

We collected data on age, sex, presence of cirrhosis, HCV genotype, type, number and date of antiviral therapies, SVR, presence of concomitant HBV and HIV infections, liver stiffness, body mass index, alcohol consumption, presence of diabetes type 2, previous history of IHT and EHT, occurrence and recurrence of IHT and EHT, death. IHT/EHT occurrence, recurrence and death were evaluated by Kaplan-Meier curves.

A semiparametric competing risk proportional hazards regression model was performed to evaluate the risk of IHT/EHT according to the exposure to DAAs, IFN or no exposure.

Results: 4082 patients (male 62.2%, median age 45 IQR [37-53] years; 48.5% genotype 1; 16.4% with cirrhosis) were included. 997 patients were treated exclusively with IFN-based regimens and 1085 only with DAAs, and 80 treated *ab initio* with both IFN-based therapy and DAAs were excluded. 1660 patients remained untreated until the last follow-up.

SVR was obtained in 652 (65.4%) of patients treated with IFN and in 933 patients (86%) with DAAs. In a median follow-up of 7.8 years (3.8-11.9), IHT developed in 179 (4.4%) patients, while EHT in 168 (4.1%). At the end of follow-up, 613 patients (15.3%) had died.

Of these 85 had a diagnosis of IHT (13.9%) and 74 (12%) of EHT. The 5-year cumulative incidence of IHT was 1.55% (95% CI 0.96-2.48) for IFN-based regimens, 4.27% (95% CI 2.93-6.2) for DAA and 0.89% (95% CI 0.4-1.99) for untreated patients. In patients with cirrhosis the 5-year cumulative incidence was higher, 4.95% (95% CI 2.78-8.81), 12.45% (95% CI 8.08-19.18) and 4.54% (95% CI 1.39-14.82), respectively.

We found no significant difference in risk of IHC (HR = 1.34; 95% CI = [0.70; 2.58]; $p = 0.380$) and death (HR = 0.66; 95% CI = [0.43; 1.03]; $p = 0.066$) between patients treated with DAAs and those treated with IFN.

After adjusting for covariates, the hazard for developing IHT was higher in patients treated with DAAs as their first line of treatment compared to patients who remained untreated (HR = 2.01; 95% CI = [1.10; 3.67], $p = 0.023$). However, the hazard for death was lower in patients treated with DAAs vs. those who remained untreated (HR = 0.49; 95% CI = [0.33; 0.72], $p < 0.001$).

Conclusion: Antiviral therapy with DAAs was not associated with an increased risk of EHT, and the risk of IHT in patients exposed to DAAs is comparable to that observed in patients exposed to IFN-based therapy.

We observed an increased risk of IHT in subjects treated with DAAs as compared to untreated patients with chronic hepatitis C; further studies should clarify this aspect. In agreement with previous data, DAAs were associated with a lower risk of death in the population of the study.

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Disclosure: Nothing to disclose.

P0741

HEPATITIS B VIRUS SCREENING AND PROPHYLAXIS THERAPY IN PATIENTS WITH SOLID TUMORS TREATED WITH ANTICANCER THERAPIES

L. Bannon¹, O. Hadad², L. Deutsch (Mlynarsky)¹, O. Shibolet¹

¹Tel Aviv Medical Center, Sackler Faculty of Medicine, Tel Aviv University, Gastroenterology and Hepatology, Tel Aviv, Israel,

²Tel Aviv Medical Center, Sackler Faculty of Medicine, Tel Aviv University, Medicine, Tel Aviv, Israel

Contact E-Mail Address: liandhn@gmail.com

Introduction: Hepatitis B virus (HBV) reactivation is defined as a rise in viral replication diagnosed by laboratory tests, sometimes resulting in hepatocellular injury. Reactivation can occur in any patient with anti-hepatitis B core (Hbc) antibodies, regardless of HBsAg status. Immunosuppression may lead to viral reactivation, and the risk is dependent on the viral status and type of immunosuppression agent used, with the highest risk documented in patients treated with anti-CD20 regimens and in hematopoietic stem-cell or solid organ transplant recipients. HBV reactivation may also occur in patients with solid tumors treated with chemotherapy. Recently the American Society for clinical Oncology (ASCO) followed suite with EASL and AASLD and suggested universal screening for all patients receiving anti-cancer therapies.

Aims & Methods: Our study aim was to find the rates of HBV reactivation in patients treated systemically for solid organ tumors.

Methods: We conducted a retrospective single-center study of 404 patients with solid tumors treated with chemotherapy and screened for HBV infection in the Tel Aviv Sourasky Medical Center between January 2014 and April 2021. Demographics, clinical and laboratory data were extracted from medical records.

Adult patients diagnosed with solid tumors and treated with chemotherapy with positive serology of anti-Hbc antibodies were included. We examined patient's reactivation of HBV, defined as seroconversion of HBsAg or increase in HBV PCR after chemotherapy treatment.

Results: Out of 404 patients diagnosed with solid tumors screened for anti-Hbc antibodies, 66 patients had positive serology and were included. Thirty-eight were males (57.6%), median age at cancer diagnosis was 66 years (range 48-88), 23 were of Russian origin (34.8%), 37 patients were smokers (56.1%), and three (4.5%) had history of alcohol consumption. The most common tumors were breast, lung and colon cancer (15 (22.7%), 11(16.6%), 10(15.1%), respectively) and 50 patients had metastatic disease (75.8%).

Seven patients had a positive HbsAg (10.6%) and most of them were treated with nucleoside analogues, none of the patients had co-infection with HDV. Among patients with negative HbsAg (59), only 5 received prophylaxis therapy.

Only one patient was diagnosed with reactivation of HBV infection (1.5%). This patient was diagnosed as chronic HBV carrier (HBsAg+/anti Hbc+ and undetected HBV PCR) before she was treated with chemotherapy (Adriamycin and Taxol). The patient did not receive prophylactic anti-viral therapy and two years after initiation of chemotherapy she had elevated liver enzymes and a positive HBV-PCR. Entecavir was started and the patient recovered without further liver related complications.

Conclusion: The rate of HBV reactivation followed chemotherapy for solid tumor is low. Nevertheless, since reactivation can be fatal it is not negligible. Further prospective controlled studies are needed to help guide the appropriate screening regimen in high-risk populations.

Disclosure: There is no conflict of interest.

P0742

PREVALENCE OF INFECTIVE AND NON-INFECTIVE HEPATITIS AND JAUNDICE IN A TERTIARY FEVER HOSPITAL: ALEXANDRIA GOVERNORATE, EGYPT

A. Aboelfetouh¹, M.A. Amin²

¹A FH Alexandria, Liver and GIT, Alexandria, Egypt, ²University of Cairo, Dept. of Internal Medicine, Cairo, Egypt

Contact E-Mail Address: amrohosny65@gmail.com

Introduction: In a developing country like Egypt, the importance of estimating the prevalence of each illness is pivotal to minimize occurrence of complications, time waste and costs of investigations and treatment. Patients with biochemical liver impairment are commonly admitted to Alexandria Fever Hospital (AFH) with a multitude of causes that might be difficult to distinguish. Every year, about one thousand patients with jaundice and hepatitis are admitted to AFH. About 15-20% (150-200 patients / year) of those patients have negative viral markers for hepatotropic viruses A, B and C, namely HAV-IgM, HBs-Ag and HCV-Ab.

Aims & Methods: The present study aims at assessing the diversity of infective and non-infective causes responsible for hepatitis with or without jaundice in AFH.

Study design, period and setting:

A hospital-based cross sectional study was conducted at AFH, a tertiary hospital in Alexandria governorate, Egypt. The Liver Investigations unit (LIU) was responsible for setting the protocol of investigations and management. The study took place over a period of 12 months from January to December 2016.

Study sample:

Admitted to AFH, a total of 111 patients of acute hepatitis and chronic liver disease with negative markers for hepatitis A, B and C.

Criteria of acute patients:

1. High serum Bilirubin.
2. ALT & AST > 3folds.
3. Negative viral markers (A, B, C).
4. No signs of biliary obstruction in abdominal U/S

Acute patient investigations protocol:

1. HEV-IgM
2. HBc-IgM (Ab)
3. Leptospira-IgM
4. Non-hepatotropic viral markers: CMV-IgM, EB-IgM, Herpes S. -IgM
5. Autoimmune markers: ANA, ASMA, Anti-Actin, LKM-AB, AMA, Ig-G, Ig-M, ANCA

If all found to be negative the following investigations were proceeded:

6. PCR for HCV (Acute HCV)
7. If +ve HBc-IgM → PCR for HBV

If these two were negative the following investigations were proceeded:

8. Metabolic markers: S.Iron, Ferritin, transferrin saturation, ceruloplasmin, urine copper, a1-antitrypsin.

Criteria of chronic patients:

Undiagnosed jaundice, chronic liver disease, or liver cirrhosis with negative markers for hepatitis A, B or C.

chronic patient investigations protocol:

1. Autoimmune markers
2. Metabolic markers
3. HBc-IgM (Ab) – (Occult HBV) → PCR for HBV

If all found to be negative the following investigations were proceeded:

4. Liver biopsy
5. Other investigations: CT, Triphasic CT, MRI, MRCP.

Results: Acute HCV was 3 patients (pts), acute HDV on chronic HBV 1 pt, alcoholic steato-hepatitis 1 pt, autoimmune hepatitis 29 pts, bacterial (septicemia, liver abscess) 2 pts, Bilharziasis 4 pts, cardiac cirrhosis 2 pts, CMV acute hepatitis 1 pt, Cryptogenic 16 pts, EBV acute hepatitis 2 pts, Gilbert Disease 3 pts, Hemochromatosis 6 pts, ischemic 1 pt, Leptospirosis 7 pts, NASH 13 pts, occult HBV 2 pts, pregnancy induced cholestasis 2 pts, primary biliary cirrhosis 1 pt, primary sclerosing cholangitis 1 pt, toxic hepatitis (Drug induced) 11 pts, Wilson disease 3 pts.

The most common causes were autoimmune hepatitis (25.2%) followed by cryptogenic (14.4%).

Most patients with toxic hepatitis (Drug induced) (81.8%), autoimmune hepatitis (72.4%), acute HCV (66.7%) were females while most cases with leptospirosis (85.7%), hemochromatosis (83.3%), Bilharziasis (75%) were males.

Conclusion: In acute hepatitis patients, autoimmune hepatitis was the most common cause followed by toxic hepatitis. In chronic hepatitis patients, nonalcoholic steatohepatitis (NASH) was the most common cause followed by metabolic causes.

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Disclosure: Ethical disclosures:

Protection of human subjects:The authors declare that the procedures followed were in accordance with the regulations of the responsible Clinical Research Ethics Committee.

Informed consent was obtained directly from each patient before data collection and after explanation of the study objectives. All procedures of data collection were treated with confidentiality according to the Helsinki declarations of biomedical ethics.

Conflict of interest: There are no conflicts of interest.

P0743

LIFESTYLE IN PRIMARY BILIARY CHOLANGITIS: LET'S PAY ATTENTION!

V. Cossiga¹, N. Cazzagon², S. Ciminnisi³, M.R. Attanasio¹, F. Pezzato⁴, M. Giacchetto³, M. Guarino⁵, V. Calvaruso⁶, A. Floreani⁴, F. Morisco⁷

¹University of Naples Federico II, Clinical Medicine and Surgery, Gastroenterology and Hepatology Unit, Naples, Italy, ²University of Padova, Surgical and Gastroenterological Sciences, and Gastroenterology, Padova, Italy, ³University of Palermo, Gastrointestinal and Liver Unit, Health Promotion Sciences Maternal and Infantile Care, Internal Medicine and Medical Specialties, Palermo, Italy, ⁴Università di Padova, Surgery, Oncology and Gastroenterology, Padova, Italy, ⁵University of Naples Federico II, Gastroenterology and Hepatology Unit, Clinical Medicine and Surgery, Napoli, Italy, ⁶University of Palermo, DI.BI.M.I.S., Palermo, Italy, ⁷University of Naples Federico II, Clinical and Experimental Medicine, Naples, Italy

Contact E-Mail Address: valentina.cossiga@gmail.com

Introduction: Primary biliary cholangitis (PBC) is a chronic cholestatic liver disease. In PBC patients, hyperlipidemia is common and it is due to an altered cholesterol metabolism as consequence of cholestasis. The hypercholesterolemia itself is not associated to an increased cardiovascular risk, but, if associated to other metabolic conditions, the risk is increased.

Aims & Methods: The aim of this study was to evaluate eating habits and physical activity in PBC patients and compare them to a control group. This is a prospective and multicenter study evaluating lifestyle in PBC patients. A group of 54 healthy subjects without liver disease, matched by age and sex, served as controls. Eating habits were evaluated with a food frequency questionnaire (FFQ) consisting of 100 different food items most consumed by Italian population. The adherence to Mediterranean diet was evaluated with the aMED (alternate Mediterranean diet) score. Physical activity was assessed with a short pre-validated questionnaire.

Results: Overall, 107 PBC patients were enrolled (92.5% female, median age 61 years). Sixty-one (57%) patients had metabolic comorbidities (58.8% with overweight/obesity, 54% with arterial hypertension, 37.8% with dyslipidemia and 8.2% with diabetes mellitus). The total fat and cholesterol intakes were higher in controls than in PBC (respectively $p=0.004$ and $p=0.015$), but above the national recommendation in both groups. Moreover, in PBC patients monounsaturated fat (MUFA) and polyunsaturated fatty acid (PUFA) intakes were lower than in the control group (respectively, $p<0.001$ and $p=0.005$). The adherence to Mediterranean diet was low in 75.7% of PBC patients. Regarding physical activity, PBC subject had a sedentary behavior, spent many hours/day sit and exercise <200 min/week, similar to controls (respectively $p=0.845$ and $p=0.115$).

Conclusion: The eating habits and lifestyle of PBC patients are unhealthy and at high risk of developing metabolic conditions and MAFLD (metabolic associated fatty liver disease). Therefore, hepatologists should pay attention to the presence of metabolic comorbidities in PBC patients, evaluate eating habits and physical activity and promote a lifestyle change to reduce liver disease progression and hepatocellular carcinoma risks.

Disclosure: The authors have no conflicts of interest to declare that are relevant to the content of this article.

P0744

COVID-19 ASSOCIATED SECONDARY SCLEROSING CHOLANGITIS - A CASE SERIES OF 4 PATIENTS

F. Bordalo Ferreira¹, S. Bragança¹, M. Mourato², J. Batista Paulo², R. Sismeiro², Z. Santos², A. Pereira³, R. Theias Manso³, A. Nassauer Mónica⁴, L. Carvalho Lourenço¹, M. Cardoso¹

¹Hospital Professor Doutor Fernando Fonseca, Gastroenterology, Amadora, Portugal, ²Hospital Professor Doutor Fernando Fonseca, Internal Medicine, Amadora, Portugal, ³Hospital Professor Doutor Fernando Fonseca, Anatomical Pathology, Amadora, Portugal, ⁴Hospital Professor Doutor Fernando Fonseca, Radiology, Amadora, Portugal

Contact E-Mail Address: filipamvpbferrera@gmail.com

Introduction: COVID-19 associated secondary sclerosing cholangitis (SSC) is a recently described cholestatic liver disease that seems to be a variant of SSC in critically ill patients (SSC-CIP). About 30 cases were described in the literature so far. In this disease, the direct cytopathic effect on cholangiocytes, the cytokine storm and hypercoagulability state add up to the mechanisms identified for SSC-CIP, such as ischemic cholangiopathy caused by invasive mechanical ventilation and hemodynamic instability, bile toxicity, biliary infection and drug-induced liver injury.

Aims & Methods: We present a case series of 4 patients who developed SSC complicating the course of severe COVID-19. These cases are illustrated by detailed iconography.

Results: Clinical cases of 63 and 64-years-old female patients and 56 and 78-years-old male patients are described. None of the individuals had a previously known liver disease. However, we documented previous hepatitis B virus (HBV) infection in one patient and chronic HBeAg negative HBV infection, with low DNA level, in another one.

All patients had long stays in the intensive care unit (ICU) with invasive mechanical ventilation (high positive end-expiratory pressure [PEEP], periods of prone positioning, difficult ventilator weaning), need for vasopressors and multiple other drugs, including various antibiotics and high dose steroid therapy. Initially, a significant raise in aminotransferases (aspartate aminotransferase 13-17x upper limit of normal [ULN] and alanine aminotransferase 20-34x ULN) was observed, with subsequent improvement, followed by marked cholestasis (alkaline phosphatase 17-23x ULN and gamma-glutamyl transpeptidase 40-99x ULN) and jaundice (total bilirubin 3-7x ULN), in spite of clinical improvement.

Magnetic resonance cholangiopancreatography (MRCP) showed similar aspects in different patients - prominence, thickening or irregularity of intra-hepatic biliary ducts (all patients), strictures and cystic dilations with a typical beaded appearance (three patients) and liver abscesses (two patients). In one patient, endoscopic retrograde cholangiopancreatography (ERCP) was performed, confirming rarefaction and focal dilations of intra-hepatic ducts and a biliary cast was extracted. The liver biopsy performed in three patients revealed significant edema and mixed inflammatory infiltrate of portal spaces, ductulitis, proliferation of the bile duct epithelia, intra-hepatic cholestasis and inflammatory aspects of a small-medium size vessel. All patients were started on ursodeoxycholic acid. None of them reached normalization of liver enzymes and at least one patient progressed to liver cirrhosis (follow-up time of 4-15 months). Two patients were referred to a liver transplant center.

Conclusion: COVID-19 associated SSC is a rare late complication of severe SARS-CoV-2 infection. These patients exhibit a spectrum of similar laboratory, cholangiographic and histological features. The prognosis is dismal with rapid progression to advanced chronic liver disease. Since effective medical treatment is lacking, early referral for liver transplantation should be considered.

Disclosure: Nothing to disclose.

P0745

COLECTOMY IN ULCERATIVE COLITIS DOES NOT PREVENT DEVELOPMENT OF PRIMARY SCLEROSING CHOLANGITIS

A. Lundberg Båve¹, O. Olén², J. Söderling³, A. Bergquist¹, C. Nordenvall⁴

¹Karolinska Institutet Stockholm, Department of Medicine Huddinge, Department of Upper GI Disease, Division of Hepatology, Karolinska University Hospital, Stockholm, Sweden, ²Karolinska Institutet Stockholm, Clinical Epidemiology Division, Department of Medicine Solna, Department of Clinical Science and Education Södersjukhuset, Sachs' Children and Youth Hospital, Stockholm, Sweden, ³Karolinska Institutet Stockholm, Clinical Epidemiology Division, Department of Medicine Solna, Stockholm, Sweden, ⁴Karolinska Institutet Stockholm, Department of Molecular Medicine and Surgery, Department of Pelvic Cancer, Karolinska University Hospital, Stockholm, Sweden

Contact E-Mail Address: aiva.lundberg.bave@ki.se

Introduction: Primary Sclerosing Cholangitis (PSC) is a hepatobiliary disease closely related to ulcerative colitis (UC). Genetics, dysregulation of bile mediated by dysbiosis of the gut, and the gut-lymphocyte homing theory all contribute to explanatory models of PSC pathogenesis. However, neither microbiome- nor immune modulating therapies have yet convincingly shown to affect the progression of disease. In PSC patients, colectomy has been shown to be associated with a better outcome, and a lower incidence of recurrent PSC following liver transplantation. These findings speak in favor for an involvement of the gut liver axis in the origin of PSC.

Aims & Methods: The aim of this study was to evaluate if colectomy in UC-patients is associated with decreased risk of development of PSC. Nationwide registers were used to identify all adult Swedish patients with ulcerative colitis (UC) in 1990-2018. Information regarding colectomy and diagnosis of PSC was retrieved.

Within the cohort of UC-patients, colectomized patients were matched to those with no colectomy, by sex, age at UC-onset (± 5 years), year of UC onset (± 3 years) and presence of proctitis at time of colectomy. Incidence rates of PSC per 1000-person year were calculated, as well as survival analyses calculating the risk of PSC using the Kaplan Meier method and Cox proportional hazard regression model.

Results: From the cohort of 61 993 UC-patients, 5 577 colectomized patients (median age 44y, 41% women) were matched to 15 078 patients with colon in situ (median age 45y, 41% women). During follow-up, 3.4% of the colectomized patients developed PSC compared with 3.0% among the comparators, yielding incidence rates/1000 person years of 2.6 and 2.4, respectively. There was no overall difference in incidence of PSC in colectomized UC-patients vs UC comparators (Hazard Ratio [HR] 1.07 [95%CI 0.90-1.28]).

Conclusion: Colectomy was not associated with a lower incidence of PSC in patients with UC, speaking against a protective effect of colectomy for the development of PSC.

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P0746

PRIMARY SCLEROSING CHOLANGITIS (PSC) AND CHRONIC INFLAMMATORY BOWEL DISEASE (IBD) ASSOCIATION

D. Azzouzi¹, R. Alaoui¹, M. Borahma¹, N. Lagdali¹, M. Kadiri¹, F.Z. Chabib¹, I. Benelbarhdadi¹, F.Z. Ajana¹

¹Mohamed V University, Gastroenterology C, Rabat, Morocco

Contact E-Mail Address: azzouzidriass.ad@gmail.com

Introduction: Primary sclerosing cholangitis (PSC) is a rare cholestatic liver disease characterised by inflammatory and fibrosing involvement of the bile ducts. It is often associated with chronic inflammatory bowel diseases.

Aims & Methods: The purpose of this work is the study of the different-clinical, morphological, therapeutic and outcomes of this association. This is a retrospective and descriptive study covering a period of 18 years from January 2003 to April 2022, including all cases of PSC. The diagnosis of PSC was based on biological, radiological and histological arguments. The diagnosis of IBD was based on a combination of clinical, endoscopic, histological and radiological evidence.

Results: Twenty-eight cases of PSC were collected. 12 were women and 16 were men. The average age was 48.9 $\pm$ 16.77 years. Out of 1590 IBD patients, PSC was detected in 1% of patients (1.27% in Crohn's disease and 0.52% in UC) and out of 28 PSC cases, IBD was noted in 57.1% of cases. The association of PSC and IBD was found in 16 patients (n=16). The association with Crohn's disease was found in 13 patients (46.42%) and with ulcerative colitis (UC) in 3 patients (10.71%).

Crohn's disease was colonic in 8 patients, ileocolic in 5 patients, UC was rectosigmoid in 2 patients and pancolic in one case.

Crohn's disease and ulcerative colitis were diagnosed on all clinical, morphological, endoscopic and histological arguments. As for PSC, it was evoked by an troubled liver test during IBD monitoring, showing cholestasis in 66.6% of cases, hyperbilirubinemia in 20.8% of cases and moderate cytotoxicity in 41.6% of cases. The cholangio-MRI was performed for each patient showing an aspect of primary sclerosing cholangitis. Cholangio-MRI showed moniliform dilatation of the intrahepatic bile ducts in 9 cases, segmental stenosis-dilatation of the intrahepatic bile ducts in 3 cases and stenosis-dilatation of the bile duct in 1 patient and was normal in 4 patients.

Liver biopsy was performed first in the 4 patients with a normal CP-MRI and then in 6 other patients (n=10), showing PSC of the small ducts in 4 patients, cirrhosis in 2 patients, portal fibrosis with rare septa in 2 patients. Colonoscopy with histological study was normal in 3 patients with UC and 4 patients with Crohn's disease as part of colorectal cancer screening.

Two patients with Crohn's disease underwent surgery for obstruction and received ileo-caecal resection and were put on combiotherapy (adalimumab+azathioprine) to avoid post-operative recurrence, the other patients were on immunosuppressive therapy. The 3 patients with UC were put on salicylates.

Treatment with urso-desoxy-cholic acid was started in all our patients. Seven of our patients were lost to follow-up. Two of our patients died (one from sepsis in the setting of stage C cirrhosis and the other from enteromesenteric ischemia) and two did not respond to treatment (One of the non-respondents progressed to cholangiocarcinoma with hepatic metastases) and five progressed well clinically and biologically.

Conclusion: Primary sclerosing cholangitis is a rare condition. Our work showed particularly that the association of PSC with Crohn's disease is higher than that of UC which is different from the literature series. These data require confirmation through more extensive prospective studies.

Disclosure: Nothing to disclose.

P0747

CROSS-SECTIONAL IMAGING BASED DIAGNOSIS OF SARCOPENIA IS ASSOCIATED WITH IMPAIRED TRANSPLANT-FREE SURVIVAL IN PATIENTS WITH PRIMARY SCLEROSING CHOLANGITIS

P. Keshoofi¹, P. Schindler², F. Rennebaum¹, F. Cordes³, M. Wildgruber⁴, H. Heinzow⁵, A. Hüsing-Kabar¹, L.L. Seifert¹
¹University Clinic Muenster, Medical Clinic B, Department of Gastroenterology, Hepatology, Endocrinology, Infectious Disease, Muenster, Germany, ²University Clinic Muenster, Department of Radiology, Muenster, Germany, ³EUREGIO-KLINIK Nordhorn, Medical Clinic II, Nordhorn, Germany, ⁴LMU München, Munich, Germany, ⁵Klinikum der Barmherzigen Brüder, Medical Clinic I, Trier, Germany

Contact E-Mail Address: p.keshoofi@uni-muenster.de

Introduction: The presence of sarcopenia is a well-validated prognostic tool in chronic liver disease (CLD) to predict morbidity and mortality. Further investigation on its value for patients with primary sclerosing cholangitis (PSC), a specific and rare form of cholestatic CLD, is lacking.

Aims & Methods: This retrospective, cross-sectional study includes 91 patients with PSC from a tertiary german liver center. Skeletal muscle index (SMI) was assessed using cross-sectional images at the third lumbar vertebra (L3) to determine sarcopenia, according to previously published cut-off values. The primary endpoint of this study was transplant-free survival at 2 and 5 years following cross-sectional imaging.

Results: Sarcopenia, assessed by SMI, is significantly associated with impaired transplant-free survival and was identified as an independent risk factor via multivariate Cox-regression analysis ($P=0.005$, B 3.129, 95%-CI 1.423-6.880).

The 2-year and 5-year transplant-free survival is significantly lower if sarcopenia is present (2-year transplant-free survival: 78.6% vs. 51.4%, $p=0.001$, log-rank test; 5-year transplant-free survival: 69.9% vs. 35.7%, $p=0.001$, log-rank test).

Conclusion: This study provides first evidence to establish imaging-based diagnosis of sarcopenia as an independent risk factor in PSC patients. Further prospective studies are required to improve diagnostic accuracy and integrate sarcopenia in future scoring systems for PSC patients.

Disclosure: Nothing to disclose.

P0748

KLF14 ALLEVIATES IMMUNE LIVER INJURY IN MICE VIA NF- κ B SIGNALING PATHWAY

X. Chen¹, W. Shi¹, P. Liu¹

¹First Affiliated Hospital of Nanchang University, Department of Gastroenterology, Nanchang, China

Contact E-Mail Address: chenxiaoyan_wow@163.com

Introduction: To date, immunopathogenic mechanisms of autoimmune hepatitis (AIH) have not been well elucidated yet. Previous studies showed macrophages were involved in the development of autoimmune hepatitis. At the same time, KLF14 was reported to moderate AIH. Thus, we attempt to study whether KLF14 could alleviate AIH through influencing the function of macrophage in liver.

Aims & Methods: At first, we identified the hepatic expression of KLF14 in human and murine AIH. Immune-mediated hepatitis was induced by concanavalin A (Con A). A KLF14 recombinant adenoviruses plasmid (Ad-KLF14) was constructed and injected into mice. Expressing of KLF14 in mechanisms were detected by immunofluorescence, inflammatory cytokines were tested by qRT-PCR. In vitro, we stimulated the KLF14/vector plasmids-transfect RAW264.7 cells with IFN- γ and examined the expression of inflammatory factors. Then we took luciferase reporter assay and co-immunoprecipitation assay to identify whether KLF14 regulated macrophage through NF- κ B.

Results: Expression of KLF14 was suppressed in liver tissues of human and murine AIH. KLF14-overexpressed mouse revealed lower degree of inflammation and pathological injury in liver compare with normal controls. In vitro, after the administration of INF- γ , the expression of inflammatory factors was down-regulated in Ad-KLF14 RAW264.7 cells. Meanwhile, the result of luciferase reporter assay and Co-IP showed KLF14 covalently bind to NF- κ B and directly inhibited it.

Conclusion: KLF14 could alleviate immune liver injury and inflammation induced by Concanavalin A in mice via blocking the NF- κ B signaling pathway. Collectively, our results point to a novel gene regulating AIH within the pathogenic, pro-inflammatory macrophage activation in the setting of liver inflammation.

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P0749

AUTOIMMUNE HEPATITIS FOLLOWING COVID-19 VACCINE

A. Izagirre Arostegi¹, T. Arzallus Marco¹, S. Torrente Iranzo¹, M. Garmendia Irizar², M. Ibarra Laresgoiti¹, I. Uribeetxebarria Agirre¹, J. Stampa¹, B. Fernandez Gonzalez¹, I. Undagoitia Gutierrez¹, M. Elfau Mur¹, A. Castiella Eguzkiza¹, E.M. Zapata Morcillo¹

¹Donostia University Hospital, Gastroenterology, Donostia San Sebastián, Spain, ²Donostia University Hospital, Pathology, Donostia San Sebastián, Spain

Contact E-Mail Address: teresa.arzallusmarco@osakidetza.eus

Introduction: Vaccination against SARS-Cov-2 infection has significantly reduced the incidence of severe cases. However, safety concerns have increased as possibly related side effects have been described. It is postulated that vaccination could induce different autoimmune diseases, probably due to cross-reactivity between SARS-Cov-2 proteins and human proteins. To date, more than 20 cases of post-vaccination autoimmune hepatitis (AIH) have been described in the literature.

Aims & Methods: The aim of this study was to collect cases of AIH that were detected after vaccination for SARS-Cov-2 in our hospital, and to analyse their characteristics and the possible causality of the vaccine. Cases of probable or definitive autoimmune hepatitis according to the simplified criteria of the International Autoimmune Hepatitis Group that presented less than 90 days after COVID-19 vaccination were collected. All cases had to have a compatible liver biopsy and response to corticosteroids in order to be included.

The following data were collected: age, sex, type of vaccine, latency, transaminase and bilirubin (BT) levels at diagnosis, liver biopsy, autoantibodies and IgG, predisposing HLA and treatment received.

Results: Since the start of vaccination, 5 cases of altered liver biochemistry after vaccination have been detected (Table 1).

Patient	Sex	Age (years)	Vaccine	Latency (days)	GPT (U/L)	GOT (U/L)	Total bilirubin (mg/dl)	ANA +	IgG (mg/dl)	Compatible biopsy	HLA	IAIHG simplified score
1	Female	47	AstraZeneca	24	353	241	0.4	1/160	2016	Yes	HLA-DRB1 *03:01,*04:03	8
2	Male	72	Pfizer	46	248	204	12.3	1/320	1670	Yes	HLA-DRB1*04	7
3	Female	62	AstraZeneca	4	655	498	2.5	1/160	1684	Yes	HLA-DRB1 *03:01 *07:01	8
4	Female	72	Pfizer	46	866	570	2.3	1/320	1916	Yes	HLA-DRB1 *03:01 *07:01	8
5	Female	59	AstraZeneca	9	1799	1292	1.3	1/640	1978	Not performed	HLA-DRB1 *01:03, *11:04	/

Table 1.

Four patients were female and one male, with a mean age of 62 years. Sixty percent received Pfizer and 40% AstraZeneca. The mean time from vaccination to detection of laboratory abnormalities was 26 days. No patients showed evidence of liver failure, although there was one case of severe acute hepatitis. ANAs were positive together with elevated IgG levels in all patients. Liver biopsy was performed in 4 cases, which were compatible with AIH. Four patients were treated with systemic corticosteroids with good outcome, and three of them were prescribed azathioprine as maintenance therapy (in one patient it was contraindicated due to a concomitant diagnosis of endometrial neoplasia). Four of the patients had HLA susceptibility for IAH. The score was calculated based on the simplified diagnostic criteria of the International Autoimmune Hepatitis Group, with all patients who underwent biopsy scoring ≥ 7 points (definite autoimmune hepatitis).

Four of the patients received a new dose of the vaccine at a later date. The second patient had a slight worsening of transaminases, which was related to the concomitant suspension of azathioprine due to digestive intolerance, with an improvement in blood tests when a new course of corticosteroids was started.

Conclusion: In all of the cases presented, there is a temporal relationship with onset of the alterations less than 90 days after vaccination. Although controversial, it is postulated that vaccination could be the cause of autoimmunity, or rather play a role as a trigger for latent disease.

At least 20 cases of probable AIH following vaccination have been reported in the literature, with characteristics similar to the cases presented in this study. However, at present, it is not possible to say with certainty whether the vaccine is the cause of the debut of IAH or whether it is a casual association in predisposed patients.

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P0750

TRAINED IMMUNITY IN LIVER CIRRHOSIS: FROM MOLECULAR MECHANISMS TO PROGNOSIS IMPLICATIONS. A PRELIMINARY OBSERVATION

M. Dallio¹, M. Romeo¹, M. Cipullo¹, L. Ventriglia¹, F. Scognamiglio¹, M. Sangineto², F. Grabherr³, B. Enrich³, J. Schwärzler³, A. Pedrini³, G. Serviddio², H. Tilg³, A. Federico¹

¹University of Campania “Luigi Vanvitelli”, Department of Precision Medicine, Hepatogastroenterology Division, Naples, Italy,

²University of Foggia, University Center for Liver Disease Research and Treatment (CURE), Liver Unit, Bari, Italy, ³Medical University Innsbruck, University Clinics for Internal Medicine I, Innsbruck, Austria

Contact E-Mail Address: marcello.dallio@gmail.com

Introduction: Trained Immunity (TI) represents a novel concept of the immunological reaction involving the innate immune cells, triggered by a second antigenic contact, gaining a long-term reversible pro-inflammatory phenotype. In liver cirrhosis, immune dysfunction impacts the onset of chronic local and systemic inflammation, the disease worsening, and the development of its complications.

Aims & Methods: The aim was to highlight TI response impairment along with the progression of chronic liver disease and to estimate its implications on the cirrhosis outcome.

Healthy subjects, patients with chronic hepatitis (CH) (alcoholic and non-alcoholic fatty liver disease ones), and liver cirrhosis (LC) were enrolled. For each patient, medical history and a peripheral venous blood sample were collected (20 ml). After a per gradient isolation, monocytes were sequentially stimulated with β -glucan for 24 h (1 μ g/mL) and lipopolysaccharide (LPS) (10 ng/mL) for 24 hours in order to assess the pro-inflammatory [tumor necrosis factor (TNF)- α , interleukin (IL)-6] and anti-inflammatory response (IL-10) (at day 3 and 6 respectively). Evaluation of blood levels of LPS, IL-6, and TNF- α was also performed.

Results: Regarding TNF- α and IL-6, the maintenance of TI was highlighted in healthy subjects (n.10) and CH (n.15) as well but not in LC patients (n.38) (TNF- α controls, LPS:2800 $\pm$ 628.8, β -glucan+LPS:5046 $\pm$ 136.2 pg/ml, p:0.008, IL-6 controls, LPS:2487 $\pm$ 562.4, β -glucan+LPS:4556 $\pm$ 190.2 pg/ml, p:0.008; TNF- α CH, LPS:1839 $\pm$ 70.7, β -glucan+LPS:4445 $\pm$ 162.6 pg/ml, p:0.007, IL-6 CH, LPS:2576 $\pm$ 177.9, β -glucan+LPS:3865 $\pm$ 332.3 pg/ml, p:0.008). IL-10 levels showed a typical TI trend only in healthy subjects (LPS:2797 $\pm$ 518.9, β -glucan+LPS:6001 $\pm$ 1523 pg/ml p: 0.001). In cirrhotic group, the bivariate analysis revealed an inverse correlation between circulating LPS, IL-6 (R = -2.511; p = 0.01) and TNF- α (R: -1.887; p = 0.02).

The Kaplan-Meier Log-Rank test analysis (24 LC patients with inefficient and 14 with efficient TI response) on not SARS-CoV-2 infections development and liver-related hospitalizations (HR 4.09, 95% CI: 1.57-10.61, p = 0.01; HR: 4.66, 95% CI: 1.5-14.47, p = 0.02 respectively) revealed lower risk for patients with efficient TI response.

	Tumor Necrosis Factor - α					Interleukin-6				
Healthy subjects (n.10)	Controls	β -glucan	LPS	β -glucan + LPS	P-value (LPS vs β -glucan + LPS)	Controls	β -glucan	LPS	β -glucan + LPS	P-value (LPS vs β -glucan + LPS)
Mean $\pm$ Standard Deviation (pg/ml)	0.6906 $\pm$ 1.544	62.57 $\pm$ 32.10	2800 $\pm$ 628.8	5046 $\pm$ 136.2	0.008	0.000 $\pm$ 0.000	62.08 $\pm$ 23.42	2487 $\pm$ 562.4	4556 $\pm$ 190.2	0.008
Chronic hepatitis (n.15)	Controls	β -glucan	LPS	β -glucan + LPS	P-value (LPS vs β -glucan + LPS)	Controls	β -glucan	LPS	β -glucan + LPS	P-value (LPS vs β -glucan + LPS)
Mean $\pm$ Standard Deviation (pg/ml)	0.000 $\pm$ 0.000	36.25 $\pm$ 28.96	1839 $\pm$ 70.71	4445 $\pm$ 162.6	0.007	0.000 $\pm$ 0.000	54.24 $\pm$ 29.50	2576 $\pm$ 177.9	3865 $\pm$ 332.3	0.01
Liver cirrhosis (n.38)	Controls	β -glucan	LPS	β -glucan + LPS	P-value (LPS vs β -glucan + LPS)	Controls	β -glucan	LPS	β -glucan + LPS	P-value (LPS vs β -glucan + LPS)
Mean $\pm$ Standard Deviation (pg/ml)	22.25 $\pm$ 65.81	65.88 $\pm$ 36.42	2065 $\pm$ 657.2	2191 $\pm$ 1106	not statistically significant	0.000 $\pm$ 0.000	56.34 $\pm$ 34.49	2329 $\pm$ 402.0	2568 $\pm$ 985.9	not statistically significant

LSP: lipopolysaccharide.

Table. Trained immune response in healthy subjects, chronic hepatitis, and liver cirrhosis patients.

Conclusion: The worsening of chronic liver disease appears related to the progressive impairment of the TI response whose maintenance seems to be associated with a lower risk of unfavorable clinical events in cirrhotic patients.

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P0751

INTERDISCIPLINARY APPROACH IS ESSENTIAL FOR SUFFICIENT DIAGNOSIS AND THERAPY IN IGG4-RELATED DISEASE INVOLVING MULTIPLE ORGANS

S. Christoph¹, G. Gerken², H. Schmidt¹, A. Kahraman³

¹University Hospital Essen, Clinic for Gastroenterology, Hepatology and Transplant Medicine, Essen, Germany, ²Helios Clinic Niederberg, Clinic for Gastroenterology, Hepatology and Palliative Medicine, Velbert, Germany, ³Max Grundig Clinic GmbH, Clinic for Gastroenterology, Hepatology and Infectiology, Bühl, Germany

Contact E-Mail Address: drsandra.christoph@gmail.com

Introduction: IgG4-related disease (IgG4-RD) is a systemic, chronic inflammatory syndrome, with enlargement of involved organs, elevated serum levels of IgG4, dense lymphoplasmocytic infiltrates, rich in IgG4-positive plasma cells, and fibrosis in involved organs. The most frequently involved organs are the pancreato-hepatobiliary tract, salivary and lacrimal glands, the retroperitoneum, kidneys, lungs, and aorta. Often multiple organ systems are involved. As an initial treatment, glucocorticoids are recommended. In patients with relapse along with glucocorticoid dose reduction, various immunosuppressive agents have been reported.

Aims & Methods: We reviewed 98 patients (2019-now) who were treated in the special outpatient unit for IgG4-RD at the University Hospital of Essen and identified 10 patients with IgG4-RD involving multiple organ systems.

Results: The first patient is a 65-year-old male diagnosed with an IgG4-RD involving parotitis, lymphadenitis, sialadenitis with orbitopathy and elevated IgG4 serum level (7400 mg/l). Clinically response to therapy with steroids was documented.

The second patient is a 63-year-old man with an IgG4-positive pancreatitis, sialadenitis, lymphadenopathy, and elevated IgG4 serum level (3960 mg/l). Immunosuppression with tacrolimus led to clinical benefit.

As the third patient, we report a 48-year-old man with IgG4-related inflammatory condition in pancreas and kidneys with high IgG4 serum levels. The patient was successfully treated with azathioprine and prednisolone. As the fourth patient, we demonstrate a 34-year-old man with IgG4-related autoimmune hepatitis, lymphadenitis, and pancreatitis. After treatment with tacrolimus in combination with rituximab, a significant decrease of IgG4-level was detected.

The fifth patient, a 65-year-old man, was diagnosed with IgG4-related fibro-inflammatory pseudotumors in the liver, esophagitis, and lymphadenopathy combined with high serum levels of IgG4 (12000 mg/l). Clinically response to therapy with steroids and azathioprine was reported.

As the sixth patient we demonstrate a 29-year-old male with IgG4-related lymphadenopathy, recurrent myocarditis, and pancreatitis.

The patient has symptom-free episodes under low-dose prednisolone. We also found an IgG4-RD with multiple organ involvement in our seventh patient. A 54-year-old man with IgG4-related cholangitis, pancreatitis, prostatitis, and very high serum level of IgG4 (26700 mg/l) were treated with steroids and azathioprine.

As our eight case, we present a 23-year-old man with congenital hepatic fibrosis, after living-donor liver transplantation, who developed an IgG4-related disease with high IgG4 serum levels (45300 mg/l) after infection

with SARS-CoV-2. Pathologically enlarged lymph nodes were detected. In a biopsy of retroperitoneal lymph nodes, IgG4-positive plasma cells were detectable. Intestinal biopsies have shown numerous positive plasma cells in the IgG4-staining (40 IgG4 positive plasma cells/HPF). Treatment with rituximab is planned.

The ninth patient is a 56-year-old woman with lymphadenitis and cholangitis, who clinically responded to a treatment with budesonide. As the last patient we present a 59-year-old man with an IgG4-related aortitis, cardiac fibrosis, cholangitis, hepatitis, exocrine pancreatic insufficiency and Hashimoto's thyroiditis responding very sufficient to rituximab.

Conclusion: An interdisciplinary approach is essential for a sufficient diagnosis and therapy in IgG4-RD involving multiple organs. This collective is extremely heterogeneous, and treatment is often based on individual concepts.

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P0752

INCIDENTAL M2-AMA POSITIVITY BY IMMUNOBLOT IS A STRONG INDICATOR OF PRIMARY BILIARY CHOLANGITIS

I. ergenc¹, B. Gözaydınlioğlu², Ç. Keklikkiran³, Y. Yilmaz⁴
¹Marmara University, Gastroenterology, Istanbul, Turkey, ²Marmara University School of Medicine, Istanbul, Turkey, ³Marmara University School of Medicine, Gastroenterology, Istanbul, Turkey, ⁴Marmara University, School of Medicine, Gastroenterology, Istanbul, Turkey

Contact E-Mail Address: ergencilkay@gmail.com

Introduction: Anti-mitochondrial antibodies (AMA) are the typical biomarkers of primary biliary cholangitis (PBC). Anti-mitochondrial M2 antibody (M2-AMA), formed against the E2 subunit of pyruvate dehydrogenase complex, is the most specific AMA subtype for PBC¹.

AMA antibodies might become positive years before the development of PBC². Furthermore, the M2-AMA dot-blot is more specific to PBC than indirect immunofluorescence based AMA (IIF-AMA).

Aims & Methods: This study aims to investigate the natural evolution of incidental AMA-M2 positivity by immunoblot test to PBC diagnosis with or without IIF-AMA positivity. The Extractable Nuclear Antibodies (ENA) Im-

munoblot (IB) panel tests (Euroimmun, Germany) including M2-AMA requested by rheumatology, endocrinology, neurology and general internal medicine to investigate autoimmune disorders were screened (n=11459) and patients with positive M2-AMA (n=120) were identified. Patients with a definite or provisional diagnosis of PBC (n=21) at the time of the ENA panel test were excluded.

Ninety-nine M2-AMA positive patients who underwent ENA panel test for suspected autoimmune disorders were invited to the study. Patients who agreed to participate in the study were tested for AMA and Antinuclear antibody (ANA) by indirect immunofluorescence method (IIF) (Euroimmun, Germany). Serum alkaline phosphatase (ALP) activity was tested and previous ALP results were noted. European Association for the Study of the Liver (EASL) criteria were used for PBC diagnosis.

Results: Among 11459 samples tested for the ENA panel, 0.1% (n=99) were M2-AMA positive by IB. A total of 99 patients were eligible for the study and 48 patients agreed to participate. The mean age was 48.5±4 and 93.75% (n=45) were female. 64.5% (n=31) of patients were followed-up in rheumatology clinic, 23% (n=11) in internal medicine clinic and 12.5% (n=6) in neurology clinic.

The median follow-up period after M2-AMA positivity was 27 months. Twenty-eight (58.5%) were ANA positive (Table 1), 21 (43.5%) were IFA-AMA positive and 31.2% were diagnosed with PBC. Thirteen out of these 21 AMA positive patients had elevated ALP levels and were eventually diagnosed with PBC.

In addition, two of AMA negative patients had persistently increased ALP levels and were diagnosed with PBC. Twelve of 15 newly diagnosed PBC patients had autoimmune disorders. Of these, 4 were diagnosed with rheumatoid arthritis, 3 with connective tissue disease, 3 with ankylosing spondylitis, 1 with Hashimoto's thyroiditis and 1 with Familial Mediterranean Fever. While six newly diagnosed PBC patients had a history of increased serum ALP levels at the time of first M2-AMA positivity, nine of them developed an increase in ALP during the follow-up.

	AMA (+) (n= 21)	AMA (-) (n=27)	Total
PBC Diagnosis	13	2	15(%31,2)
ANA positivity	12	16	28(%58,3)
Accompanying autoimmune disorders	12	19	31(%64,5)

AMA: Anti-mitochondrial antibody, PBC: Primary Biliary Cholangitis, ANA: Antinuclear antibody

Table 1: Antibody positivity and PBC diagnosis rates.

Conclusion: Immunoblot AMA M2 positivity was only 0.1% in the suspected autoimmune disorders patients. Two-thirds of M2-AMA positive patients were diagnosed with PBC, 6 of these patients were missed the diagnosis although they met the EASL criteria at test day, remaining 9 patients were diagnosed in a median follow-up of 27 months. This study demonstrates that M2-AMA positivity in patients with autoimmune disorders is extremely valuable and should alert the physicians for current and future diagnosis of PBC.

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P0753

ANTI-MITOCHONDRIAL ANTIBODY-NEGATIVE PRIMARY BILIARY CHOLANGITIS: EPIDEMIOLOGICAL, CLINICAL, BIOLOGICAL, HISTOLOGICAL AND EVOLUTIONARY CHARACTERISTICS

R. Ayadi¹, D. Cherif², H. Debbabi¹, H. Yacoub¹, H. Hajer³, H. Kchir¹, N. Maamouri⁴

¹La Rabta University Hospital, Gastroenterology Department B of La Rabta Hospital in Tunis, Tunisia, ²Rabta, Gastroenterology, Tunisia, ³La Rabta University Hospital, Gastroenterology, Ben Arous, Tunisia, ⁴La Rabta Hospital, Tunisia

Contact E-Mail Address: ayadirahmaa018@gmail.com

Introduction: Primary biliary cholangitis (PBC) is a chronic inflammatory liver disease with an autoimmune mechanism. Its diagnosis is based on the presence of biological cholestasis, positive anti-mitochondrial antibodies (AMA) type 2 and suggestive histological lesions. AMA- negative PBC represents a rare form of PBC with misleading signs that can lead to misdiagnosis.

The main objective of this study was to determine the epidemiological, clinical, biological, histological and evolutionary characteristics of this particular form compared to the seropositive form.

Aims & Methods: A retrospective, descriptive, comparative, mono-centric study was carried out at the gastroenterology B department of La Rabta hospital in Tunis over a period of 23 years. Medical records of 108 patients admitted for PBC during the study period were collected. The diagnosis of seronegative PBC was made when biological cholestasis was associated with characteristic histological signs in the absence of anti-mitochondrial antibodies (AMA).

Results: Among the 108 patients followed for PBC, we collected 11 cases of seronegative PBC (11,88%). The mean age was 51 years with a predominance of women (75%). PBC was asymptomatic in 45% of cases and was most often discovered incidentally in an abnormal liver blood test (36%). Immunologically, only anti-nuclear antibodies (ANA) were positive (63%). Liver biopsy confirmed the diagnosis in all patients. Histologically, lymphocytic destructive cholangitis was the most frequent lesion (63%) as well as Scheuer stage 4 (36%). At least one associated autoimmune disease was present in 45% of patients. All patients received ursodeoxycholic acid (UDCA) at a dose of 12-15 mg/Kg/d. Three patients with overlap syndrome received corticosteroids in combination with UDCA. The mean follow-up was 60 months (0-200 months).

A complete response was noted in 5 cases. Four patients were lost to follow-up. Only one patient had a relapse due to poor compliance with treatment. An hepatocellular carcinoma was observed in only one case during the course of the disease. No significant differences were found between seropositive and seronegative groups for any of the studied characteristics of the disease.

Conclusion: Although AMA-negative PBC is a rare form of PBC, it is associated with similar rates of complications as the seropositive form. Only the early initiation of UDCA can control the progression of the disease. However, its misleading signs can delay the diagnosis and the management of patients.

Therefore, AMA- negative PBC should be considered in the presence of any hepatic cholestasis and the treatment with UDCA must be provided at an early stage to improve the prognosis of the disease.

Disclosure: Nothing to disclose.

P0754

THE PREVALENCE OF SEROLOGICAL MARKERS OF HEPATITIS E VIRUS AND ITS IMPACT ON CLINICAL COURSE OF AUTOIMMUNE HEPATITIS

M.K. Janik¹, A. Kempńska-Podhorodecka², J. Raszeja-Wyszomirska¹, M. Milkiewicz², M. Krawczyk^{3,4}, P. Milkiewicz^{1,5}

¹Medical University of Warsaw, Liver and Internal Medicine Unit, Department of General, Transplant and Liver Surgery, Warszawa, Poland, ²Pomeranian Medical University, Department of Medical Biology, Szczecin, Poland, ³Medical University of Warsaw, Laboratory of Metabolic Liver Diseases, Centre for Preclinical Research, Warszawa, Poland, ⁴Saarland University, Department of Medicine II Saarland University Medical Center, Homburg, Germany, ⁵Pomeranian Medical University, Translational Medicine Group, Szczecin, Poland

Contact E-Mail Address: mjanik24@gmail.com

Introduction: Reported prevalence of hepatitis E virus (HEV) in patients with autoimmune hepatitis (AIH) varies markedly (8 - 40%). A recent study in non-alcoholic fatty liver disease (*Paternostro et al. Hepatol Res. 2021*) showed a relationship between HEV seropositivity and more advanced liver fibrosis and cirrhosis. This aspect has not yet been evaluated in AIH.

Aims & Methods: Here we assessed the prevalence of HEV seropositivity in patients with AIH and its impact on disease course. A group of 398 non-transplant adult patients (female 68%, mean age 38 ± 16 years, liver cirrhosis 38%), including 270 (68%) with AIH and 128 (32%) with its variants (AIH-PSC and AIH-PBC) was enrolled.

The serum concentration of HEV IgG and IgM antibodies was measured by enzyme-linked immunosorbent assay (ELISA). Liver cirrhosis was diagnosed by liver biopsy or imaging studies.

Moreover, in patients with AIH in remission, liver fibrosis was assessed as liver stiffness measurement (LSM) by 2D-Shear Wave Elastography (Aixplorer, SuperSonic), used to measure spleen stiffness as well.

Results: In total, 59 (15%) patients were HEV IgG positive, and 5 (1%) were HEV IgM positive. This proportion was lower than previously reported (Grabarczyk et al. Transfusion 2018) in Polish blood donors (43%; $p < 0.001$). The HEV IgG-positive patients were older both at the study time (45.6 vs 36.7 years, $p < 0.001$) and at the diagnosis of their disease (39.0 vs 30.6 years, $p < 0.001$), as compared to IgG-negative patients. They also had higher BMI (25.0 vs 23.7 kg/m², $p = 0.031$), liver stiffness (17.2 vs 14.7 kPa, $p = 0.014$) and spleen stiffness (29.7 vs. 26.8 kPa, $p = 0.043$).

In patients with AIH in biochemical remission ($n = 198$), the multivariate analysis revealed that the risk of liver cirrhosis (LSM > 16.1 kPa) was increased by HEV seropositive status (OR 2.46, CI 95% 1.03 - 5.87) and older age (OR 1.03, CI 95% 1.01-1.06).

However, there was no impact of HEV seropositivity or age in the entire cohort on the clinically diagnosed liver cirrhosis. There was no difference between patients with AIH and with or without HEV IgG positive regarding biochemistry at the time of diagnosis (i.e. ALT, bilirubin, IgG) or the enrolment in the study and treatment regime.

Conclusion: Despite a lower prevalence of HEV IgG in patients with AIH than in the general population, these patients might be more prone to have advanced liver fibrosis. Nevertheless, the impact of HEV infection on the disease course of AIH needs to be fully elucidated in prospective studies.

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P0755

LONG-TERM OUTCOMES IN PEDIATRIC LIVER TRANSPLANTATION: A SINGLE CENTER 20 YEARS EXPERIENCE

M. Guarino¹, F. Di Dato², L. Pignata¹, M. Capasso¹, F.M. Cutolo¹, V. Esposito², V. Cossiga¹, R. Iorio², F. Morisco¹

¹University of Naples Federico II, Department of Clinical Medicine and Surgery, Gastroenterology and Hepatology Unit, Napoli, Italy,

²University of Naples Federico II, Department of Translational Medical Sciences, Section of Pediatrics, Napoli, Italy

Contact E-Mail Address: maria.guarino86@gmail.com

Introduction: Liver transplantation (LT) provides life-saving therapy for children with end-stage liver disease and liver-based metabolic defects. Over the last decades important advances have been made both from the surgical and clinical point of view making LT an effective and widely available treatment in children ensuring notable results in terms of patient and graft survival rates [1-3].

Since LT in pediatric age is a relatively recent reality, there is still limited knowledge about its long-term impact in terms of quality of life and chronic immunosuppression long-term effects [4-5].

Aims & Methods: This study aimed to describe long-term outcomes in LT children followed-up for more than two decades, with particular interest to late post-transplant complications and patient survival rates.

We conducted a single-center retrospective study including all pediatric patients who underwent LT from 1987 to 2011 and followed-up until 2021 at the "Federico II" University Hospital of Naples.

Results: A total of 119 patients have been enrolled, 62 males and 57 females, with a median age at the time of enrollment of 24.3 years (25th-75th percentile: 18.7-32.4). The median age at the time of LT was 1.71 years (25th-75th percentile: 0.73-6.14) with a median follow-up time of 21.6 years (25th-75th percentile: 15.7-25.7).

The main indication for LT was biliary atresia (63%), followed by liver-based metabolic defects (10.1%), autoimmune liver diseases (7.6%), progressive familial intrahepatic cholestasis (5.9%) and Alagille syndrome (3.4%). Immunosuppressive regimens undertaken in the immediate post-transplant period were in all patients based on calcineurin inhibitors (119/119). Tacrolimus-based regimens were used in 85 patients (71.4%), in the majority as monotherapy (75 patients).

During the post-LT follow-up in 34 patients (28.6%) a therapeutic switch was necessary, mostly due to chronic rejection (16 cases). Twenty-two re-transplantations were performed in 13 patients with a 20-year graft survival rate of 81.56%. Vascular complications represented the most frequent cause of graft failure (8/22). The most common comorbidities were allergic ones (29.4%). Long-term immunosuppression-related complications included metabolic bone diseases (12.6%), arterial hypertension (10.1%) and chronic kidney dysfunction (10.1%). De novo malignancies occurred in 20 patients (16.8%), mostly represented by lymphoproliferative disorders (18/20). No skin neoplasms were reported. Six deaths (5.04%) have been registered (for malignancies in 2 cases, for sepsis in 2 cases and for cirrhosis in 2 cases) with a 20-year survival rate of 94.96%.

Conclusion: The present study shows a significant increase in survival of LT pediatric patients and grafts and confirms the less frequent onset of complications compared to the adult setting but also highlights the emerging and still unresolved issues.

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P0756

ELASTOGRAPHY BY FIBROSCAN AND POINT SHEAR WAVE FOR ANALYSIS OF LIVER STIFFNESS: A PROSPECTIVE STUDY

G. Losurdo¹, I. Dittonno¹, D. Novielli¹, N. Ranaldo¹, E.G. Ierardi¹, M. Rendina¹, A. Di Leo¹

¹Section of Gastroenterology, DETO, University of Bari, Bari, Italy

Contact E-Mail Address: ilaria.dittonno@gmail.com

Introduction: Liver stiffness measurement (LSM) by fibroscan is the most used non invasive method to assess the fibrosis of the liver. Recently, point shear wave elastography (pSWE) has been introduced as a simple alternative non invasive test. Therefore, we aimed to compare the results of these two techniques.

Aims & Methods: Consecutive patients attending our ultrasound facility in our outpatient clinic in the period January-December 2021 were recruited. For each patient, LSM was performed by both Fibroscan (Echosens, Paris, France) and pSWE (Esaote Mylab Xpro80, Genova, Italy).

At least 10 measurements were performed, and results were expressed as median with interquartile range. Staging of fibrosis was assigned according to Metavir classification. Statistical analysis was conducted by Pearson's test for correlation and linear regression. Bland-Altman graphs were drawn.

Results: Sixty-three patients (35 males, 28 females, mean age 56.7 ± 13.0) were recruited. The most common indications to perform LSM were chronic viral hepatitis (14.3%), unexplained hypertransaminasemia (36.5%), non alcoholic steatohepatitis (14.3%), and autoimmune liver diseases (6.3%). LSM measurements of pSWE and Fibroscan showed a poor correlation (r=0.56, p<0.001) and linear regression (b=0.93 ± 0.03, p<0.0001). Bland-Altman graph found only 4 outliers.

The best correlation was observed in patients with non alcoholic steatohepatitis (r=0.81), while those with unexplained hypertransaminasemia had r=0.76.

Overall, Fibroscan classified one patient as F4, one as F3, three as F1 and 13 as F0. Concordance with pSWE for F staging was observed in 16 (84.2%) patients. A full concordance in fibrosis Metavir staging was recorded in 47 cases (74.6%), while in 9 patients (14.3%) SWE overestimated and in 7 (11.1%) underestimated fibrosis.

Conclusion: In most of cases, pSWE shows LSM estimation in agreement with Fibroscan, and the best concordance was observed for non alcoholic steatohepatitis. A slight trend of stiffness overestimation by pSWE was observed, despite only for mild, non significant fibrosis.

Disclosure: Nothing to disclose.

P0757

PERFORMANCE OF A 2D-SWE FOR THE DIAGNOSIS OF LIVER FIBROSIS USING TRANSIENT ELASTOGRAPHY AS REFERENCE METHOD

C.G. Foncea^{1,2}, A. Popescu^{1,2}, R. Lupusoru^{1,2,3}, R. Cotrau^{1,2}, F. Bende^{1,2}, R. Sirli^{1,2}, I. Sporea^{1,2}

¹University of Medicine and Pharmacy "Victor Babes", Department of Gastroenterology and Hepatology, Department of Internal Medicine II, Center for Advanced Research in Gastroenterology and Hepatology, Timisoara, Romania, ²Center for Advanced Hepatology Research of the Academy of Medical Sciences, Timisoara, Romania, ³"Victor Babes" University of Medicine and Pharmacy, Center for Modeling Biological Systems and Data Analysis, Department of Functional Sciences, Timisoara, Romania

Contact E-Mail Address: foncea.camelia@gmail.com

Introduction: Liver fibrosis is a progressive process leading to liver cirrhosis. Several non-invasive elastography techniques were developed for liver stiffness measurements (LS) as a marker of liver fibrosis.

The aim of this study was to evaluate the performance and feasibility of 2D-Shear Wave Elastography (2D-SWE) for liver fibrosis (LF) assessment using Transient Elastography (TE) as the reference method.

Aims & Methods: 67 subjects were included, 65% (44/67) male, mean age 55.6 ± 13.2 , in which LS was evaluated in the same session by TE (FibroScan Compact M 530) and 2D-SWE (Samsung-Medison RS85). Reliable LS measurements were defined for TE the median value of 10 measurements with an IQR/M $\leq 30\%$, while for 2D-SWE the median value of 10 measurements, with a reliability measurement index (RMI) ≥ 0.5 and IQR/M $\leq 30\%$. For classification of LF severity we used TE as reference method with cut-off value ≥ 7 kPa for at least significant liver fibrosis (1).

Results: Reliable measurements by TE and 2D-SWE were obtained in all 67 cases. A strong correlation was found between 2D-SWE and TE, $r=0.83$. The best cut-off value for 2D-SWE in identifying at least significant fibrosis ($F \geq 2$) was >7 kPa [AUROC=0.91, 95% CI (0.82;0.97), $p<0.0001$, Se=81.8%, Sp=80.0%, PPV=66.7%, NPV=90.0%].

Conclusion: 2D-SWE is a feasible method for assessing liver fibrosis, that strongly correlates with TE results.

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P0758

POSSIBLE THERAPEUTIC IMPACT OF LONG NON-CODING LINC01018 ON AN EXPERIMENTALLY INDUCED MODEL OF HEPATOCELLULAR CARCINOMA

M. Elzallat¹, M. Hassan¹, N. El Kramani², T. Aboushousha³, A. Abdellatif², M. Zoheiry¹, H. Abu-Taleb⁴, E. El-Ahwany¹

¹Theodor Bilharz Research Institute, Immunology & Therapeutic Evaluation Department, Giza, Egypt, ²American University in Cairo, School of Science and Engineering, Cairo, Egypt, ³Theodor Bilharz Research Institute, Pathology Department, Cairo, Egypt, ⁴Theodor Bilharz Research Institute, Environmental Research Department, Giza, Egypt

Contact E-Mail Address: zallatzallat@gmail.com

Introduction: Hepatocellular carcinoma (HCC) is the most frequent subtype of primary liver cancer and one of the leading causes of cancer-related mortality worldwide. Emerging evidence has recently suggested that long noncoding RNAs (lncRNAs) have tumor-suppressive roles in cancers. LINC01018 can inhibit the proliferation of tumor cells and promote cell differentiation in HCC.

Aims & Methods: In this study, a new therapeutic modality using lncRNA LINC01018 was designed to control HCC progression. sixty mice were included and categorized into 3 groups. The 1st group acted as a normal control group whereas the 2nd group acted as a pathological control group and was injected with N-Nitrosodiethylamine (DEN) weekly for 16 weeks. The 3rd Group was injected intrahepatically with lncRNA LINC01018 once/week for four weeks starting from the 12th week after initiating DEN injection. After 16 weeks, animals were euthanized, and liver specimens and blood samples were collected for pathological, biochemical, and assessment.

Results: Our results showed that lncRNA LINC01018 administration leads to inhibition of cell proliferation of HCC. It was observed that there was an improvement in histopathology in the 3rd group when compared to the pathological control group. The levels of AFP, VEGF, TNF- α , PD-EGF, and EpCAM decreased significantly ($P<0.001$) and the Relative expression of hepatic B-Catenin and SENP was significantly down-regulated ($P<0.001$) after LINC01018 administration.

Conclusion: lncRNA LINC01018 can be considered a new target for therapeutic intervention in HCC.

References:

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P0759

CHARACTERISTICS AND SURVIVAL OF PATIENTS WITH HEPATOCELLULAR CARCINOMA IN NATURAL HISTORY IN A WESTERN COUNTRY

H. González-Sánchez¹, A. Castaño-García¹, M. Celada-Sendino¹, P. Flórez-Díez¹, M. García-Calonge¹, D. Muiño-Domínguez¹, C. Álvarez-Navascués¹, V. Cadahía-Rodrigo¹, M.L. González-Diéguez¹, L. Franco-Aguirre¹, M. Rodríguez^{1,2,3}, M. Varela^{1,3,2,4}

¹Hospital Universitario Central de Asturias, Liver Unit, Oviedo, Spain, ²Universidad de Oviedo, Oviedo, Spain, ³ISPA (Instituto de Investigación Sanitario del Principado de Asturias), Oviedo, Spain, ⁴IUOPA (Instituto Universitario de Oncología del Principado de Asturias), Oviedo, Spain

Contact E-Mail Address: helenagonzalezsanchez@hotmail.com

Introduction: Hepatocellular carcinoma (HCC) arises from a liver cirrhosis in more than 80% of cases and this condition could determine the beginning and/or maintenance of the HCC treatment. In addition, comorbidities and frailty of the patients may induce a treatment stage migration or even be the reason to leave them without specific treatment for the HCC.

Aims & Methods: The aim of our study is to assess the characteristics and survival of patients with HCC in natural history in our setting.

Unicentric retrospective cohort study with the inclusion of all consecutive HCC patients diagnosed at our Unit between Jan 27th 2015 and Dec 27th 2021. The main inclusion criterion was the selection of “non treatment” as first and sole therapy for HCC. Baseline clinical variables, reason of non-treatment and period from diagnosis to death/end of follow-up were systematically recorded.

Results: A hundred eighty-one patients from 685 met our inclusion criterion: 82% were men, median age 71 years, 93% with cirrhosis, 55% alcohol related vs 34% viral, 54% with previous decompensation (73% ascites). After a median follow-up of 9.98 months, 84% had died.

There were statistical differences in median survival according to 1) tumor-related symptoms [ECOG PS-0: 13 months, ECOG PS-1: 6 months, ECOG PS $\geq$ 2: 2 months; $p < 0.001$], 2) tumor stage [BCLC 0-A: 13 months, BCLC-B: 12 months, BCLC-C: 4 months, BCLC-D: 2 months; $p < 0.001$], 3) baseline AFP [AFP < 200 ng/mL: 9 months vs AFP ≥ 200 : 3 months; $p < 0.001$] and 4) baseline Child-Pugh [A: 8 months vs B: 4 months vs C: 6 months; $p = 0.003$].

The most common reasons for non-treatment were: cirrhotic decompensation / BCLC-D stage (51%), frailty/advanced age (25%), comorbidity (16%) and patient refusal (8%). Baseline factors independently associated with survival were the absence of previous decompensation (HR 0.492, IC 95% 0.331-0.733, $p < 0.001$), BCLC stage (HR 0.389 IC 95% 0.183-0.813, $p = 0.012$) and diagnosis during screening program (HR 1.614, IC 95% 1.058-2.463, $p = 0.026$).

Conclusion: Twenty-six percent of HCC patients remain in their natural history without HCC-specific therapy at our center. The main reasons were liver impairment/BCLC-D stage, followed by frailty/old age and extrahepatic comorbidity. Baseline BCLC stage, absence of prior cirrhosis decompensation and diagnosis during the screening program were independently associated with increased survival.

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P0760

IMPACT OF THE COVID-19 PANDEMIC IN THE DIAGNOSIS AND THERAPY OF SINGLE HEPATOCELLULAR CARCINOMA LESS THAN 3 CM IN A WESTERN COUNTRY

M. Garcia-Calonge¹, L. Martinez Cambor¹, H. González Sánchez¹, D. Muiño Domínguez¹, M. Celada Sendino¹, P. Flórez-Díez¹, A. Castaño¹, C. Alvarez Navascues¹, M.L. Gonzalez Dieguez¹, V. Cadahia Rodrigo¹, M. Rodriguez Garcia¹, M. Varela¹

¹Hospital Universitario Central de Asturias, Oviedo, Spain

Contact E-Mail Address: martagcalonge@gmail.com

Introduction: The aim of a cancer screening program is to reduce cancer-related mortality. For that reason patients with liver cirrhosis are enrolled into surveillance through biannual ultrasonography plus AFP to detect single hepatocellular carcinomas (HCC) less than 3 cm, best candidates to apply therapies with curative intent.

This study evaluates the impact of the COVID-19 pandemic in the time between detection, diagnosis, and treatment in patients with uninodular HCC ≤ 3 cm. The secondary objective is to assess the number and sequence of tests needed to achieve the final diagnosis.

Aims & Methods: Retrospective inclusion of consecutive patients with final diagnosis of single HCC ≤ 3 cm at our centre. Baseline clinical and analytical variables, date of detection, diagnosis, treatment / entry on the transplant waiting list and the sequence of tests performed (CT, MRI, biopsy) were recorded. Time to diagnosis (period from detection to diagnosis), time to treatment (from diagnosis to date of treatment/entry on the waiting list) and overall time (the sum of the above) were defined. The results were analyzed globally and divided into two periods: pre-COVID (Jan-15 to Feb-2020) and COVID (Mar-20 to the present).

Results: From Jan 27th 2015 to Dec 27th 2021, 128 patients of 685 had a final diagnosis of single HCC ≤ 3 cm, 18% in the pre-COVID era and 22% in the COVID era. Baseline characteristics: median age 64 years old, 84% males, aetiology: alcohol 46%, hepatitis C 39%, fatty liver disease 5%. Child-Pugh class A 86%, BCLC-0 29%, BCLC-A 71%. Median size 20.5 mm, median AFP 5 ng/mL. Only 74% were diagnosed within the screening program. Thermal ablation was applied in 58 patients, liver transplantation in 29, surgical resection in 21 and intraarterial therapy in 16. Twelve patients were left in natural history.

Diagnosis was reached by non-invasive criteria (imaging) in 112 patients and by biopsy in 16. The tests performed are shown in the TABLE 1. No statistically significant differences were found in the diagnostic capacity between multiphasic CT (67.6%) and dynamic MRI (73.3%), p -value 0.113. There were no differences in the diagnostic method (imaging versus biopsy) according to the size of the nodule (21.43 mm vs. 21.13 mm), p -value 0.199; nor in the number of studies performed according to the sequence (CT-MR-Biopsy vs MR-CT-Biopsy vs others), p -value 0.746.

There were no significant differences neither in the proportion of tumors diagnosed between 10-20 mm and 21-30 mm on the pre-COVID vs COVID era, p -value 0.80, nor in the therapy applied (surgical versus loco-regional, p -value 0.639).

Time to diagnosis, time to treatment, and overall time are shown in TABLE 2. Significant differences were found in the time to treatment between the pre-COVID and COVID eras: 8 weeks vs 11 weeks, p -value 0.038.

Conclusion: The COVID pandemic did not affect the proportion of single HCC ≤ 3 cm diagnosed, but it increased the median time from diagnosis to treatment.

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P0761

PREVALENCE AND PATTERN OF ALCOHOL CONSUMPTION IN PATIENTS WITH HEPATOCELLULAR CARCINOMA

D. Muiño Domínguez¹, A. Mínguez Sabater², M. García Calonge¹, H. González Sánchez¹, A. Castaño García¹, E. Junquera³, A.M. Piedra Cereza¹, M. Rodríguez^{1,4,5}, M. Varela^{1,4,5,6}

¹Hospital Universitario Central de Asturias, Liver Unit, Oviedo, Spain, ²Hospital Universitari i Politècnic la Fe de Valencia, Liver Unit, Valencia, Spain, ³Hospital Universitario San Agustín, Department of Gastroenterology and Hepatology, Avilés, Spain, ⁴Universidad de Oviedo, Department of Medicine, Oviedo, Spain, ⁵Instituto de Investigación Sanitaria del Principado de Asturias. ISPA, Oviedo, Spain, ⁶Instituto Universitario de Oncología del Principado de Asturias. IUOPA, Oviedo, Spain

Contact E-Mail Address: daniel.muinho@gmail.com

Introduction: Abstinence from alcohol is associated with a lower risk of hepatocellular carcinoma (HCC) in patients with compensated cirrhosis. However, the evolution of HCC in relation to the maintenance of alcohol abstinence is unknown.

Aims & Methods: Firstly, to determine the prevalence of alcohol consumption (AC) in HCC patients regardless of its etiology, presence of cirrhosis and previous AC. Secondly, to assess the usefulness of the AUDIT-C to detect any AC in HCC patients. Thirdly, to compare AUDIT-C with other commonly used methods (CAGE and biological markers). Alcohol was measured in standard alcohol units (1 containing 10 g of pure alcohol). Cross-sectional study including 100 consecutive HCC patients who attend the outpatient clinic. Exclusion criteria: hepatic encephalopathy at the moment of the interview, patients with HCC in the waiting list/ followed after liver transplantation. Clinical and sociodemographic variables were collected. AUDIT-C, CAGE questionnaire and collection of AC through a semi-structured survey were performed. Alcohol-free beer consumption was also registered, because this is associated with a higher rate of abstinence in patients without alcohol cessation.

Results: One hundred and two HCC patients were prospectively included. The average time to complete the interviews and questionnaires was 6 min per patient. No patient refused to enter the study. The median time from HCC diagnosis to the date of the study was 25 months (mean 33 months, range 1-72).

Alcohol was the underlying cause of HCC in 60 (58.8%) patients, alone or associated with hepatitis C, metabolic syndrome, hemochromatosis, etc. The prevalence of AC was 35.29% (n=36). The prevalence of alcohol-free beer consumption was 49.02% (n=50). Only 10 patients (9.8%) drank > = 10 standard alcohol units per week.

There were no differences in AC regarding age, educational level, concomitant medications (benzodiazepines, antipsychotic, antidepressant). However, those who lived in urban areas had a higher AC than those who lived in rural areas (p-value 0.04) and those who never smoked drank significantly less than smokers/ex-smokers (p-value 0.002).

AC was not different regarding the presence of underlying cirrhosis (p-value 0.35), alcohol aetiology (p-value 0.66) or in patients with active treatment vs those under surveillance of HCC relapse (p-value 0.32).

In contrast, AC was significantly higher in males (p-value <0.001), in patients diagnosed more than 1 year ago vs newly diagnosed (p-value 0.01), and in patients with early/very early BCLC stages vs others (p-value 0.05).

Regarding alcohol-free beer consumption, patients with alcohol etiology drank more than patients with other etiologies (p-value 0.0001), without differences regarding the HCC BCLC-stage (p-value 0.95).

The AUDIT-C score = > 3 (AUROC 0.849) predicts any AC with a sensitivity of 75% (95% CI 59.47-90.53) and a specificity of 84% (95% CI 74.70-94.05). Instead, the CAGE questionnaire and the analytical values [mean corpuscular volume, gamma-glutamyl transpeptidase] have a low sensitivity and specificity to discriminate against any AC in this population. CAGE > 1 [AUROC 0.626] sensitivity 72.22 (56.20-88.24) specificity 53.03 (40.23-65.83); CAGE > 2 [AUROC 0.615] sensitivity 47.22 (29.53-64.92) specificity 75.76 (64.66-86.85); MCV > 85 fL (AUROC 0.509) sensitivity 0.81 (68.94-96.08) specificity 21.2% (6.2-26.5); GGT > 40 IU/L (AUROC 0.487) sensitivity 75% (62.81-92.75) specificity 33% (18.46-42.15).

Conclusion: One third of HCC patients consume alcohol, however less than 10% consume more than 10 standard alcohol units per week. This consumption is higher in urban area, males, smokers/ex-smokers, in HCC patients diagnosed more than 1 year ago and in patients with early/very early staged tumors.

Patients with alcohol-related HCC consume more alcohol-free beer. The AUDIT-C score >= 3 discriminates against any alcohol consumption with a sensitivity of 75% and a specificity of 84% in this population.

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P0762

WHAT CHANGED IN HEPATOCELLULAR CARCINOMA PRESENTATION IN THE LAST ELEVEN YEARS? COMPARISON OF TWO SEQUENTIAL TIME SERIES FROM A TERTIARY HOSPITAL

D. Conceição¹, J. Serrazina², I. Coelho Rodrigues², A. Craciun², J. Lemos Garcia¹, M. Moura², C. Freitas², S. Carvalhana², R. Tato Marinho², H. Cortez Pinto^{2,3}

¹Portuguese Oncology Institute, Gastroenterology, Lisboa, Portugal, ²Hospital de Santa Maria, Centro Hospitalar Universitário Lisboa Norte, Gastroenterology and Hepatology, Lisboa, Portugal, ³Faculty of Medicine, University of Lisbon, Clínica Universitária de Gastroenterologia, Lisboa, Portugal

Contact E-Mail Address: dgc1990@gmail.com

Introduction: Hepatocellular carcinoma (HCC) is the sixth most common cancer and the second leading cause of cancer mortality worldwide. Hepatitis B virus (HBV) and hepatitis C (HVC) remain, at present, the most important worldwide risk factors for HCC. Nevertheless, universal HBV vaccination of new-borns and effective treatments for chronic HCV infection, will likely decrease the rates of viral-associated HCC.

Aims & Methods: Our main aim was to analyse the changes in demographics and risk factors for HCC in the last 11 years.

Retrospective single-centre study, including all patients with HCC diagnosis between 2011 and 2021 who have been referred to the multidisciplinary hepatic tumours team, in a Portuguese tertiary hospital.

We compared two subgroups, according to the diagnosis date: Group 1 from 01/2011 to 06/2016; Group 2 from 07/2016 to 12/2021. We analysed the patients' demographics, the presence of liver cirrhosis aetiology of liver disease, Child-Pugh score, ECOG score; alcohol abstinence, ALBI score, the presence of portal vein thrombosis and the imaging appearance of HCC. We performed a T-test to analyse the mean difference between the two different groups.

Results: From the total of 173 patients included, 141 were males, with a mean age of 66 years at diagnosis. Liver cirrhosis was present in 96% of patients with alcohol as main aetiology (50%), followed by HCV infection (25%), HBV (10%) and non-alcoholic fatty liver (8%).

Comparing the two series (Table), during the same length of time, the more recent one had more patients referred, patients had a worst performance status and there were more patients non-Child A. In what regards aetiology there was a percentual increase in NASH and alcohol-related cases, and a decrease in HBV and HCV related cases, although it did not reach statistical significance.

	Total (173)	Group 1(64) 01/2011 to 06/2016	Group 2 (109) 07/2016 to 12/2021	p-value
Age at diagnosis (mean)	66	67	66	0,798
Gender				
Male	141 (82%)	47 (73%)	94 (86%)	0,036
ECOG 0	130	58 (90%)	72 (66%)	0,001
Liver cirrhosis	167	62 (96%)	105 (98%)	0,848
Child-Pugh score A	135	57 (89%)	78 (72%)	0,003
Liver cirrhosis main etiology				
alcohol	86	26 (41%)	60 (55%)	0,587
HCV	43	21 (33%)	22 (25%)	
HBV	17	8 (13%)	17 (10%)	
NASH	13	3 (4%)	10 (8%)	

Table.

Conclusion: There seems to a trend for a change of HCC aetiology, as expected, with a relative increase in fatty liver disease, either alcohol or non-alcohol related. The observation that patients are referred even with decompensated liver disease, and without a good performance status, may indicate that consideration is now given to the management of HCC even in more advanced states, since there is a large array of options, that that may include active palliative care.

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P0763

CLINICAL CHARACTERISTICS AND RISK FACTORS OF EXTRAHEPATIC RECURRENCE AFTER HEPATECTOMY OF HEPATOCELLULAR CARCINOMA WITHOUT INTRAHEPATIC HEPATOCELLULAR CARCINOMA: A MULTI-INSTITUTIONAL 15-YEAR OBSERVATIONAL STUDY

W.R. Kang¹, J.H. Yoon¹, S.B. Cho¹, J.-Y. Hong¹, Y.S. Ko¹, S.K. Choi¹

¹Chonnam National University Hospital and Medical School, Department of Gastroenterology, Gwangju, Korea (Republic of)

Contact E-Mail Address: kwoorim89@hanmail.net

Introduction: Extrahepatic recurrence (EHR) is a well-known poor prognostic factor regarding hepatocellular carcinoma (HCC). Although EHR after hepatectomy of HCC may occur in high risk group of patients, little is known about EHR when there are no intrahepatic HCC. We investigated the clinical features and risk factors regarding EHR without remnant intrahepatic HCC at the time of EHR diagnosis.

Aims & Methods: This retrospective study included 1,069 treatment-naive patients who underwent curative hepatectomy for HCC at four tertiary academic hospitals from January 2004 to December 2019. Multivariate analysis via Cox-regression was performed to identify the variables associated with EHR.

Results: One hundred and sixty five patients developed EHR after hepatectomy of EHR during median follow-up duration of 4.01 years. Among patients with EHR, 58 patients (35.2%) had no viable intrahepatic HCC at EHR diagnosis. There was no significant difference in time to initial HCC recurrence and EHR development between patients group with intrahepatic HCC and without intrahepatic HCC at EHR diagnosis; 18.16 vs. 19.79 months, and 37.14 vs. 28.43 months (p=0.337), respectively.

Compared to patients with intrahepatic HCC at EHR, patients without intrahepatic HCC at EHR showed higher portion of worst Edmondson Steiner grade ≥ 3 (74.8 vs. 89.7, p=0.022), mUICC stage ($\geq III$) at 1st recurrence (45.8 vs. 74.1, p<0.001) and with lower mUICC T stage ($\geq III$) at 1st recurrence (34.6 vs. 13.8, p=0.004).

On multivariate analysis, presence of metastatic lymph nodes at pathologic examination, tumor necrosis, micro-/macro-vascular invasion, and HCC stage beyond Milan criteria was closely associated with EHR without intrahepatic HCC.

Conclusion: EHR without remnant viable HCC may occur in considerable number of patients after hepatectomy for HCC. Close monitoring for EHR is warranted in high risk group of patients despite of no HCC in liver.

Disclosure: Nothing to disclose.

P0764

EARLY EXTRAHEPATIC RECURRENCE AFTER HEPATECTOMY FOR HEPATOCELLULAR CARCINOMA SIGNIFICANTLY REDUCES SURVIVAL: A 15-YEAR OBSERVATIONAL STUDY

W.R. Kang¹, J.H. Yoon¹, S.B. Cho¹, Y.S. Ko¹, S.K. Choi¹

¹Chonnam National University Hospital and Medical School, Department of Gastroenterology, Gwangju, Korea (Republic of)

Contact E-Mail Address: kwoorim89@hanmail.net

Introduction: Extrahepatic recurrence (EHR) after curative hepatectomy for hepatocellular carcinoma (HCC) is closely associated with a poor prognosis. We investigated the features and mortality regarding early EHR and identified the predictive factors and its association with survival.

Aims & Methods: This retrospective study included 779 treatment-naive patients who underwent curative hepatectomy for HCC at two tertiary academic hospitals from January 2004 to December 2019. Multivariate analysis via Cox-regression was performed to identify the variables associated with EHR. Early EHR was defined as EHR development within 2 years after curative hepatectomy.

Results: Early EHR was diagnosed in 74 patients (9.4%) over a median follow-up period of 14.3 years, most commonly in the lungs (36.5%) followed by lymph nodes (32.4%), bone (20.3%), peritoneum (13.5%), and adrenal gland (13.5%). The median time to EHR was 0.73 year in early EHR group and 4.87 years in non-early EHR group.

The median survival duration of early EHR group, non-early EHR group, and non-EHR group was 3.05, 6.62 and 11.53 years, respectively (p<0.001) and early EHR was significantly associated with survival duration (Exp(B)=7.897, p<0.001).

On multivariate analysis, serum albumin < 4.0g/dL, serum alkaline phosphatase > 100U/L, surgical margin involvement, venous and/or lymphatic involvement, satellite nodule, tumor necrosis at pathology, sum of tumor size ≥ 7 , and macrovascular invasion at diagnosis were predictive of early EHR.

As the numbers of the risk factors increased, the probability of early EHR and the overall mortality rate inclined exponentially. (Probability of early EHR; 0/1/2/3/4/5≥ risk factors, 4.1/5.0/13.2/21.1/42.5/44.6%, respectively, median survival duration; 0/1/2/3/4/5≥ risk factors, 12.1, 11.5, 8.4, 7.0, 5.0, 2.7 years, respectively).

Conclusion: Early EHR significantly deteriorates the prognosis of HCC patients and our risk factors clarifies the clinical course of EHR and could improve the follow-up strategy to improve outcomes in high risk patients.

Disclosure: None.

P0765

IDENTIFICATION OF CT VALUES THAT COULD BE PREDICTIVE OF NECROSIS (N-CTAV) IN HEPATOCELLULAR CARCINOMA AFTER LENVATINIB TREATMENT

M. Chuma¹, H. Yokoo², H. Toyoda³, K. Ueda⁴

¹Yokohama City University Medical Center, Gastroenterological Center, Yokohama, Japan, ²Asahikawa Medical University, Division of Hepato-Biliary-Pancreatic Surgery, Asahikawa, Japan, ³Ogaki Municipal Hospital, Gastroenterology and Hepatology, Ogaki, Japan, ⁴Cancer Institute Hospital of Japanese Foundation for Cancer Research, Diagnostic Imaging Center, Tokyo, Japan

Contact E-Mail Address: chumamakoto@gmail.com

Introduction: It has been clinically shown that molecular targeted agents (MTAs) targeting vascular endothelial growth factor (VEGF) and other molecules can significantly reduce tumor blood flow on CT images. The modified response evaluation criteria in solid tumors (mRECIST) have been developed to overcome the limitations of standard RECIST criteria in assessing the response to therapy of HCC, including evaluation of tumor blood flow.

Currently, mRECIST has become the standard tool for the measurement of radiological endpoints in the early/intermediate stages of HCC. The mRECIST has been proven to capture higher objective response rates in tumors treated with molecular therapies, and these responses have been shown to be independently associated with better survival.

Although evaluation using mRECIST is an excellent tool, it is not clear whether the site of decreased “early enhancement” in the tumor (suggestive of a complete response (CR) or partial response (PR) by mRECIST evaluation) after MTA treatment is pathologically necrotic or viable.

Moreover, the future course of HCC patients with CR according to mRECIST following MTA therapy is uncertain. In terms of continuing MTA treatment or predicting the course of treatment, it is clinically important to determine whether the area in the HCC with a CR after MTA treatment according to mRECIST pathologically consists of necrotic or viable tissue.

Furthermore, it is significant to determine the criteria that might predict subsequent tumor progression following a diagnosis of CR with MTA therapy.

Aims & Methods: In this study, we attempted to identify CTav that can be used to identify necrosis in HCC tumors after lenvatinib treatment (N-CTav), and to clarify the association between the tumor N-CTav occupancy rate and maintenance of CR following lenvatinib treatment.

We compared CTav in arterial phase CT images with postoperative histopathology in four patients who underwent HCC resection after lenvatinib treatment, to determine CTav thresholds indicative of histological necrosis (N-CTav). Next, we confirmed the accuracy of the determined N-CTav in 15 cases with histopathologically proven necrosis in surgical specimens. Furthermore, the percentage of the tumor with N-CTav, i.e. the N-CTav occupancy rate, assessed using Image J software in 30 tumors in 12 patients with CR out of 571 HCC patients treated with lenvatinib, and its correlation with local recurrence following CR were examined.

Results: Receiver operating characteristic (ROC) curve analysis revealed an optimal cut-off value of CTav of 30.2 HU, with 90.0% specificity and 65.0% sensitivity in discriminating between pathologically identified necrosis and degeneration, with a CTav of less than 30.2 HU indicating necrosis after lenvatinib treatment (N30-CTav).

Furthermore, the optimal cut-off value of 30.6% for the N30-CTav occupancy rate by ROC analysis was a significant indicator of local recurrence following CR with 76.9% specificity and sensitivity (area under the ROC curve; 0.939), with the CR group with high N30-CTav occupancy (≥ 30.6%) after lenvatinib treatment showing significantly lower local recurrence (8.3% at 1 year) compared with the low (< 30.6%) N30-CTav group (P<0.001, 61.5% at 1 year).

Conclusion: The cut-off value of 30.2 HU for CTav (N30-CTav) might be appropriate for identifying post-lenvatinib necrosis in HCC, and an N30-CTav occupancy rate of >30.6% might be a predictor of maintenance of CR. Use of these indicators have the potential to impact systemic chemotherapy for HCC.

Disclosure: Nothing to disclose.

P0766

THE VALUE OF THIOREDOXIN LEVEL AND ITS GENE POLYMORPHISM IN THE DIAGNOSIS OF POST- HCV HEPATOCELLULAR CARCINOMA

M. Yousry¹, Y. Aboamer², S. Abd-Elsalam³, A. Mehrez⁴, E. Abdel-Monsef⁴, M. Saleh⁵, R. Samir⁶, A. Fouad⁶, O. Mahmoud⁷, H. Samir⁸, M. Alborae⁹

¹Faculty of Medicine for Boys, Al-Azhar University, Hepatology, Gastroenterology and Infectious Diseases, Cairo, Egypt,

²Mahala Hepatology Teaching Hospital, Hepatology, Gastroenterology and Infectious Diseases, Gharbia, Egypt,

³Faculty of Medicine, Tanta University, Tropical Medicine Department, Tanta, Egypt, ⁴Mahala Hepatology Teaching Hospital, Hepatobiliary Surgery, Gharbia, Egypt, ⁵National Hepatology and Tropical Medicine Research Institute, Internal Medicine, Cairo, Egypt, ⁶National Hepatology and Tropical Medicine Research Institute, Clinical Pathology, Cairo, Egypt, ⁷Ahmed Maher Teaching Hospital, Internal Medicine, Cairo, Egypt, ⁸Faculty of Medicine, Benha University, Hepatology, Gastroenterology and Infectious Diseases, Benha, Egypt, ⁹Al-Azhar University, Cairo, Egypt, Department of Internal Medicine, Cairo, Egypt

Contact E-Mail Address: alborae@earth-eg.org

Introduction: Hepatocellular carcinoma (HCC) is one of the most common malignancies and a leading cause of cancer-related death worldwide. Indeed, we need a novel tumor marker other than AFP for early detection and to improve the outcome. Serum thioredoxin is a promising protein involved in the pathogenesis of many malignancies.

Aims & Methods: The study aims to evaluate serum thioredoxin and its gene polymorphism in HCC in cirrhotic patients due to HCV infection. Three hundred fifty patients with HCC, 350 patients with chronic liver diseases, and 300 healthy controls were enrolled in our study. Serum thioredoxin level was measured by ELISA and a molecular study of thioredoxin domain-containing 5 (TXNDC5) gene polymorphism (rs1225943) polymorphism using real-time PCR by Taqman allele discrimination was done for all subjects.

Results: Our study revealed a significant increase in serum thioredoxin levels in patients with HCC compared to chronic liver diseases and healthy controls. Using the receiver operating characteristic (ROC) curve at the area under the curve (AUC) 0.917 and a cut-off value of >14.6 U/ml, our overall sensitivity and specificity for the HCC group over the other groups

were 86 % and 92.15%, respectively with 92.2% positive predictive value and 54.9% negative predictive value. The molecular study of TXNDC5 gene polymorphism (rs1225943) polymorphism revealed no significant difference between the studied groups.

Conclusion: Serum thioredoxin may be used as a promising tumor marker for HCC. Future researches are needed to assess its use as a single or combined with other markers in the diagnosis and follow-up of the patients after interventions.

Disclosure: Nothing to disclose.

P0767

PAROXYSMAL NOCTURNAL HEMOGLOBINURIA: A RARE CAUSE OF VASCULAR LIVER DISEASE

L. Khalif¹, M. Borahma², M. Kadiri³, F.-Z. Chabib⁴, N. Lagdali¹, C. Berhili¹, I. Benelbarhdadi¹, F.Z. Ajana⁵

¹Mohammed V University in Rabat, Hepatogastroenterology : Medecine C, CHU Ibn Sina, Rabat, Morocco, ²Mohammed the Vth University, Ibn Sina Hospital, Department of Gastroenterology C, Rabat, Morocco, ³Ibn Sina Hospital, Rabat, Rabat, Morocco, ⁴Ibn Sina university Hospital, Rabat, Morocco, Medical Unit C, Seclin, France, ⁵CHU Ibn Sina, SMMAD, Moroccan Society of Digestif Diseases, Rabat, Morocco

Contact E-Mail Address: dr.ibtissamkhalif@gmail.com

Introduction: Paroxysmal nocturnal hemoglobinuria (PNH) is a genetic pathology due to a clonal acquired somatic mutation of the PIGA gene in one or more hematopoietic stem cells, responsible for a partial or complete deficiency of glycosylphosphatidylinositol (GPI) anchor synthesis. The prognosis of this pathology is particularly related to thromboembolic complications.

The aim of our work was to specify the prevalence of this pathology in patients with vascular liver diseases (VLD) and specifying their epidemiological, clinical, therapeutic profiles, and outcomes.

Aims & Methods: It was a retrospective and descriptive study conducted over 19 years, from 2003 to march 2022, including all patients followed for vascular liver diseases, and having the presence of a positive PNH clone. The PNH clone was searched by flow cytometry to demonstrate a deficiency in GPI-linked markers on a maximum of two distinct bloodlines, in addition to an exhaustive thrombosis work-up (thrombophilia test, antiphospholipid syndrome, JAK2 mutation, neoplasia...)

Results: Out of 119 patients with vascular liver diseases, six patients had the presence of an erythrocytic and granular PNH clone, which represented a prevalence of 5.04%, including 2.5% for Porto-sinusoidal vascular disease (PSVD), 1.7% for portal cavernoma, and 0.84% for Budd Chiari syndrome (BCS).

The mean age was 42.8 years (24-65 years), and all were female.

The circumstances of discovery were variable, the pain of the left hypochondria in 66% of the cases (n=4), an upper digestive hemorrhage in 50% of the cases (n=3), and one only patient had abdominal distension (16.6%). Clinical examination revealed an enlarged spleen in 83.4%, collateral venous circulation in both flanks in 50%, and the thorax in 16.6%, and one patient only had ascites grade II. Clinical examination of the liver revealed a firm liver in 50%, a cirrhotic-looking liver in 33.4%, and a clinically normal liver in 16.6%.

Abdominal ultrasound coupled with Doppler showed a heterogeneous liver with irregular contours in 50% of cases, chronic portal thrombosis with portal cavernoma in 33.4% of cases, and BCS in 16.6% of cases.

All our patients (n=6) had portal hypertension (PH). The upper endoscopy showed endoscopic signs of PH (esophageal varices with red signs) in all patients.

Liver function tests were normal in 67% of cases, and in 33% of cases, they showed isolated anicteric cholestasis. Liver biopsy showed obliterative portal venopathy in 33% (n=2) and sinusoidal dilatation in 17% (n=1).

The etiological workup revealed an isolated PNH clone in three patients, associated with a combined protein S and C deficiency in two patients, and associated with an antiphospholipid syndrome in one patient.

The treatment was symptomatic (beta-blockers and esophageal varicose vein ligation) for all patients, AVK anticoagulation in 33% of patients (n=2); however, due to lack of resources, none of the patients was put on the specific treatment Eculizumab.

The patients were monitored every six months, with good evolution, marked by the absence of AVK-related hemorrhagic events, and eradication of esophageal varices in all patients (100%).

Conclusion: The presence of the PNH clone is a rare cause of vascular liver disease, in our small series the prevalence was 5.04%, dominated by intrahepatic block (PSVD) in 2.5% of cases.

In the setting of thrombosis, the search for PNH clone should be systematic, and the main treatment relay on Eculizumab, because anticoagulant treatment alone does not reduce the thrombotic risk in patients with PNH.

Disclosure: Nothing to disclose.

P0768

LIVER VASCULAR DISEASE AND MYELOPROLIFERATIVE SYNDROMES

Z. Amzal¹, M. Borahma², M. Kadiri³, F. Chabib⁴, N. Lagdali¹, C. Berhili¹, I. Benelbarhdadi¹, F.Z. Ajana⁴

¹Mohammed V University, Department of Hepatogastroenterology, Medecine C, CHU Ibn Sina, Rabat, Morocco, ²Mohammed V University, Ibn Sina Hospital, Department of Gastroenterology C, Rabat, Morocco, ³Ibn Sina Hospital, Rabat, Rabat, Morocco, ⁴CHU Ibn Sina, SMMAD, Moroccan Society of Digestif Diseases, Rabat, Morocco

Contact E-Mail Address: Zinebamzal199@gmail.com

Introduction: Myeloproliferative disorders are a group of diseases characterized by clonal and malignant proliferation of one or more myeloid cell lines. The platelet and leukocyte changes characteristic of these syndromes facilitate the formation of Platelet-leukocyte aggregates and therefore the development of venous and arterial thrombosis. it may involve Hepatic venous and the entire splanchnic system (portal vein, intrahepatic vessels, hepatic vein).

Our work aimed to report the epidemiological, clinical, etiological, therapeutic profiles, and outcomes of our patients.

Aims & Methods: This was a retrospective, descriptive study over 9 years, from 2013 to March 2022, and including all patients with portal hypertension (PH) by suprahepatic block (Budd Chiari), intrahepatic in the context of Liver vascular diseases (LVD), and infrahepatic (portal thrombosis).

Results: Out of 119 patients followed for liver vascular disease, 17 patients had a myeloproliferative syndrome, which represented a prevalence of 14. The average age was 44.5 years, with extremes ranging from 20 to 74 years, with a sex ratio F/H = 1.83% with a clear female predominance of 65% (n=11), the circumstances of discovery were variable: digestive hemorrhage and abdominal pain in 59%(n=10), jaundice in 24%(n=4), ascites in 18%, the clinical examination revealed the presence of splenomegaly in 94%(n=16), collateral venous circulation in 47%(n=8). Forty-seven percent (n=8) of our patients had an overloaded liver, 35% (n=6) normal liver, and 6% liver with a cirrhotic appearance.

Ultrasound coupled with Doppler showed chronic portal thrombosis with portal cavernoma in 35% (n=6), acute thrombosis in 29% (n=5), and Budd Chiari syndrome in 24% (n=4). The liver was heterogeneous in 47% (n=8),

dysmorphic in 29% (n=5) and normal in 24% (n=4). All our patients were in the stages of the PH, and the block 47% (n=8) was infrahepatic, 29% (n=5) intrahepatic and 24% (n=4) suprahepatic.

Liver biopsy confirmed intrahepatic origin (Porto-sinusoidal vascular disease (PSVD)) in 24%. The Upper endoscopy showed signs of PH esophageal varices in 95%, gastroesophageal in 59% (n=10) and isolated gastric varices in 53% (n=9). The workup showed cholestasis in 47% of cases (of which 3 patients had icteric cholestasis), cytolytic in 35%, anemia in 88%, polycythemia in 12%, hyperleukocytosis in 59% and thrombocytosis in 24%. The etiological workup (bone marrow biopsy, and JACK 2 mutation) were performed in all our patients. The bone marrow biopsy revealed the presence of primary myelofibrosis in 41% (n=7), chronic myeloid splenomegaly, and essential thrombocythemia in 18% (n=3), and Polycythemia vera in 12% (n=2).

The JAK2 gene mutation was positive in 53% (n=9). The treatment was mainly based on symptomatic treatment (beta-blockers, esophageal varices ligation if red signs, anticoagulation treatment in 77% (n=13), specific treatment of myeloproliferative syndrome based on hydroxyurea capsules in 47% (n=8).

The evolution was marked by the death of 2 patients before treatment (one patient by bleeding and another by acute myeloid leukemia at the stage of acutisation) and 1 patient after the beginning of the treatment (following an acute hepatocellular insufficiency), the rest of the patients were followed up twice a year with good clinical and biological evolution.

Conclusion: In our series, the prevalence of myeloproliferative syndrome was 14.28%. Primary myelofibrosis was the most dominant etiology. The outcomes of our patients were favorable under symptomatic and specific treatment.

Disclosure: Nothing to disclose.

P0769

VASCULAR LIVER DISEASE AND THROMBOPHILIA

Y. Jebari¹, M. Borahma², M. Kadiri³, F.-Z. Chabib⁴, C. Berhili¹, N. Lagdali¹, I. Benelbarhadi¹, F.Z. Ajana⁵

¹University Mohammed V, Rabat, Morocco, ²Mohammed the Vth University, Ibn Sina Hospital, Department of Gastroenterology C, Rabat, Morocco, ³Ibn Sina Hospital, Rabat, Morocco, ⁴Ibn Sina University Hospital, Medical Unit C, Rabat, France, ⁵CHU Ibn Sina, SMMAD, Moroccan Society of Digestif Diseases, Rabat, Morocco

Contact E-Mail Address: yousrajabari91@gmail.com

Introduction: Biological abnormalities exposed to thrombotic risk are multiple, the most commonly explored are constitutional coagulation inhibitor deficiencies. Our study aimed to determine the prevalence of constitutional coagulation inhibitor deficiencies in liver vascular diseases (LVD) and the different sites of these thromboses.

Aims & Methods: This was a retrospective, descriptive, single-center study conducted over 29 years from 2010 to April 2022, including 119 patients followed in our department. All our patients benefited from an abdominal echography completed by an abdominal CT angiography.

Results: A total of 119 patients followed for LVD, the prevalence of constitutional coagulation inhibitor deficiencies was 40.35% (n=46). The average age of our patients was 39.86 ± 12.69 years with a sex ratio F/H of 2.8. Two patients had a personal history of thrombosis, the first one had a femoral and cerebral thrombosis, and the second one had a deep vein thrombosis (DVT).

Abdominal pain was present in 56.5% (n=26) followed by digestive bleeding in 54% of cases (n=25). The clinical examination showed signs of Portal hypertension including splenomegaly in 85% (n=39), CVCs in 45.6% (n=21)

and ascites in 13% (n=6). The liver was normal in 64% (n=44), and cirrhotic in 8.7% (n=4). CT angiography showed portal thrombosis in 32.7% of cases, all of which were in the portal cavernoma stage, and Budd Chiari syndrome in 26% of cases.

Liver biopsy showed Porto-sinusoidal vascular disease (PSVD) in 41.3% of cases (n=19), five of which were complicated by portal cavernoma (10.8%). An upper endoscopy was performed for all patients and showed hypertensive gastropathy in 50% (n=23), esophageal varices grade I in 13%, grade II in 34.4%, grade III in 37%, and Gastric varices in 47.7%.

The thrombophilia etiology workup revealed a protein S (PS) deficiency in 82.6% of cases (n=38), a protein C (PC) deficiency in 69.5% of cases (n=32), antithrombin (AT) deficiency in 19.5% of cases (n=9) and a Factor V mutation in 4.3% of cases (n=2) complicated to SBC and PSVD.

A combined deficiency was found in 71.7% of cases (n=33). Half of the cases (n=23) were deficient in PC and PS, PS and AT in 4.3% of cases (n=2), and deficient in PC and AT was found in 8.7% of cases (n=4).

Three factors (PS, PC, and AT) were found in 8.7% of cases (n=4). In our series, 37% of the cases (n=17) received anticoagulant treatment, 17.5% of which were on oral anticoagulation (n=8) and 19.5% were on vitamin K antagonists (VKAs) (n=9). No cases of re-permeabilization were found, but no cases of thrombosis extension were noted under treatment. Hemorrhagic decompensation was noted in 6.5% of cases (n=3), two of which died.

Conclusion: Constitutional coagulation inhibitor deficiencies are frequent causes of vascular liver disease. In our series, they had a prevalence rate of 40.35%.

Disclosure: Nothing to disclose.

P0770

ORAL MUCOSAL HEALTH IN LIVER TRANSPLANT RECIPIENTS

A. Santonicola¹, S. Camera¹, M. Mercurio¹, F. Spirito¹, L. Sisalli¹, M. Amato¹

¹University of Salerno, Department of Medicine, Surgery and Dentistry, Scuola Medica Salernitana, Salerno, Italy

Contact E-Mail Address: antonellasantonicola83@gmail.com

Introduction: Liver transplantation (LT) is the therapeutic option of choice for acute and chronic end-stage liver disease. However, chronic immunosuppressive treatment may impact the oral health of LT recipients, although data are limited.

Aims & Methods: To evaluate the prevalence of oral mucosal lesions (OMLs) in a cohort of LT patients.

We recruited 68 LT recipients (79.4% men, mean age 64.54±10.1 years, mean BMI= 26.88±6.48 Kg/m²) from the Liver Transplant Follow-up Center of the University of Salerno. We collected demographic characteristics (gender, age, smoking habits), anthropometric data (weight, height, and BMI), the prevalence of comorbidities (hypertension, dyslipidemia, type II diabetes mellitus, chronic kidney disease, osteoporosis), LT data, and type of immunosuppressive therapy.

All patients underwent a clinical oral examination and laboratory tests. We compared data obtained with those of 34 controls, similar in age, sex, and smoking habits, recruited from the Odontostomatology clinic.

Results: 62/68 (91.2%) LT patients showed oral mucosal lesions (OMLs), in particular 40(58.8%) patients parodontopathy; 25(36.8%) Candidiasis; 20(29.4%) reduced salivary flow; 15 (22.1%) atrophic tongue, 13(19.1%) recurrent aphthous stomatitis; 10(14.7%) fissured tongue; 5(7.4%) angular cheilitis, 3(4.4%) keratotic lesions, and 1(1.5%) lichen planus-like lesions. The prevalence of OMLs was statistically higher in LT patients than in the controls (91.2% vs. 61.8%, p<0.001). In particular, LT patients showed a significantly higher prevalence of recurrent aphthous stomatitis, hypostomia, and plicated tongue than controls (p<0.05 in all cases).

The prevalence of OMLs was not significantly different in LT patients on treatment with calcineurin inhibitors (cyclosporine A and tacrolimus) compared to mTOR inhibitors (everolimus) ($p=0.33$). There was no correlation between LT time and the prevalence of OMLs ($p=0.75$). Non-smoker LT patients showed a significantly higher prevalence of recurrent aphthous stomatitis than smokers (25% vs. 0%, $p=0.026$).

Conclusion: There is a high prevalence of OMLs in LT recipients. In particular, parodontopathy is the most frequently diagnosed lesion. LT patients showed a significantly higher prevalence of OMLs than controls, probably due to chronic immunosuppressive therapy. However, the type of immunosuppressive drugs and the time from LT do not influence the prevalence of OMLs. A regular oral examination should be recommended in all LT patients.

Disclosure: Nothing to disclose.

P0771

THE ASSOCIATION BETWEEN COFFEE CONSUMPTION AND NON-ALCOHOLIC FATTY LIVER DISEASE: A CASE-CONTROL STUDY

N. Anass¹, O. Zineb¹, M. Meryem², F. Rouibaa³

¹Faculty of Medicine, Mohammed VI University of Health Sciences, Gastroenterology, Casablanca, Morocco, ²Faculty of Medicine, Mohammed VI University of Health Sciences, Casablanca, Morocco, ³Military Hospital Mohamed V-Souissi University, Rabat, Morocco

Contact E-Mail Address: anas21nadi@gmail.com

Introduction: Non-alcoholic steatotic liver disease (NAFLD) is the most common chronic liver disease worldwide. No pharmacological treatment is approved for the treatment of this disease, and all therapeutic recommendations are based on compliance with hygienic-dietary rules, weight loss, and physical activity.

Coffee is the most consumed beverage in the world and its consumption is said to reduce mortality and the risk of metabolic syndrome and type 2 diabetes. Several studies have suggested a protective role for coffee against chronic liver disease, hepatic fibrosis, and hepatocellular carcinoma; however, this finding comes from observational studies and remains controversial, particularly in the presence of confounding factors such as diabetes and low alcohol consumption.

Aims & Methods: This study aims to assess the association between coffee consumption and the prevalence and severity of NAFLD in a non-diabetic population who has never consumed alcohol. Secondly we aimed to study the other factors associated with NAFLD.

This case-control study was conducted from December 2020 to December 2021 at Cheikh Khalifa International University Hospital, Casablanca, Morocco. The target population included 157 participants seeking care in the outpatient and inpatient units of the gastroenterology and internal medicine department. Cases were defined by the presence of steatosis on liver ultrasound, the severity of which was assessed by the Bright Liver Steatosis Score. Controls were defined by the absence of steatosis on liver ultrasound. All patients with cytotoxicity and/or cholestasis had an etiological investigation (serologic testing for HBV and HCV infection, autoimmune investigation). All participants underwent liver ultrasound, clinical assessment (blood pressure, waist circumference and BMI), and biological assessment (blood count, lipid profile test, liver function tests, FBG). Dietary assessment was conducted using a food frequency questionnaire, coffee consumption was dichotomized into present or absent and then categorized according to the number of cups consumed per day.

Results: The study included 94 NAFLD and 63 controls, the two groups were comparable in demographic characteristics. The means of SBP, BMI, waist circumference, AST, ALT, Gamma-GT, Alkaline Phosphatase, and FBG were significantly higher in the NAFLD group.

The study of the association between coffee consumption and NAFLD showed a significant decrease in the risk of its occurrence ($OR=0.39$) and its severity ($OR=0.32$) in coffee consumers, mainly in those consuming 3 or more cups. In multivariate analysis, the following factors were associated with increased prevalence of NAFLD: metabolic syndrome, high mean levels of Alkaline phosphatase, Gamma-GT, ALT, FBG, BMI, and waist circumference. However, Green tea consumption was not associated with either prevalence or severity of NAFLD ($OR=1.02$, $p=0.82$).

Conclusion: The relationship between coffee and steatotic liver disease is not fully understood, and the results of studies are disparate. Our work suggests that coffee plays a protective role against the prevalence and severity of NAFLD. As coffee is an accessible and relatively inexpensive beverage, it could be included in dietary rules for a healthier diet and implemented as a preventative strategy if future studies were to confirm our data. Further prospective studies are needed to establish a cause-effect relationship between coffee and NAFLD.

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Disclosure: Nothing to disclose.

P0772

ASSESSMENT OF ACCESSIBILITY TO DIAGNOSIS AND TREATMENT OF HEPATITIS C: A LARGE RETROSPECTIVE COHORT FROM A TERTIARY CARE HOSPITAL IN TURKEY

M. Eren Durmuş¹, G. Köker¹, A.H. Cekin², S. Öcal², F. Akbay Harmandar²

¹University of Health Sciences Antalya Training and Research Hospital, Internal Medicine, Antalya, Turkey, ²University of Health Sciences Antalya Training and Research Hospital, Gastroenterology, Antalya, Turkey

Contact E-Mail Address: drmerveeren@gmail.com

Introduction: Hepatitis C virus (HCV) infection is a major public health problem. According to 2015 data, approximately 71 million people have chronic HCV viremia globally. It is one of the leading causes of liver-related morbidity and mortality in the world. The seroprevalence of anti-HCV in our country has been detected 0.5-1%. Due to its silent progress many patients may be unaware of the situation.

Aims & Methods: In our study, we aimed to determine the rate of the anti-HCV positive patients who were able to achieve viral elimination and also the number of the patients who were possibly under-diagnosed or lost to follow-up. Subjects who had anti-HCV positivity between 2014-2019 and older than 18 have been reviewed retrospectively.

The data of the patients were recorded and patients referred for further evaluation and accessed to the treatment and the ones who achieved sustained viral response after twelve weeks from the end of the therapy (SVR12) were identified.

Results: There were 7260 anti-HCV positive patients in 5-years period. 5685 of them were tested for HCV viremia (78.3 %). HCV-RNA was positive in 1620 of them (22.3 %), corresponding to 28.4 % of the patients who have been tested for HCV-RNA. Among the patients with HCV-RNA positivity, 1288 of them were tested for HCV genotype (17.7 %). Only 848 of them could access to treatment (11.6 %). The patients were treated with either an interferon-based regimen (n= 143, 16.9 %) or direct acting antivirals (n= 705, 83.1%). Only 607 of the patients were tested for SVR12 and 568 of them could achieve viral clearance.

Conclusion: The World Health Organization has been set international targets for the elimination of HCV infection by 2030, which is a public health threat. According to our study, there are significant deficiencies in several stages of the treatment cascade, which is consistent with world data. Recently, highly efficient oral direct acting antivirals have made the treatment of HCV infection more practical. Both improving patients' awareness and knowledge of all physicians is essential to prevent losses and delays in the diagnosis and treatment of HCV infection.

Disclosure: Nothing to disclose.

P0773

INCREASING OF GUT BACTERIAL BILE SALT HYDROLASE ACTIVITY BY PROBIOTIC LACTOBACILLUS PLANTARUM IN PATIENTS WITH DYSLIPIDEMIA: A RANDOMIZED STUDY

A. Neverovsky¹

¹Bogomolets National Medical University, Internal Medicine #1 with a course of Gastroenterology, Kyiv, Ukraine

Contact E-Mail Address: artemneverovskiy@gmail.com

Introduction: Supplementation with probiotic bacteria may be effective in the treatment of hypercholesterolemia due to different mechanisms. One of them is a modification of bile acid metabolism by gut bacterial bile salt hydrolase (BSH).

Aims & Methods: Aim of study was to assess the effectiveness of additional supplementation with probiotic Lactobacillus plantarum (LP) in modification of gut bacterial BSH relative activity (RA) in patients with dyslipidemia. The trial included 77 patients aged 40-74 years with dyslipidemia that were randomly divided in two groups: case group (n=41) that were treated with combination of simvastatin 20 mg once daily and probiotic LP in the amount of 2×10^9 CFU once daily and control group (n=36) that were treated with simvastatin monotherapy 20 mg once daily during 12 weeks.

Fecal samples were collected for assessment of RA of gut bacterial BSH using the ultra-performance liquid chromatography-mass spectrometry (UPLC-MS) method. For determining the differences between groups, the unpaired, paired t-tests, Wilcoxon signed-rank and matched pairs tests were used.

Results: The baseline demographic and clinical characteristics were not different between trial's groups. It was shown that baseline levels of RA of gut bacterial BSH were not significantly different between case group (0,1 (0,06-0,14) U/ml) and control group (0,086 (0,05-0,13) U/ml), p=0,4. But after 12 weeks of treatment it was revealed that RA of gut bacterial BSH: in case group began significantly higher ($0,2 \pm 0,07$ U/ml) comparing with baseline levels, p<0,001; in control group there was no difference between baseline levels and after 12 weeks of investigation (0,085 (0,05-0,14) U/ml), p=0,53. RA of gut bacterial BSH after 12 weeks of trial was significantly higher in case group comparing to control group, p<0,001.

Conclusion: Additional supplementation with probiotic Lactobacillus plantarum during 12 weeks was effective in increasing of relative activity of gut bacterial BSH in patients with dyslipidemia.

Disclosure: Nothing to disclose.

P0774

EFFECT OF ANTIBIOTICS AND ERCP STENT PLACEMENT IN THE BILIARY MICROBIOME IN THE CHOLEDOCHOLITHIASIS PATIENTS WITH ACUTE BILIARY INFECTION

Y.-C. Chen¹, T.-K. Fang¹, X.-H. Huang¹, T.-Y. Chiang¹, Y.-N. Huang¹, Y.-B. Lu¹, Y.-C. Weng¹

¹Xiamen Chang Gung Hospital, Department of Digestive Disease, Xiamen City, China

Contact E-Mail Address: yuchieh.j.weng@gmail.com

Introduction: It is generally believed that endoscopic retrograde cholangiopancreatography (ERCP) is the vital treatment for those choledocholithiasis patients with acute biliary infection. However, administration of antibiotics before ERCP treatment is usually the clinical routine medicine therapy for acute biliary infection.

In addition, endoscopic sphincterotomy in ERCP is common procedure prior to the retrieval of common bile duct stones. Some studies indicated that endoscopic sphincterotomy (EST) damaged the function of sphincter

of Oddi, leading to further regurgitation of the duodenal contents and gut bacteria into the bile duct, biliary tract infection due to biliary microbiome alteration and choledocholithiasis recurrence.

However, there is lacking of study to prove the effect of antibiotic agents and ERCP biliary plastic placement procedure whether affect the variety of biliary microbiome. Therefore, in this study, we try to investigate whether ERCP biliary plastic stent placement and usage of antibiotics affect the characteristic of biliary microbiome.

Aims & Methods: 10 choledocholithiasis patients with acute biliary infection, diagnosed basing on Tokyo guideline 2018(TG18), were recruited at Xiamen Chang Gung Hospital from 2019 to 2021. At beginning of admission, all patients were administrated antibiotic agents (3rd generation ciprofloxacin or quinolone) for the medical therapy of acute biliary infection. The bile samples were collected during the 1st time ERCP treatment. And we all preformed EST for stone retrieval and biliary plastic stent was placed to avoid the complication of biliary obstruction related to blood clot and the complication of post-ERCP cholangitis.

The 2nd time ERCP was executed to remove the biliary plastic stent and collect the bile samples in these same patients without usage of antibiotics at least over 21 days. The method of DNA extraction and 16s rRNA gene sequencing of bile samples was used to analyze and compare the biliary microbiome composition between 1st and 2nd time ERCP group.

Results: The result revealed that Firmicutes (44.7%), Actinobacteriota (15.9%), Bacteroidota (13.5%) and Proteobacteria (11.2%) were the most dominant phyla in these 20 bile samples. The beta-diversities of bile juice from 2nd time ERCP group were significantly different to 1st time ERCP group (Anosim; R= 0.2037; p=0.001), but the alpha-diversities were comparable (Chao1; p=0.2899). LefSe results showed that 1st time ERCP group had higher abundance in Streptococcus (LDA=4.02; p=0.028) and Cyanobacteria (LDA=4.38; p=0.049), while the 2nd time ERCP group had higher levels of Blautia(LDA=4.08; p=0.018)and Gammaproteobacteria (LDA=4.16; p=0.049).PICRUST2 analysis revealed that KEGG Level 2 of 1sttime ERCP group was significantly difference to 2nd time ERCP group(Anosim; R=0.1867; p=0.012).

Conclusion: Our study showed that under the treatment of antibiotics and ERCP plastic stent placement, the choledocholithiasis patients with acute biliary infection demonstrated microbial dysbiosis with a significant reduction in microbial beta-diversity in bile of 1st time ERCP group comparing to the 2nd time ERCP group. In addition, the Streptococcus and Cyanobacteria were abundant in the 1st ERCP group; microbiota functional capacities with significant differences between 1st and 2nd time ERCP group which suggested that they can be used as predictive indicators for acute biliary infection in choledocholithiasis patients.

Disclosure: Nothing to disclose.

P0775

EFFECTS OF BILE ACIDS ON METABOLIC PROFILE IN OBESE ANIMAL MODEL

C.H. An¹, K.H. Ryu¹, H.Y. Chon¹, D.S. Kim¹, S.H. Lee¹, Y.W. Choi¹
¹Konyang University College of Medicine, Gastroenterology, Daejeon, Korea (Republic of)

Contact E-Mail Address: anchy92@naver.com

Introduction: Microbiotas in the body affect metabolism. Some studies show that sterile laen mouse receiving intestinal microbiota from obese mouse gained more weight. Bile acids are inhibitor of intestinal microorganisms. Each of bile acids have a varying degree of hydrophobicity and pH, so the influence on microbiotas also varies.

Therefore, the administration of bile acids are expected to change the microbial environment in the intestine microbiota and would affect metabolic indicators including body weight.

Aims & Methods: The first study was conducted for 8 weeks by comparing the weight change of three groups: control, high fat diet (HFD) and HFD + ursodeoxycholic acid (farenoid X receptor[FXR] antagonist; UDCA).

The second study compared the two groups of HFD, HFD + UDCA for 5 weeks to confirm reproducibility, and as another control, HFD + obeticholic acid(FXR agonist; Ocaliva®) was added. In the study, serum metabolic indices were evaluated and homeostatic model assessment for insulin resistance(HOMA-IR) were also measured.

Results: Compared to the control group, the weight gain rate of the HFD group was significantly increased, but the increase was slowed in the group receiving the UDCA together. In the second experiment, although the rate of weight gain was slowed in the group treated with obeticholic acid, it was less than that of UDCA.

Compared to the high-fat diet alone group, liver enzymes were significantly decreased in the UDCA group. There was no statistically significant difference in blood glucose in the UDCA group, but significantly decreased in the obeticholic acid group. HOMA-IR also decreased in the UDCA group, but more significantly in the obeticholic acid group.

Both UDCA and obeticholic acid co-administration with high-fat diet group showed an increased Firmicutes/Bacteroidetes ratio in the intestinal microbiota, more clearly observed in the obeticholic acid group.

Conclusion: Coadministration of obeticholic acid slowed weight gain but was less potent than UDCA. In high-fat diets, UDCA administration had a positive effect on values reflecting hepatobiliary inflammation. UDCA did not have a positive effect on blood glucose or lipid level but reduced insulin resistance. Obeticholic acid administration had a strong positive effect on blood sugar, lipid levels, and insulin resistance in high-fat diets than UDCA. The experimental results showed that the intestinal Firmicutes/Bacteroidetes ratio increased in the UDCA and obeticholic acid co-administration group, Contrary to past reports.

This result is paradoxical to the slowing of weight gain by bile acid administration. In conclusion, weight gain due to high fat diet may be slowed down by bile acids. However, It is not likely to be due to microbial changes in the intestinal tract but is likely to be involved in the direct effect of body metabolism of bile acids.

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P0776

DELAYED VERSUS EARLY LAPAROSCOPIC CHOLECYSTECTOMY POST PERCUTANEOUS CHOLECYSTOSTOMY. DOES IT MATTER?

K. Abdelsaid¹, M. Hassan¹, B. Jayasanakar¹, Y. Abdul Aal¹

¹Maidstone and Tunbridge Wells NHS trust, General Surgery, Tunbridge Wells, United Kingdom

Contact E-Mail Address: Kirolos.Abdelsaid@nhs.net

Introduction: Percutaneous cholecystostomy (PC) is an effective option for high risk and delayed presented Acute cholecystitis (AC). However, the optimal timing for subsequent laparoscopic cholecystectomy (LC) as a definitive treatment remains controversial.

Aims & Methods: This study includes 41 patients who underwent LC following PC for severe AC. We compared the length of tube insertion, the period from PC till LC and the period from PC removal till LC against comorbidities, another attack of AC, subsequent pancreatitis/jaundice and operative difficulties in terms of intraoperative adhesions, drain insertion, conversion to open, length of operation.

To compare the effectiveness, possible advantages, and complications of early cholecystectomy versus delayed cholecystectomy following Percutaneous Cholecystostomy in patients with Acute Cholecystitis.

Results: The median time of the length of tube insertion was 36 days (range 5-208), while the median time of PC insertion till LC was 144 days (range 31-744), and for the period from PC removal till LC was 78 days (range 0-714).

In addition, patients with prolonged tube insertion (more than a month) showed a higher risk of developing subsequent pancreatitis and jaundice ($P=0.04$). At the same time, intraoperative adhesions were associated with prolonged time from tube insertion to operation (more than four months). However, there was no significant association between the length of tube insertion, period from PC insertion till LC, period from PC removal till LC, and other studied parameters.

Conclusion: Prolonged time of PC insertion and prolonged time from PC insertion till LC in patients with AC have a higher risk of pancreatitis and surgical difficulties. Further studies, including a more significant number of patients sample, are warranted to confirm the outcomes and determine the optimal time of LC following PC in those patients.

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P0777

RISK FACTORS ASSOCIATED WITH HEMORRHAGIC AND THROMBOEMBOLIC COMPLICATIONS AFTER ENDOSCOPIC RETROGRADE CHOLANGIOPANCREATOGRAPHY (ERCP)

J. Castro Rodríguez¹, R.M. Alejandro Altamirano¹,

M. Pleguezuelo Navarro¹, F.J. Serrano Ruiz¹, A.J. Hervás Molina¹

¹Hospital Universitario Reina Sofía, Department of Gastroenterology, Córdoba, Spain

Contact E-Mail Address: jcastorodriguez01@gmail.com

Introduction: Endoscopic retrograde cholangiopancreatography (ERCP) is a growing procedure in the diagnosis and treatment of biliary and pancreatic obstructive pathologies. Among its complications are: pancreatitis (the most frequent 1.3-9.7%), hemorrhage (0.76-2.3%) and others such as perforation and cholangitis. Thrombotic complications have been less studied.

Aims & Methods: The aim of the study was to identify risk factors associated with the occurrence of hemorrhagic complications and thromboembolic events in the 30 days post-ERCP.

We conducted an observational study that included a total of 644 therapeutic ERCPs performed on 544 patients at the Hospital Universitario Reina Sofia in Cordoba (Spain) in 2019, with prospective follow-up within 30 days after the procedure.

Results: A total of 51.6% of ERCPs were performed in men, with a mean age of 72 ± 15.1 years. There were history of hypertension (64.9%), diabetes (26.4%), stroke (8.9%), ischemic heart disease (9%), atrial fibrillation (15.5%) and thromboembolic event (2.8%). The most frequent indication for ERCP was the presence of choledocholithiasis (73.3%), with malignant stenosis accounting for 15.2%. Prior anticoagulant and antiplatelet medication was present in 17.4% and 24.2% of procedures, respectively.

Bleeding occurred in 9.8% of procedures. The only variable associated with an increased risk of bleeding was the performance of sphincterotomy, with biliary prosthesis placement after sphincterotomy being a protective factor (Table 1), both of them in univariate and multivariate logistic regression.

Six thromboembolic events were identified in the 30 days after ERCP (0.93%): 3 strokes, 2 deep venous thromboses of the lower limbs and 1 portal thrombosis. The variables associated with an increased thrombotic risk were: atrial fibrillation, recurrent thromboembolism (TE) and rheumatic valve disease (Table 1).

The recurrent TE maintains statistical significance in multivariate analysis. The incidence of thrombosis was also higher in patients taking apixaban and heparin compared to other anticoagulants ($X^2: 81.19$ $p < 0.001$, $R^2: 1.96$). Correct or inadequate discontinuation and/or reintroduction of anticoagulant and/or antiaggregant drugs was not associated with an increased risk of thromboembolic or hemorrhagic events.

	X ²	p	OR (IC95%)	p
Sphincterotomy	92,1% vs 7,9% X ² :14,11	0,001	4,56 (1,86-11,2)	0,001
Biliary prosthesis	11,85% vs 5,07% X ² :7,12	0,006	0,17 (0,07-0,39)	0,013
Atrial fibrillation	50% vs 15,2% X ² :10,91	0,05	5,57 (1,14-27,23)	0,037
Recurrent thromboembolism	16,7% vs 0,15% X ² :52,34	0,001	64,10 (12,45-329,78)	0,001
Rheumatic valve disease	16,7% vs 0,2% X ² :6,58	0,037	9,71 (1,21-77,36)	0,039

Table 1.

Conclusion: The occurrence of bleeding and thrombosis after ERCP or other endoscopic procedures has been well established in several studies. Identifying predisposing risk factors allows close monitoring of the most

vulnerable patients to prevent the appearance of these complications or to detect them early. Although in our study inadequate periprocedural management of antithrombotic therapy was not associated with a significant increase in the incidence of hemorrhagic or thromboembolic events 30 days after ERCP, it is advisable to follow the recommendations of the different clinical practice guidelines, since this relationship has been established in other studies.

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P0778

THE IMPACT OF HOSPITAL LEVEL OF CARE ON THE MANAGEMENT OF ACUTE CHOLECYSTITIS: A POPULATION-BASED STUDY

L. Lindqvist¹, A. Andersson¹, J. Österberg^{2,3}, G. Sandblom⁴, O. Hemmingsson¹, P. Nordin¹, L. Enochsson¹

¹Umeå University, Department of Surgical and Perioperative Sciences, Surgery, Umeå, Sweden, ²Karolinska Institutet, Department of Clinical Sciences, Intervention and Technology (CLINTEC), Stockholm, Sweden, ³Mora Hospital, Department of Surgery, Mora, Sweden, ⁴Karolinska Institutet, Department of Clinical Science and Education, Södersjukhuset, Stockholm, Sweden

Contact E-Mail Address: lars.enochsson@umu.se

Introduction: Acute cholecystitis (AC) is the most common complication of gallstone disease, affecting about 20% of patients admitted for biliary tract disease (1,2). Several studies have shown that early cholecystectomy performed within the first week decreases overall morbidity and the total length of stay compared to delayed operation (3,4). The organisation of healthcare might also have an impact on when patients with AC are treated which in turn may affect the outcome.

Aims & Methods: The aim of this study was to analyse how patients with AC are treated in relation to the number of hospital beds as well as level of care at the respective hospital. Data were collected from the Swedish Register for Gallstone Surgery and ERCP (GallRiks). Cholecystectomies between 2010 and 2019 were included. The inclusion criterion was acute cholecystectomy in patients with ongoing AC.

Results: Of 120 655 cholecystectomies, 24 194 (20%) met the inclusion criterion. There was a positive correlation between number of hospital beds at the surgical clinics and number of days between admission and surgery ($R^2=0.132$; $p=0.0075$).

Furthermore, the time between admission and surgery was significantly extended at Tertiary Referral Centres (TRC) compared to regional hospitals (2.2 ± 1.7 days vs. 1.6 ± 1.4 days, mean $\pm$ SD; $p<0.0001$). However, there was no correlation between time of cholecystectomy and intra- and/or postoperative complications at the respective hospital levels ($R^2=0.002$; $p=0.7618$).

Conclusion: An increased number of surgical hospital beds did not shorten the time to acute cholecystectomy on patients with AC. However, the time to cholecystectomy was significantly longer at TRCs compared to regional hospitals. Although it is not certain that these findings can be generalised to healthcare organisations outside Sweden, these results indicate that logistic differences as well as different levels of hospital care may affect the management of patients with AC.

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P0779

EFFECTIVENESS AND FACTORS AFFECTING TECHNICAL SUCCESS OF AN ENDOSCOPIC SPHINCTEROTOMY IN PATIENTS WITH LARGE STONES AND COMMON BILE DUCT EMPYREMENT

B. Aourarh¹, A. Benhamdane¹, T. Addajou¹, K. Boualiten¹, E. ilham¹, F. Rouibaa¹, A. Benkirane¹, H. Seddik¹

¹Mohamed V Military Hospital, Gastroenterology II, Rabat, Morocco

Contact E-Mail Address: benayad.aourarh@gmail.com

Introduction: Biliary endoscopic sphincterotomy stands as a gold-standard in the treatment of the common bile duct (CBD) stones. Its efficiency can be nevertheless limited by the presence of large stones or CBD empyrement.

The aim of our study is to evaluate the effectiveness of biliary endoscopic sphincterotomy (EST) in patients with large stones (more than 15mm), patients with one or two stones and patients with a CBD empyrement; and also, to identify the factors affecting technical success of endoscopic drainage and its complications in the management of large bile duct stones.

Aims & Methods: In this monocentric study, conducted in the gastroenterology department, 1011 patients with CBD stones treated by EST were included retrospectively over a period of 19 years between April 2002 and September 2021.

The common bile duct empyrement was defined by the presence of multiple stones (more than 3) while the large stone was defined by a stone with a size >15mm.

Our patients were divided in two groups:

Group 1. (n=143): Patients with a large stone

Group 2. (n=868): Patients with one or two stones; or a CBD empyrement.

All the demographic, clinic, endoscopic and therapeutic data was collected, and entered then analyzed on the program JAMOV 2.0 using the logistic regression model in univariate and multivariate analyses.

Results: Patients in group 1 represented 14.1% of the patients included whereas the group 2 included 85.9% of the patients.

Success rate after one catheterization was 55.2% in group 1 versus 81% in group 2 ($p < 0.001$).

An endoscopic revision was noted in 14.7% of the patients in group 1 versus 8% in group 2 ($p = 0.009$). Complementary maneuvers were performed in 46.2% of cases in group I versus 16.1% in group II.

Global success rate after the endoscopic revision and/or complementary maneuvers was of 88.7% in group 1 versus 10.5% in group 2 ($p = 0.125$).

The overall rate of early complications was 10.5% in group 1 versus 5.1% in group 2 with a statistically significant difference between the two groups ($p = 0.017$).

In univariate analysis, the factors that reduce significantly the overall success of endoscopic treatment were: age, a cholangitis, a stenosis or an important dilation ($> 15\text{mm}$) of the CBD.

In a multivariate analysis and by adjusting the parameters studied, namely age, sex, surgical treatments, acute pancreatitis, cholangitis, perampullary diverticulum, CBD diameter and a CBD stenosis; only the presence of a cholangitis (OR: 0,295 IC 95%: [0,164 – 0,532] $p < 0.001$) and the presence of a CBD stenosis (OR: 0,53 IC 95%: [0,922 – 1,051] $p: 0.001$) were statistically significantly associated with the reduction of the overall success of endoscopic treatment.

Conclusion: Our study showed that there was no significant statistical difference of effectiveness in the endoscopic treatment between patients with a large stone and those with a simple stone.

The presence of a cholangitis and a CBD stenosis seem to be factors affecting the decrease of the overall success of an endoscopic treatment.

Disclosure: Nothing to disclose.

P0780

LOW-PHOSPHOLIPID-ASSOCIATED CHOLELITHIASIS (LPAC) SYNDROME - CLINICAL, RADIOLOGICAL AND GENETIC ASPECTS OF A CASE SERIES

F. Bordalo Ferreira¹, L. Martins Figueiredo¹, M. Cardoso¹, J. Carvalho e Branco¹, L. Carvalho Lourenço¹, D. Horta¹

¹Hospital Professor Doutor Fernando Fonseca, Gastroenterology, Amadora, Portugal

Contact E-Mail Address: filipamvpbferreira@gmail.com

Introduction:

LPAC (low-phospholipid-associated cholelithiasis) syndrome is a genetic condition associated with increased incidence of gallstone disease. This disorder is caused by mutations in ABCB4 and related genes, which reduce the biliary concentration of phosphatidylcholine, contributing to lithogenic bile and biliary epithelium lesion.

This diagnosis should be suspected when at least two clinical criteria are present: age less than 40 years at onset of biliary symptoms, recurrence of biliary symptoms after cholecystectomy or intrahepatic hyperechogenic foci detected by ultrasound suggestive of intrahepatic sludge or stones. Clinical suspicion should be raised by personal history of intrahepatic cholestasis of pregnancy or by first degree family history of gallstones. Treatment with ursodeoxycholic acid is usually effective.

Aims & Methods: We describe a series of 5 patients with an established diagnosis of LPAC syndrome. Patients with at least two clinical criteria and confirmed mutations in ABCB4 and/or ABCB11 genes were included. These cases are illustrated by detailed iconography.

Results: Three male and two female patients were included, with ages at

diagnosis of 38 to 55 years-old. Clinical manifestations and outcomes were variable. The description of cases encompasses personal and family history, clinical presentation, findings of diagnostic and therapeutic exams (abdominal ultrasound, computed tomography, magnetic resonance cholangiopancreatography [MRCP] and endoscopic retrograde cholangiopancreatography [ERCP]), genetic testing and clinical outcomes.

We describe different manifestations, including acute pancreatitis, acute cholangitis and their complications (liver abscesses and portal vein thrombosis), recurrent choledocholithiasis and intrahepatic lithiasis, and chronic complications, namely secondary sclerosing cholangitis and biliary cirrhosis.

Conclusion: This case series alerts to clinical manifestations which should raise suspicion for LPAC syndrome, such as recurrent biliary gallstones, especially after cholecystectomy, and intrahepatic foci of lithiasis. Recognizing this diagnosis has important therapeutic implications and allows for genetic counseling, essential for timely detection of at risk relatives.

Disclosure: Nothing to disclose.

P0781

THE RISK FACTORS OF RECURRENT CHOLEDOCHOLITHIASIS IN PATIENTS AFTER GASTRECTOMY

M.K. Jung¹, J. Heo¹, C.-M. Cho², D.W. Lee², J.-K. Lim³

¹Kyungpook National University Hospital, Internal Medicine, Daegu, Korea (Republic of), ²Kyungpook National University Chilgok Hospital, Internal Medicine, Daegu, Korea (Republic of),

³Kyungpook National University Hospital, Radiology, Daegu, Korea (Republic of)

Contact E-Mail Address: hero797@hanmail.net

Introduction: The incidence of cholelithiasis was reported to be higher in patients after gastrectomy than in the general population. However, there is no study for recurrent choledocholithiasis incidence in patients after gastrectomy.

Aims & Methods: The aim of this study is to evaluate the risk factors contributing to the recurrence of choledocholithiasis in patients after gastrectomy. A retrospective analysis was made of the patients after gastrectomy who underwent choledocholithiasis removal between January 2011 and December 2019 in Kyungpook National University Hospital.

Results: The choledocholithiasis was treated by endoscopic retrograde cholangiopancreatography (ERCP) ($n = 41$) or percutaneous transhepatic biliary drainage (PTBD) ($n = 90$). The type of gastrectomy was classified as subtotal gastrectomy with Billroth-I (18.3%), Billroth-II (45.0%), and total gastrectomy with Roux-en-Y (35.1%). The recurrence of choledocholithiasis was found in 18 of 131 patients (13.7%) during mean follow-up period of 31.5 months (range 6-105 months). The recurrent choledocholithiasis was higher in ERCP group (24.4%) than in PTBD group (8.9%). Stone removal modality (ERCP), no use of balloon sphincteroplasty, sphincteroplasty balloon size less than 12 mm, the presence of perampullary diverticulum and common bile duct (CBD) stricture were the significant risk factors for recurrent choledocholithiasis.

On univariate analysis, CBD stricture (HR 5.73, 95% CI: 1.53-21.48) was risk factor for recurrent choledocholithiasis after ERCP stone removal. The balloon sphincteroplasty (HR 0.23, 95% CI: 0.06-0.94) and balloon size larger than 12 mm (HR 0.88, 95% CI: 0.78-1.00) were factors that decrease the recurrent choledocholithiasis after PTBD stone removal.

By multivariate analysis of Cox proportional hazard model, stone removal modality (ERCP) ($P = 0.024$), no use of balloon sphincteroplasty ($P = 0.005$), and sphincteroplasty balloon size less than 12 mm ($P = 0.027$) were associated with recurrent choledocholithiasis after gastrectomy.

Conclusion: This study demonstrates the balloon sphincteroplasty with

balloon size over 12mm could decrease the recurrence of choledocholithiasis following gastrectomy regardless of the stone removal modality.

Disclosure: Nothing to disclose.

P0782

CAN DI-ISOPROPYL IMINODIACETIC ACID (DISIDA) SCAN PREDICT THE RECURRENT BILIARY EVENTS?

S.J. Hwang¹, W.C. Chung¹

¹St. Vincent's Hospital, College of Medicine, The Catholic University of Korea, Department of Internal Medicine, Suwon, Korea (Republic of)

Contact E-Mail Address: niledelta@naver.com

Introduction: A Tc-99m di-isopropyl iminodiacetic acid (DISIDA) scan is a specialized radiology procedure used to assess the function and structure of the gallbladder. We aim to whether DISIDA scan predict the recurrent biliary events after recovers from mild cholecystitis or removal of the common bile duct (CBD) stones.

Aims & Methods: A consecutive series of the patients were undertaken from March. 2010 to March. 2020. A total of 121 patients were enrolled. The mean follow-up period was 58 months (range 6–125 months).

The patients with mild cholecystitis, and those with CBD stone with or without gallbladder stones were enrolled. Due to mild symptoms, all of them did not have cholecystectomy.

After the improvement of symptoms, they underwent DISIDA scan and regular follow-up was done. We checked whether there were recurrent biliary events. Patients were categorized into two subgroups: recurrent biliary events (n = 55), and symptom-free group (n = 66).

Results: In patients having the positive results of non-visualization of the gallbladder or gallbladder ejection fraction (GBEF) <40 %, the risk of cholecystectomy due to event recurrence was significantly higher ($P < 0.01$). In patients with cholecystitis, the patients with positive DISIDA scan had the higher rate of recurrent biliary events regardless of gallbladder stones ($P < 0.01$). In patients with CBD stone, the results of DISIDA scan was a good predictor for recurrent biliary events ($P < 0.01$).

Conclusion: DISIDA scan could be a good tool to predict recurrent biliary events in patients who had cholecystitis or CBD stone.

Disclosure: Nothing to disclose.

P0783

CHOLECYSTECTOMY REDUCES THE RISK OF MYOCARDIAL INFARCTION AND CEREBRAL INFARCTION IN PATIENTS WITH GALLSTONE-RELATED INFECTION

S.-M. Park^{1,2}, H.S. Ahn³, H.J. Kim³, S.M. Lee², C. Park², H.B. Kwon²

¹Chungbuk National University College of Medicine, Internal Medicine, Cheongju, Korea (Republic of), ²Chungbuk National University Hospital, Internal Medicine, Cheongju, Korea (Republic of), ³Korea University College of Medicine, Preventive Medicine, Seoul, Korea (Republic of)

Contact E-Mail Address: jyoosin@hanmail.net

Introduction: Gallstones are positively associated with myocardial infarction (MI) and cerebral infarction (CI). However, risk changes of MI or CI in the condition of gallstone-related infection (GSI) or by cholecystectomy are still controversial.

Aims & Methods: We compared the risks of MI or CI in patients with GSI or not-GSI and risk changes of them by cholecystectomy. GSI (n=84,467) and non-GSI (n=406,800) patients with age- and sex-matched controls (n=4,912,670) were identified from Korean National Health Insurance and

Korean National Health Screening Exam database. Adjusted hazard ratios (aHRs) of MI or CI were analyzed in both groups treated by cholecystectomy or not.

Subgroup analysis was performed in both sexes and in different ages. Cardio-metabolic risk factors such as blood pressure, pulse pressure, fasting plasma glucose, body mass index, cholesterol, smoking, alcohol drinking and physical activity were adjusted.

Results: Risks of MI or CI were higher in GSI group compared to non-GSI group (aHR of MI; 1.32 vs. 1.07, aHR of CI; 1.24 vs. 1.06, respectively). Risk of MI was reduced by cholecystectomy in GSI group, while it was equivocal in non-GSI group (risk reduction rates by cholecystectomy; 11.4% and 0%, respectively).

Risks of CI were reduced by cholecystectomy in both GSI and non-GSI groups, while its effect was greater in GSI group (16.1% and 4.7%, respectively). Original risks of MI or CI in gallstone patients and risk reduction rates by cholecystectomy were higher in females and in younger patients compared to those in males and in older ones, respectively.

Conclusion: Increased risks of MI or CI and greater risk reduction by cholecystectomy were seen in patients with GSI. Therefore, cholecystectomy is strongly recommended for patients with GSI, especially in females or in young patients.

Disclosure: No conflict of Interest.

P0784

THE YIELD OF ENDOSCOPIC ULTRASOUND IN INVESTIGATION OF INCIDENTAL COMMON BILE DUCT DILATATION

T. Khoury¹, A. Shahin², W. Sbeit²

¹Galilee Medical Center, Department of Gastroenterology, Naharia, Israel, ²Galilee Medical Center, Gastroenterology, Naharia, Israel

Contact E-Mail Address: tawfik.khoury.83@gmail.com

Introduction: There are controversies regarding the upper normal diameter of the common bile duct (CBD) but it is accepted to be 7 mm. Dilated bile ducts are usually caused by an obstruction of the biliary tree, which can be due to stone, tumors (usually of either the papilla of Vater or the pancreas), benign strictures (due to chronic pancreatitis or primary sclerosing cholangitis) benign stenosis of the papilla (ie, papillary stenosis), and papillary diverticulum.

Factors like age, height, weight, BMI, previous cholecystectomy, drugs, and type of imaging modality affect CBD diameter, but the duct significantly dilated due to obstructive biliary pathology.

With the widespread use of abdominal imaging, an incidentally found dilated common bile duct (CBD) is a common radiographic finding. Endoscopic ultrasound (EUS) provides high-resolution, real-time imaging of the gastrointestinal tract and surrounding extramural structures.

Aims & Methods: The aim of the study is to explore the yield of EUS in investigation of incidental common bile duct dilatation according to computed tomography (CT) scan. This is a retrospective single-center study with inclusion of all patients who referred for EUS performed for evaluation of incidental CBD dilatation according to CT in the Gastroenterology department at Galilee Medical Center from 2016 till 2020.

Results: Overall, 65 patients were included in the study. All of them were referred for further investigation of dilated CBD according to CT. The average age of the entire cohort was 67.2 ± 16.1 (28-97) years. Twenty-one patients (32.3%) were males.

The rate of smoking, obesity, diabetes mellitus, hypertension, hyperlipidemia, congestive heart failure and alcohol drinking were 15.4%, 27%, 32.3%, 52.3%, 53.8%, 6.2% and 1.54% respectively. Notably, the rate of personal and family history of cancer was 12.3% and 1.54%, respectively. EUS examination was normal in 29 patients (44.6%), while the other

patients had pathological findings. Three patients (4.6%) had hypoechoic mass on EUS (2 in the pancreas and 1 in the CBD). Nineteen patients (29.2%) had gallstone disease (10 patients within the CBD, 5 within the GB and 4 within both the CBD and the gallbladder ((GB)). Ten patients had pancreatic cysts. Three patients had main pancreatic duct dilatation and 1 patient had GB polyp.

Comparing the patients who had normal EUS examination, with those who had abnormal EUS examination, only two parameters showed a trend for significance with abnormal EUS findings including: age and personal history of cancer (69.4 years and 17.5% vs. 63.7 years and 4%, $P=0.08$ and $P=0.05$), respectively.

Conclusion: EUS for investigation of idiopathic CBD dilation showed pathology in more than 50% of cases. Predictors for abnormal findings were including advanced age and personal history of cancer. Further larger studies are needed to better elucidate the role of EUS in this setting.

Disclosure: Nothing to disclose.

P0785

ULTRASOUND-BASED ASSESSMENT OF BILIARY MANIFESTATIONS IN ADULT PATIENTS WITH CYSTIC FIBROSIS. PREVALENCE AND RISK FACTORS

A. Marinero Martínez-Lázaro¹, R.M. Girón Moreno^{2,3}, F. Casals Seoane^{4,3}, Ó. Cano-Valderrama⁵, L. García-Buey^{4,3}
¹Hospital Clínico San Carlos, Department of Gastroenterology, Madrid, Spain, ²Hospital Universitario de La Princesa, Department of Pneumology, Madrid, Spain, ³Universidad Autónoma de Madrid, Instituto de Investigación Sanitaria Princesa (IIS-IP), Madrid, Spain, ⁴Hospital Universitario de La Princesa, Department of Gastroenterology, Madrid, Spain, ⁵Complejo Hospitalario Universitario de Vigo, Department of General and Gastrointestinal Surgery, Vigo, Spain

Contact E-Mail Address: almunenamarinero@hotmail.com

Introduction: Biliary pathology is thought to be highly prevalent in patients with Cystic Fibrosis. However, the published data vary widely regarding its exact frequency and clinical impact, especially in adult patients. More so, to date, the underlying pathophysiological mechanism is not completely understood.

Aims & Methods: The aim of the study was to evaluate the prevalence of biliary manifestations in a cohort of adult Cystic Fibrosis patients in a tertiary referral hospital and to evaluate the possible risk factors that influence its development. Adult patients with Cystic Fibrosis were recruited and laboratory tests and abdominal ultrasound were performed. Clinical characteristics of the patients with biliary disease were collected and possible risk factors for the development of the most frequent manifestations were studied.

Results: Ninety-five patients were included, 48 (50.5%) women, with a mean age of 30.4 (28.6-32.2) years and a mean value of FEV1 of 81.5 (77.9-85). 71 (74.7%) were F508del mutation carriers. 35 (37.2%) of patients presented biliary abnormalities in abdominal ultrasound. The different biliary findings observed are shown in Table 1.

Mean values of the different laboratory parameters were as follows: total bilirubin mean value of 0,5 (0,4-0,5) (mg/dl), a mean value of 21,2 (19,3-23,1) (U/l) for aspartate aminotransferase; 23,7 (20,8-26,6) (U/l) for alanine aminotransferase, 24 (17,2-30,8) (U/l) for gamma glutamyltransferase and 92,7 (84,5-100,9) (U/l) for alkaline phosphatase. 4 (4,4%) of the patients were above the upper normal limit of the laboratory values regarding total bilirubin, 2 (2,2%) regarding aspartate aminotransferase levels and 11 (12,1%) regarding alanine aminotransferase, and 5 (5,5%) and 17 (18,7%) regarding levels of gamma glutamyltransferase and alkaline phosphatase,

respectively. Therapy with Cystic Fibrosis Transmembrane Modulators was a risk factor for the development of cholelithiasis (Odds Ratio 3.53 [1.10-11.44] $p=0.05$).

Body Mass Index was a risk factor for cholecystectomy (Pearson coefficient 0.26 $p=0.05$) but male sex (Odds Ratio 0 [0-0.6] $p=0.02$), pancreatic insufficiency (Odds Ratio 0.12 [0-0.65] $p=0.02$) and having been diagnosed with Cystic Fibrosis in the paediatric age (OR 0.07 [0.01-0.51] $p=0.03$) were protective factors. History of meconium ileus (Odds Ratio 16.87 [5.54-51.33] $p=0.001$) and Bhalla Score (Pearson coefficient -0.25 $p=0.02$) were risk factors for the development of microgallbladder.

Biliary manifestations	Patients (n)	Total prevalence (%)	Relative prevalence within affected individuals (%)
Cholelithiasis/biliary sludge	20	21.3 %	57.1%
Microgallbladder	7	7.4%	20%
Cholecystectomy	6	6.4%	17.1%
Gallbladder agenesis	1	1.1%	2.9%
Cholangiopathy (bile duct dilation)	2	2.1%	5.7%
Gallbladder polyps	1	1.1%	2.9%

Table 1.

Conclusion: Biliary involvement reached a prevalence of 37.2%. Cholelithiasis was the most frequent finding, with a prevalence similar to that described in previous publications, and clearly more prevalent than in general population. The administration of Cystic Fibrosis Transmembrane Modulators was a risk factor for its development. History of meconium ileus and Bhalla score were risk factors for microgallbladder, which was the second most frequent finding.

It seems that a milder phenotype of the disease (regarding mutations, pancreatic function and possibly, lung function) may pose a risk for developing gallbladder complications that require cholecystectomy.

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P0786

RISK FACTORS FOR GALLSTONES IN PATIENTS WITH LIVER CIRRHOSIS

R. Ennaifer¹, Z. Benzarti¹, B. Bouchabou¹, S. Chtioui¹, A. Nakhli¹, M. Kefi¹, N. Hemdani¹

¹Mongi Slim Hospital, Department of Hepatology, Marsa, Tunisia

Contact E-Mail Address: zeinebbenzarti9@gmail.com

Introduction: Gallstone disease is one of the most prevalent and costly digestive disorders in the world. Recent studies have indicated that cirrhosis is a relevant risk factor for gallstone formation. However, risk factors for lithogenesis in cirrhotic patients are still incompletely elucidated.

Aims & Methods: The aim of this study was to estimate the risk factors for gallstone formation in cirrhotic patients.

A total of 84 patients with liver cirrhosis between 2019 and 2020 were studied. Patients were divided into two groups according to the presence of cholelithiasis evaluated by ultrasonography. Thirty one (36,9%) had gallstones (Group 1) while 53 patients (63,1%) had no gallstone disease (Group 2). The groups were compared in terms of basal characteristics (age, gender, obesity, diabetes meelitus and dyslipidemia) and characteristics of liver cirrhosis (etiology, duration and Child class) to determine risk factors for gallstone formation. SPSS version 26.0 was used for the descriptive and comparative analysis.

Results: The study included 52 males (62%) and 32 females (38%) with a mean age of 61 years. The etiologies of cirrhosis in all patients were as follows: cryptogenic n = 28 (33,3%), viral n = 42 (50%), alcoholic n = 6 (7,2%), autoimmune n = 7 (8,3%) and Wilson n=1 (1,2%). Child score was A in 33 patients, B in 38 patients and C in 13 patients.

Cholecystectomy was performed in 11% of patients of the first group.

Advanced age, female gender, obesity, diabetes, and cryptogenic cirrhosis were significantly associated with gallstone disease by the univariate analysis ($p=0,01$; $p=0,004$; $p<0,001$; $p=0.006$; $p=0.01$ respectively). Alcohol use, cirrhosis duration and the stage of liver disease were not associated to lithogenesis. On multivariate analysis, only obesity was independently associated with cholelithiasis ($p=0,04$; OR = 2,34 CI 95%).

Conclusion: In our study, risk factors for lithogenesis in cirrhotic patients are predominantly related to metabolic syndrome. Further study of the relationship between cirrhosis and gallstones is critical for predicting clinical outcomes in patients with liver disease, as it seems to be associated to a poorer prognosis.

Disclosure: Nothing to disclose.

P0787

FLUORESCENCE IN SITU HYBRIDIZATION IN PRIMARY DIAGNOSIS OF BILIARY STRICTURES

V. Zoundjiekpon¹, P. Falt¹, D. Kurfurstova², J. Zapletalova³, D. Skanderova², P. Vanek¹, M. Lovecek⁴, O. Urban¹

¹Faculty of Medicine and Dentistry, Palacky University and University Hospital Olomouc, Department of Internal Medicine II – Gastroenterology and Geriatrics, Olomouc, Czech Republic,

²Faculty of Medicine and Dentistry, Palacky University and University Hospital Olomouc, Institute of Clinical and Molecular Pathology, Olomouc, Czech Republic, ³Faculty of Medicine and Dentistry, Palacky University, Department of Medical Biophysics, Olomouc, Czech Republic, ⁴Faculty of Medicine and Dentistry, Palacky University and University Hospital Olomouc, Department of Surgery I, Olomouc, Czech Republic

Contact E-Mail Address: vincent.zoundjiekpon@fnol.cz

Introduction: Diagnosis of malignant biliary stricture remains a challenge. With regard to low sensitivity of brush cytology (BC), fluorescence in situ hybridization (FISH) has been reported as a useful adjunctive test.

Aims & Methods: We aimed to determine performance characteristics of both BC and FISH alone and in combination (BC+FISH).

This single center prospective study was conducted between April 2019 and January 2021. Consecutive patients with biliary strictures undergoing ERCP were included. Tissue specimens from 2 independent brushings were examined by routine cytology and FISH using the UroVysion probes. Histopathological confirmation after surgery or 12-month follow-up were considered as the reference standards for final diagnosis.

Results: From a total of 109 enrolled patients, 7 were lost to follow-up. In the remaining 102 patients (61% males, median age 67, range 25–92 years), the proportion of benign and malignant strictures was 28 (27.5%) and 74 (72.5%), respectively; the proportion of proximal and distal strictures was 26 (25.5%) and 76 (74.5%), respectively. Performance characteristics for each diagnostic test are shown Table 1.

Study cohort (n=102)	BC	BC + FISH	p-value
Sensitivity (95% CI)	0.361 (0.251–0.483)	0.507 (0.387–0.626)	0.076
Specificity (95% CI)	0.852 (0.663–0.958)	0.741 (0.537–0.889)	0.311

Table 1: Performance characteristics of selected diagnostic tests in diagnosis of biliary strictures (BC – brush cytology, FISH – fluorescence in situ hybridization, 95% CI – 95% confidence interval)

Conclusion: Dual-modality tissue sampling using BC + FISH demonstrated an improving trend in sensitivity for primary diagnosis of biliary strictures when compared with BC alone ($p=0.076$).

Disclosure: Nothing to disclose.

P1035

KNOCKDOWN OF HSDL2 PROMOTES CELL PROLIFERATION, MIGRATION AND INVASION BY INHIBITING FERROPTOSIS VIA P53PATHWAY IN CHOLANGIOCARCINOMA

Z. Lu¹, D. Zhang¹

¹The First Affiliated Hospital of Bengbu Medical College, Anhui, China

Contact E-Mail Address: zdy527897470@126.com

Introduction: Cholangiocarcinoma (CCA) is a malignant tumor of the bile duct epithelium, including intrahepatic, perihilar, and distal CCA based on anatomical location. However, the precise underlying mechanisms are not yet fully understood. Hydroxysteroid dehydrogenase-like 2 (HSDL2) belongs to the SDR subfamily of oxidoreductases, involved in the development of a variety of cancers. In a previous study, we found that overexpression of HSDL2 suppresses cell proliferation in cholangiocarcinoma.

Aims & Methods: This study aimed to investigate the potential molecular mechanisms of HSDL2 affecting the development of cholangiocarcinoma. The cells knockdown and overexpressed HSDL2 were constructed by a stable lentivirus-mediated transduction strategy, respectively. Transcriptome and proteome sequencing were performed on knockdown and negative control cells, and relevant mRNA and protein expression were determined by qRT-PCR and Western blotting. T

he levels of glutathione and lipid peroxidation were measured using related kits, and changes in reactive oxygen species were detected using flow cytometry. CCK8 assay, colony formation assay and 5-Ethynyl-2-Deoxyuridine(EDU) incorporation assay were used to detect cell proliferation ability, and wound healing assay and transwell assay were used to detect cell migration and invasion ability.

Results: Through the transcriptome and proteome data analysis, we found that differential genes and proteins were significantly enriched in cell proliferation and death, and were closely related to P53 signaling. Knockdown of HSDL2 promotes cell proliferation, migration and invasion, and inhibits ferroptosis.

The reversed assay showed that the overexpression of p53 partially reversed the above phenomenon. However, the inhibition of ferroptosis counteracted the effect of overexpressed p53 on the proliferation, migration and invasion capacity.

Conclusion: The knockdown of HSDL2 inhibits ferroptosis via the p53 pathway to promote cell proliferation, migration and invasion in cholangiocarcinoma.

Disclosure: There is no Conflict of Interest.

P0788

IMPACT OF METFORMIN ON THE INCIDENCE OF HUMAN CHOLANGIOCARCINOMA IN DIABETIC PATIENTS: A SYSTEMATIC REVIEW AND META-ANALYSIS

S. Massironi¹, A. Laffusa¹, A. Ciaccio¹, A. Elvevi¹, C. Gallo¹, L. Ratti¹, P. Invernizzi²

¹University of Milano-Bicocca, San Gerardo Hospital, Department of Medicine and Surgery, Monza, Italy, ²University of Milano-Bicocca, Center for Autoimmune Liver Diseases, Department of Medicine and Surgery, Monza, Italy

Contact E-Mail Address: a.laffusa@campus.unimib.it

Introduction: Cholangiocarcinoma (CCA) is the second most common liver cancer. Diabetes is a major risk factor; however, treatment with metformin has been reported to be protective for several cancers, but data on CCA are still sparse and heterogeneous.

Aims & Methods: The aim of this meta-analysis is to investigate the role of metformin as a potential protective factor for CCA.

In this systematic review and meta-analysis, we searched PubMed/MEDLINE and EMBASE databases from the date of inception to May 2021, for studies analyzing the CCA rate in patients taking metformin.

Results: Twenty-eight articles were initially identified, of which three were eligible and included in our systematic review and meta-analysis estimating the relative risk (RR). The rate of CCA was lower for diabetic patients taking metformin than diabetic patients without metformin intake (RR 0.34, 95% CI 0.51-0.35, $p < 0.001$), without significant statistical heterogeneity ($I^2 = 35.08\%$, $P = 0.2143$) among studies.

Conclusion: Our study demonstrated a significant impact of metformin in reducing the risk of CCA by nearly 66% in diabetic patients taking metformin.

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Disclosure: Nothing to disclose.

P0789

LONG-TERM EFFICACY OF PLASTIC VERSUS METAL STENTS IN INOPERABLE PERIHILAR CHOLANGIOCARCINOMA; A RETROSPECTIVE COHORT STUDY

J.A. Fritzsche^{1,2,3}, D.M. de Jong⁴, J.J.M.M. Borremans¹, M.J. Bruno⁴, O.M. van Delden^{2,3,5}, J.I. Erdmann⁶, P. Fockens^{1,2,3,7}, P. de Gooyer¹, B. Groot Koerkamp⁸, H.J. Klümpen^{3,9}, A. Moelker¹⁰, L.E. Nuijten^{3,11}, C.Y. Ponsioen^{2,1}, R.L.J. van Wanrooij^{2,3,7}, L.M.J.W. van Driel⁴, R.P. Voermans^{1,2,3}

¹Amsterdam UMC Location University of Amsterdam, Gastroenterology and Hepatology, Amsterdam, Netherlands,

²Amsterdam Gastroenterology Endocrinology Metabolism, Amsterdam, Netherlands, ³Cancer Center Amsterdam, Cancer Treatment and Quality of Life, Amsterdam, Netherlands,

⁴Erasmus University Medical Center, Gastroenterology and Hepatology, Rotterdam, Netherlands, ⁵Amsterdam UMC Location University of Amsterdam, Interventional Radiology, Amsterdam, Netherlands, ⁶Amsterdam UMC Location University of Amsterdam, Surgery, Amsterdam, Netherlands, ⁷Amsterdam UMC Location Vrije Universiteit, Gastroenterology and Hepatology, Amsterdam, Netherlands, ⁸Erasmus MC Cancer Center, Surgery, Rotterdam, Netherlands, ⁹Amsterdam UMC Location University of Amsterdam, Medical Oncology, Amsterdam, Netherlands, ¹⁰Erasmus University Medical Center, Radiology, Rotterdam, Netherlands, ¹¹Amsterdam UMC Location Vrije Universiteit, Surgery, Amsterdam, Netherlands

Contact E-Mail Address: j.a.fritzsche@amsterdamumc.nl

Introduction: In patients with inoperable perihilar cholangiocarcinoma (pCCA) uncovered metal stents are preferred over plastic stents because of longer stent patency and fewer re-interventions in the short term.(1-4) However, concerns have risen regarding the number and complexity of re-interventions in the long term.(5)

This is of increasing importance considering the expected improvement in systemic and/or locoregional therapy and subsequent increase in life expectancy.(6)

Aims & Methods: Aim of the study was to assess the long-term efficacy (>6 months) of metal versus plastic stents. This retrospective study was performed at two Dutch tertiary referral hospitals and consisted of patients with inoperable pCCA who underwent biliary drainage between 2001 and 2021 and survived at least 6 months. Patients were divided in two groups; 1. plastic stent placement(s) for the full extent of follow-up and 2. metal stent(s) which had been in situ for at least 6 months.

Primary outcome was the estimated number of re-interventions per patient-year and need for permanent external or internal/external percutaneous drainage catheters. Secondary outcomes included re-interventions between 6 and 12 months in patients with at least 12 months follow-up and time to recurrent biliary obstruction.

Results: A total of 127 patients were found eligible, of whom 40 patients (31%) only underwent plastic stent placement(s) and 87 patients (69%) had metal stent(s) placed. Metal stents were placed at the initial procedure in 7 patients. In the remaining 80 patients, the first metal stent was placed after a median of 2 months (IQR 1-5) and a median of 3 interventions (IQR 1.75-4) in which plastic stent(s) or percutaneous biliary drainage catheter(s) were placed.

Patients in the metal stent group underwent fewer re-interventions compared with the plastic stent group corrected for the length of follow-up (4.8 vs. 3.1 per patient-year; incidence rate ratio (IRR), 0.64; 95% CI, 0.47 to 0.88). When only non-elective re-interventions were included no significant difference between the groups was present (2.8 vs. 2.1 per patient-year; IRR, 0.77; 95% CI, 0.55 to 1.09).

At final follow-up, 7 patients (18%) had a percutaneous drainage catheter in situ in the plastic stent group versus 12 patients (14%) in the metal stent group (risk ratio (RR), 0.79; 95% CI, 0.34 to 1.85).

In patients who had at least 12 months follow-up (n=71) patients in the plastic stent group (n=16) underwent a median of 2 re-interventions (IQR 1-2) between 6 and 12 months versus 1 re-intervention (IQR 0-3) in the metal stent group (n=55; p=0.229).

One-hundred and ten patients (87%) experienced recurrent biliary obstruction during follow-up. The median time to recurrent biliary obstruction was 2 months (IQR 0-7.25) in the plastic stent group versus 6 months (IQR 3-11) in the metal stent group (p=0.001).

Conclusion: This study confirms previous short-term data that the placement of metal stent(s) leads to fewer re-interventions compared with plastic stent(s) in patients with inoperable pCCA. Also in patients who survive beyond 6 months. To confirm this conclusion prospective data with long-term sufficient follow-up is warranted.

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P0790

ENDOSCOPIC RADIOFREQUENCY ABLATION FOR MALIGNANT BILIARY OBSTRUCTION: RISK FACTORS FOR BILIARY INFECTION

H. Haitao¹, W. Gu¹, H. Khizar², X. Zhang¹, Y. Jianfeng¹

¹Hangzhou First People Hospital, Department of Gastroenterology, Hangzhou, China, ²Zhejiang Chinese Medical University, International Education College, Hangzhou, China

Contact E-Mail Address: yjf3303@zju.edu.cn

Introduction: The aim of this study is to investigate risk factors for early adverse events in endoscopic radiofrequency ablation (RFA) for unresectable malignant biliary obstructions.

Aims & Methods: We performed a retrospective review of 148 patients with malignant biliary obstruction who had undergone endoscopic RFA between January 2012 and January 2022 at a single tertiary care center. Data obtained through the medical records included ERCP indication, patient factors (biliary anatomy, demographics, and comorbidities), stent characteristics (material, length, and design), change in serum bilirubin, rates and etiologies of bacteremia, and the mortality rate.

Results: Adverse events occurred in 34 cases (23.0%), including postoperative biliary infection in 28 cases (acute cholangitis (15.5%, 23/148), acute cholecystitis (3.4%, 5/148)), acute pancreatitis in 4 cases (2.7%), and hemobilia in 2 case (1.4%). There was no perforation. Patients with postoperative biliary infection had a higher proportion of type 2 diabetes, hypoproteinemia (<30g/L), bile duct stenosis length > 2.5 cm, segmented RFA, drainage by single stent was significantly higher than patients without biliary infection ($P < 0.05$). Logistic regression analysis showed the combination of type 2 diabetes, segmented RFA, and single stent drainage were the independent risk factors for biliary infection.

Conclusion: The most common adverse event of endoscopic RFA treatment for unresectable malignant biliary obstruction is biliary infection. History of type 2 diabetes, biliary stricture length > 2.5 cm, single stent drainage were high risk factors for biliary infection.

Disclosure: Nothing to disclose.

P0791

EFFICACY OF ENDOSCOPIC PAPILLECTOMY FOR EARLY AMPULLARY CARCINOMA

K. Suzuki¹, Y. Kurita¹, Y. Fujita², S. Tsujino², S. Hasegawa¹, K. Hosono¹, T. Kessoku¹, N. Kobayashi³, I. Endo⁴, K. Kubota¹, A. Nakajima¹

¹Yokohama City University School of Medicine, Gastroenterology and Hepatology, Yokohama, Japan, ²NTT Medical Center Tokyo, Hepato-Biliary-Pancreatic Medicine, Tokyo, Japan, ³Yokohama City University School of Medicine, Oncology, Yokohama, Japan, ⁴Yokohama City University School of Medicine, Gastroenterological Surgery, Yokohama, Japan

Contact E-Mail Address: kosuzuki.ycu@gmail.com

Introduction: The indication for endoscopic papillectomy (EP) for duodenal papillary tumors is considered to be benign lesions such as adenomas, but recently the indication has been expanded to include early-stage cancer. However, there is currently no sufficient evidence or consensus regarding the efficacy of EP for papillary carcinoma. In this study, we conducted a retrospective review of the prognosis of cancer patients who underwent EP at our hospital.

Aims & Methods: We included 107 patients who underwent EP for duodenal papillary tumors at our department between 2005 and 2020. The residual rate, recurrence rate, and prognosis of neoplastic lesions (adenocarcinoma) were evaluated. The resection was performed in the endcut mode.

Results: There were 30 cases of adenocarcinoma (17 with localized Tis, 10 with T1a, and 3 with T1b), 8 with hyperplastic changes, 2 with NETs, and 13 with other conditions. Median tumor diameter (range) was 11 (5-25) mm for adenomas, 15 (8-25) mm for Tis-T1a, and 15 (10-21) mm for T1b.

Mean observation time (range) after EP was 43.9 (0.7-185.7) months for adenomas, 41.8 (2.1-139.0) months for Tis-T1a, and 33.5 (0.7-185.7) months for T1b. b: 33.9 (4.7-87.8) months. The post-EP remnant rate of adenocarcinoma was 34.5% (29/84) in 10 cancer cases (Tis-T1a: 7, T1b: 3).

Five patients (Tis-T1a: 3, T1b: 2) underwent additional pancreaticoduodenectomy (PD), and 3 of them (Tis-T1a: 1, T1b: 2) had no malignant findings in the resection specimens, indicating that complete resection had been performed by EP. None of the 10 cancer remnants, including 5 additional untreated cases, progressed or recurred during the observation period. One case of recurrence after adenocarcinoma EP was adenocarcinoma (Tis). The patient with T1a recurrence of adenocarcinoma was treated with PD, and the patient was free of recurrence during the follow-up period.

Conclusion: EP can provide local control not only in Tis-T1a but also in T1b in the majority of cases, suggesting that EP may be an alternative treatment for patients who cannot tolerate surgical resection because of its relatively minimally invasive nature.

Disclosure: Nothing to disclose.

P0792

PROGNOSTIC FACTORS IN PATIENTS RECEIVING PEMBROLIZUMAB WITH ADVANCED BILIARY TRACT CANCER

C.S. Park¹, M.J. Sung², H.S. Lee¹, M.-J. Chung³, S. Bang¹, S.W. Park⁴, S.-Y. Song¹, J.Y. Park¹

¹Yonsei University College of Medicine, Internal Medicine, Seoul, Korea (Republic of), ²CHA Hospital, CHA University College of Medicine, Internal Medicine, Bundang-gu, Korea (Republic of), ³Yonsei University, Gastroenterology, Seoul, Korea (Republic of), ⁴Severance Hospital, Yonsei University College of Medicine, Internal Medicine, Seoul, Korea (Republic of)

Contact E-Mail Address: wpakcs@yuhs.ac

Introduction: The biliary tract cancer (BTC) has very poor prognosis. Some BTC has been shown to respond to pembrolizumab, but there are no known clinical prognostic factors to predict its treatment effects. In this study, we tried to find prognostic factors associated with pembrolizumab as 2nd-line treatment for gemcitabine plus cisplatin refractory BTC.

Aims & Methods: This is a retrospective, single tertiary-center study that involved all consecutive patients with refractory advanced BTC who was treated with pembrolizumab between August 2017 and February 2021. Patients who received pembrolizumab as the first treatment choice were excluded. And prognostic factors affecting overall survival were analyzed through cox regression analysis.

Results: Total 93 patients enrolled in this study according to the inclusion criteria. We found statistically significant factors for overall survival. It contains albumin, ALP, CA19-9, Lymphocyte-Monocyte-Ratio (LMR), Neutrophil-Lymphocyte-Ratio (NLR), and Platelet-Lymphocyte-Ratio (PLR). In multivariate cox regression analysis, albumin and LMR were identified as significant variables associated with overall survival. (adjusted HR=0.358 [95% CI: 0.205-0.627]; $p=0.000$, adjusted HR=0.279 [95% CI: 0.161-0.485]; $p=0.000$) Contrary to expectations, TPS and CPS were not significant variables affecting overall survival. (HR=1.00 [95% CI: 0.992-1.008]; $p=0.937$, HR=0.995 [95% CI: 0.986-1.003]; $p=0.215$).

Conclusion: Higher albumin and LMR were significantly associated with better overall survival. Further studies are needed to find genetic and clinical factors to predict who would be benefited from pembrolizumab as treatment for advanced biliary tract cancer.

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P0793

IGG4-RELATED SCLEROSING CHOLANGITIS MAY BE A RISK FACTOR FOR BILE DUCT CANCER

Y. Kurita¹, K. Kubota¹, K. Suzuki¹, S. Yagi¹, S. Hasegawa¹, K. Hosono¹, A. Nakajima¹

¹Yokohama City University, Yokohama, Japan

Contact E-Mail Address: kuritay@yokohama-cu.ac.jp

Introduction: The potential risk for bile duct cancer in patients with immunoglobulin 4-related sclerosing cholangitis (IgG4-SC) is unclear.

Aims & Methods: The present study aimed to evaluate the incidence of bile duct cancer in patients with IgG4-SC.

We retrospectively collected clinical data for 121 patients diagnosed with IgG4-SC. We calculated the standardized incidence ratio (SIR) of cancer in IgG4-SC patients based on the national cancer rates. The SIR of bile duct cancer and that of the period after the diagnosis of IgG4-SC were also calculated.

Results: The mean follow-up period was 6.4 years, with 121 IgG4-SC patients. During the follow-up period, 26 patients had cancer, and 29 cancers were diagnosed. Three bile duct cancer cases were diagnosed. The SIR of cancer after the diagnosis of IgG4-SC was 1.90 (95 % confidence interval [CI] 1.67-2.21). The SIR of bile duct cancer was 8.88 (95 % CI 7.81-10.30). The SIR of cancer in <1 year, 1-5 years, and > 5 years after diagnosis of IgG4-SC were 2.58 (95 % CI 2.53-2.64), 1.01 (95 % CI 0.91-1.12), and 2.44 (95 % CI 1.92-3.37), respectively.

Conclusion: IgG4-SC patients have a high risk of cancer. IgG4-SC may be associated with the development of bile duct cancer. The risk of cancer was high less <1 year and >5 years after diagnosis of IgG4-SC. Therefore, IgG4-SC patients may require careful long-term follow-up.

Disclosure: Nothing to disclose.

P0794

TIMING OF ERCP AND OUTCOMES IN PATIENTS ADMITTED WITH ACUTE GALLSTONE CHOLANGITIS: A RETROSPECTIVE MULTICENTRE AUDIT

C. Watters¹, J Fox², N. Elamin³, H Benzeglam³, W. Gaba⁴, K. Koss³, S Ramakrishnan⁴, G Fisher², N Stern⁵, W. On⁶, MaNET Research Group

¹Liverpool University Hospitals NHS Foundation Trust, Gastroenterology, Liverpool, United Kingdom, ²Countess of Chester Hospital, Gastroenterology, Chester, United Kingdom, ³Macclesfield District General Hospital, Gastroenterology, Macclesfield, United Kingdom, ⁴Warrington Hospital, Gastroenterology, Warrington, United Kingdom, ⁵Liverpool University Hospitals NHS Foundation Trust, Gastroenterology Department, Aintree Hospital, Liverpool, United Kingdom, ⁶Leeds Teaching Hospitals NHS Trust, Department of Gastroenterology, Leeds, United Kingdom

Contact E-Mail Address: christopher.watters@nhs.net

Introduction: Acute gallstone cholangitis necessitates biliary decompression and stone extraction with endoscopic retrograde cholangiopancreatography (ERCP).

The European Society of Gastrointestinal Endoscopy 2019 guideline¹ stipulates timeframes for ERCP in these patients in accordance with severity of disease, as stratified by the Tokyo 2018 guidelines² (Severe – within 12 hours, moderate – within 72 hours, mild – elective).

Aims & Methods: We aimed to assess current performance and compare outcomes in relation to time to ERCP, in multiple centres with differing hepatobiliary endoscopy services and ERCP availability. A retrospective multicentre audit of patients admitted to four institutions within the Merseyside and Cheshire region, United Kingdom between January 2016 and December 2019, with probable or definite episodes of acute cholangitis (as per Tokyo 2018 criteria) was performed.

Cases were assessed for severity of illness as per Tokyo criteria and time to ERCP, with outcomes including length of hospital stay, procedure-related complications and all-cause 30 day mortality recorded.

Results: In total, 390 patients were included for analysis across the four centres, with one hospital providing an out-of-hours emergency ERCP service. Overall, 283 patients (72.6%) presented within 'normal working hours.' Successful biliary decompression and stone extraction was achieved in 83.6% (n=326) of patients with a median time to ERCP of 5.8 days (range 0.1 – 37.5).

	Mild	Moderate	Severe
Number of pts	174	156	60
Age (range) - Male:Female	68 (19-96) - 65:109	80 (34-98) - 78:78	78 (52-94) - 36:24
ICU admissions (%)	1/174 (0.6)	1/156 (0.6)	15/60 (25)
Median time to ERCP in days (range)	5 (0.1-35.1)	6 (0.1-25)	7.3 (0.5-37.5)
Complete decompression (%)	C - 153 (87.9)	C - 124 (79.4)	C - 49 (81.7)
Partial decompression (%)	P - 12 (6.9)	P - 16 (10.3)	P - 9 (15)
Unsuccessful decompression (%)	U - 9 (5.2)	U - 16 (10.3)	U - 2 (3.3)
Adverse events (%)	6.9	3.2	3.3
Median LOS (range)	7 (1-44)	8 (1-64)	9.5 (1-40)
30 day all-cause mortality (%)	1 (0.6)	2 (1.3)	3 (5)
30 day readmission rates (%)	11 (6.3)	11 (7.1)	4 (6.7)

Table 1 - Summary across four centres (n=390)

When stratified by severity, median time to ERCP was 7.3 days (range 0.5 – 37.5) in severe cases, 6.0 days (range 0.1 – 25) in moderate cases and 5.0 days (range 0.1 – 35.1) in mild cases. 17 of the 390 patients (4.4%) required intensive care (ICU) input, with 25% (15/60) of patients classified as severe having an ICU stay.

There was a higher proportion of those presenting outside of normal working hours requiring ITU admission (37.5%, 6/16), having all been classified as severe at presentation. Those with severe cholangitis also had a longer length of stay (median 9.5 days) compared to 8.0 days for those with moderate disease.

Table One summarises the outcomes assessed across the four participating centres - one centre provided an out-of-hours ERCP service as required.

Conclusion: Median time to ERCP did not differ when stratified by severity of cholangitis and did not meet ESGE recommendations. However, patients with severe disease were able to receive emergency ERCP if clinically indicated. Provisions for emergency ERCP centred at a tertiary institution within a regional network is required.

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Disclosure: Nothing to disclose.

Poster presentations

Pancreas

Poster Presentations Pancreas

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P0795

SILENCING OF *AHR* AND *ELAVL1* GENES INFLUENCES POST-TRANSCRIPTIONAL EXPRESSION OF EACH OTHER AND CHEMORESISTANCE OF PANCREATIC CANCER CELLS, IN VITRO

D. Stukas¹, A. Jasukaitiene¹, J. Matthews², A. Gulbinas¹,
Z. Dambrasukas¹

¹Lithuanian University of Health Sciences, Institute for Digestive Research, Kaunas, Lithuania, ²University of Oslo, Institute of Basic Medical Sciences, Oslo, Norway

Contact E-Mail Address: Zilvinas.Dambrasukas@ismuni.lt

Introduction: Pancreatic cancer (PC) is a devastating disease that has less than 10 % five-year survival rate [1]. There is an urgent need to find new therapies to treat PC patients. HuR protein (*ELAVL1* gene) expression in cell cytoplasm is positively associated with PC response to gemcitabine which is currently first-line treatment for PC [2].

The aryl hydrocarbon receptor (*AHR*) is a ligand-dependent transcription factor that among other purposes modulates RNA-binding protein *ELAVL1* signaling pathway by blocking HuR protein (*ELAVL1*) translocation from nucleus to cytoplasm which consequently leads to overexpression of cytoprotective, anti-apoptotic proteins and chemoresistance [3].

Overexpression of *AHR* leads to decreased cytoplasmic levels of HuR protein (*ELAVL1*) which in turn might contribute to chemoresistance of PC patients and their survival.

Aims & Methods: The aim of this research was to investigate how *AHR* and *ELAVL1* gene silencing affects the post-transcriptional expression of related genes, each other, and chemoresistance of PC cell lines.

Three PC cell lines were used (T3M4, BxPc3, Su.86.86). *AHR* and *ELAVL1* genes were silenced for 24-hours by lipofectamine mediated siRNA transfection. Afterwards the cells were treated with IC50 of gemcitabine for 48-hours (calculated for each cell line independently). After treatment gene expression was measured by RT-PCR and protein expression by Western Blot assay. Metabolic activity was measured by MTT assay.

Results: The results showed that silencing of *AHR* and/or *ELAVL1* resulted in decreased cell viability and increased sensitivity to gemcitabine in all three PC cell lines. Silencing of *AHR* gene resulted in increase of *ELAVL1* RNA expression, however, HuR protein (*ELAVL1* gene) expression was not affected by silencing of *AHR*. Silencing of *ELAVL1* resulted in reduced *AHR*RNA as well as reduced *AHR* protein expression. Results show that *AHR* could be involved in regulation of *ELAVL1* expression in post-transcriptional level and vice versa. The results of *AHR* and/or *ELAVL1* gene silencing and expression of cytoprotective molecules of *ELAVL1* pathway differed between cell lines.

Conclusion: Both *AHR* and *ELAVL1* may play a role in regulation of each other and chemoresistance of PC cell lines. However different response of protein and RNA together with different response of cytoprotective molecules between PC cell lines shows that the effect of gene modulation is hard to predict and should be investigated further.

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P0796

WHAT IS THE SIGNIFICANCE OF A FAECAL ELASTASE-1 LEVEL BETWEEN 200 – 500MG/G?

A. Mathew¹, D. Fernandes², J. Andreyev^{2,3}

¹Royal Derby Hospital, Derby, United Kingdom, ²Lincoln County Hospital, Gastroenterology, Lincoln, United Kingdom, ³University of Nottingham, The Biomedical Research Centre, Nottingham Digestive Diseases Centre, School of Medicine, Nottingham, United Kingdom

Contact E-Mail Address: dcrfernandes@gmail.com

Introduction: Pancreatic exocrine insufficiency (PEI) is a common cause of gastrointestinal (GI) symptoms relating to malabsorption. It is commonly diagnosed if faecal elastase-1 (FE-1) levels are below 200mg/g. However, there is insufficient data to define the significance of faecal elastase levels above 200mg/g but less than 500mg/g, with a suggestion that levels between these values being a deviation from normal pancreatic exocrine function. This study therefore sought to assess the response to treatment in patients who had a FE-1 level between 200-500mg/g.

Aims & Methods: This was a retrospective study that was approved by our local audit committee, audit registration L0448. Patient information was requested from the pathology laboratory at United Lincolnshire Hospitals NHS Trust for all FE-1 samples taken between April 2019 and March 2021. Those with results of <200 or >500 were excluded.

Notes and medical records of those remaining were reviewed with any seen in an outpatient setting having their presenting symptoms recorded before trialling Creon. Subsequent clinic letters were then reviewed following commencement and a positive response noted if the initial symptoms responded to treatment.

Results: 82 patients had a FE-1 result between 200-500. Ages ranged from 27 to 90 (median = 63). 78 were referred to the Gastroenterology department with a wide range of non-specific GI symptoms. 28 patients were given a trial of Creon. The dosing regime varied, with the majority being trialled on two capsules (50,000 units) with meals and one capsule (25,000 units) with snacks. Adjuvant treatment was given, with 8 taking multivitamins and 3 taking Proton Pump Inhibitors (PPIs). 20 patients showed an improvement in symptoms of diarrhoea, steatorrhoea and bloating. 3 patients did not tolerate Creon, developing nausea and vomiting and the remaining 5 showed no response.

Conclusion: Our results show that clinicians should exercise caution when using defined reference ranges to diagnose PEI and provide treatment with PERT. Although it is often believed patients with PEI will only display symptoms when pancreatic function has dropped to <10%, there

is now a consensus that these patients may instead demonstrate a graded response to reduced exocrine function and so will benefit from having earlier testing and treatment [4]. Indeed, our findings support this suggestion, with nearly ¼ of patients with a FE-1 of between 200-500 showing a response following treatment with PERT.

Disclosure: No conflict of interest.

P0797

NOVEL PANCREAS PERFUSION CIRCUIT WITH PRE-DETERMINED PHYSIOLOGICAL PARAMETERS; A PILOT STUDY

Z. Rai^{1,2}, K. Doyle¹, M. Magbagbeola¹, L. Lindenroth¹, G. Dwyer¹, A. Stilli¹, D. Stoyanov¹, B. Davidson^{1,2}

¹University College London, London, United Kingdom, ²Royal Free Hospital NHS Trust, London, United Kingdom

Contact E-Mail Address: zainab.raai.19@ucl.ac.uk

Introduction: Recent work has demonstrated the potential of machine perfusion (MP) to extend the period during which organs remain viable from hours to days (1). MP is considered to be superior in organ preservation compared to traditional static cold storage (SCS) in high-risk kidney and liver donor organs (2).

Whilst these preservation methods have enjoyed success in *ex vivo* kidneys and livers, pancreatic perfusion has been slow to progress and the current gold-standard for storage and transport of human pancreas remains SCS (3). This is due to the unique and challenging physiological parameters the pancreas demands to maintain its viability and functionality, namely tightly controlled pressure, and flow parameters and significant susceptibility to reperfusion and ischaemic injury (4).

A novel perfusion circuitry has been developed with an objective to produce a system to evaluate whole organs in a temperature-controlled, adaptable chamber with tightly regulated, pre-determined parameters. Here we present data from 3 porcine pancreatic head perfusions using autologous oxygenated blood with a pre-set pressure and flow rate and continuous real-time monitoring.

Aims & Methods: To investigate the machine perfusion parameters of isolated pancreas associated with maintaining physiological function.

Porcine pancreases were obtained from domestic pigs immediately after termination at an abattoir. 5 cm of the distal aorta was preserved, dissected, and flushed with 2 litres of heparinised normal saline. The pancreatic head and duodenum was dissected and transported to the lab on ice with attached major vessels. Blood from autologous porcine donation was collected in a pre-heparinised receptacle.

The perfusion circuit was designed to continuously monitor and control pre-determined flow and pressure measurements and was coordinated by a raspberry pi microcontroller using a MODBUS and RS232 serial communication protocol to communicate with the sensors. The aortic patch was cannulated directly as the inflow branch and passive venous drainage was returned to the reservoir, where it was filtered, re-oxygenated and reperfused. The organ was weighed immediately prior to the perfusion and at its conclusion.

Results: 3 porcine pancreatic heads were perfused for a maximum of 60 minutes. Input pressure was predetermined by directly adjusting the duty cycle of the centrifugal pump using a closed-loop proportional-integral-derivative (PID) controller. PID is a commonly used feedback controller to regulate process variables such as pressure or flowrate. Continuous measurement of input pressure and flow taken during the perfusion was set to a maximum input pressure of 22mmHg and flow rate of 400 litres/minute. Inspection of the pancreas during perfusion showed uniform perfusion and not organ oedema. The absence of oedema was confirmed by weighing the organ before and after perfusion.

Conclusion: Whole organ pancreatic perfusion is feasible and may provide an innovative research platform. Our perfusion system is unique in its capability to set a predetermined pressure and/or flow rate, making it of significant relevance to pancreatic perfusion due to the pancreas' susceptibility to excessive pressure and flow rates. The association between perfusion parameters and histological appearances of the graft is currently being addressed.

Future work: Work is underway to histologically assess for evidence of oedema and necrosis to demonstrate preserved viability of the perfused pancreas.

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Disclosure: Nothing to disclose.

P0798

OPTIMIZATION OF DOSE LEVELS OF ORALLY ADMINISTERED PANCREATIC ENZYME SUPPLEMENTS IN THE TINY-TIMSG DYNAMIC IN-VITRO GASTROINTESTINAL MODEL

M.-L. Orera-Peña¹, H. de Voogd², S. Bellmann³, T. Garcia³

¹Viatris, Global Medical Affairs, Madrid, Spain, ²Viatris, Global Clinical Development, Amstelveen, Netherlands, ³The TIM Company, Delft, Netherlands

Contact E-Mail Address: luisa.orera@viatris.com

Introduction: In diseases like chronic pancreatitis or cystic fibrosis, pancreatic exocrine insufficiency (PEI) is common and is treated by orally administered pancreatic enzyme supplements

Aims & Methods: The aim is to establish the optimal dose range of orally administered pancreatic enzymes (Pancreatin/PANC), to improve food digestion in patients suffering from PEI, by using the tiny-TIMsg dynamic in vitro GI model.

Fat digestion of a high-fat meal was investigated in the tiny-TIMsg system set to mimic severe pancreatic insufficiency, using 5% pancreatin and no TIM gastric lipase, as seen in chronic pancreatitis conditions. Four PANC dose levels were tested containing 35,000, 70,000, 80,000 and 150,000 lipase units.

The 'healthy' level of fat digestion was measured (positive control), as well as fat digestion during simulation of severe pancreatic insufficiency without supplementation (negative control).

Administered pancreatic enzyme efficacy was established indirectly, by measuring digestibility of total fatty acids (TFA) in the small intestinal compartment.

Results: TFA bioaccessibility after 6 hours in the tiny-TIMsg model, expressed as a percentage of TFA input from the meal and bile, is shown in the table. All PANC doses effectively increased fat digestion compared to the negative control. Bioaccessibility was dose-dependent after the housekeeper wave at 180 min and most clear at doses from 70k PANC.

Conclusion: PANC increased the lipid digestion in simulated pancreatic enzyme deficient conditions at all dose levels, in a dose-dependent manner.

Disclosure: The study has been funded by Viatris. Hanka de Voogd and Maria-Luisa Orera-peña are Viatris employees

	positive control mean $\pm$ SD	negative control mean $\pm$ SD	35k PANC mean $\pm$ SD	70k PANC mean $\pm$ SD	80k PANC mean $\pm$ SD	150k PANC mean $\pm$ SD
Intake total fatty acids in mg; i.e.meal+ bile	11270 $\pm$ 60.9	11156 $\pm$ 108	11230 $\pm$ 42.7	11232 $\pm$ 6.68	11160 $\pm$ 38.5	11184 $\pm$ 34.4
Filtrate (mg) 0-60 min	300 $\pm$ 74.5	281 $\pm$ 26.5	236 $\pm$ 4.71	236 $\pm$ 5.19	242 $\pm$ 20.5	295 $\pm$ 26.4
Filtrate (mg) 60-120 min	1537 $\pm$ 270	809 $\pm$ 44.2	1217 $\pm$ 39.1	1186 $\pm$ 36.3	1267 $\pm$ 30.7	1488 $\pm$ 201
Filtrate (mg) 120-180 min	1738 $\pm$ 231	989 $\pm$ 89.3	1499 $\pm$ 33.1	1570 $\pm$ 45.6	1569 $\pm$ 83.4	1653 $\pm$ 104
Filtrate (mg) 180-240 min	1564 $\pm$ 55.9	785 $\pm$ 37	1216 $\pm$ 76.9	1283 $\pm$ 128	1299 $\pm$ 31.6	1363 $\pm$ 97.4
Filtrate (mg) 240-300 min	1402 $\pm$ 50.5	774 $\pm$ 80.1	912 $\pm$ 101	917 $\pm$ 24.8	969 $\pm$ 13.3	1010 $\pm$ 57
Filtrate (mg) 300-360 min	1305 $\pm$ 117	828 $\pm$ 140	889 $\pm$ 52.5	846 $\pm$ 2.4	875 $\pm$ 19.7	928 $\pm$ 63.3
Total 0-360 min (mg)	7846 $\pm$ 565.1	4465 $\pm$ 364	5968 $\pm$ 220	6037 $\pm$ 232	6221 $\pm$ 199.2	6737 $\pm$ 496
Bioaccessibility 0-360 min % of input	69.6 $\pm$ 5.39	40.1 $\pm$ 3.66	53.2 $\pm$ 2.16	53.8 $\pm$ 2.1	55.8 $\pm$ 1.98	60.3 $\pm$ 4.62

Table.

P0799

LOSS OF ONECUT1 ALTERS PANCREATIC EXOCRINE DEVELOPMENT

J. Krüger¹, S. Heller¹, M. Breunig¹, M.K. Melzer^{1,2}, A. Kleger¹

¹Ulm University Hospital, Internal Medicine 1, Ulm, Germany, ²Ulm University Hospital, Department of Urology, Ulm, Germany

Contact E-Mail Address: jana.krueger@uni-ulm.de

Introduction: Mutations or loss of One Cut Homeobox 1 (ONECUT1) have recently been associated with an impairment in endocrine pancreatic development and early onset of diabetes. Additionally, ONECUT1^{-/-} mice have been shown to present with enlarged, cystic pancreatic ducts, indicating a broader role of the gene in pancreatic development and lineage segregation.

Aims & Methods: To further unravel the role of ONECUT 1 in human pancreatic development with a focus on the exocrine department, we implemented a human embryonic stem cell (hESC) derived pancreatic duct-like organoid (PDLO) model to investigate the effect of ONECUT1 loss *in vitro*.

Results: Wildtype (WT) and ONECUT1 knockout (KO) cell lines were differentiated to pancreatic progenitor cells and further matured to PDLOs in 3D matrigel culture. Already at PP stage, KO cells harbored an altered expression of genes important for exocrine development and increase of markers relevant for other lineages, such as intestinal or biliary development. At PDLO stage, KO organoids showed an enlarged, cyst-like morphology, which was discovered to be caused by higher proliferation and reduced apoptosis compared to WT organoids.

Additionally, polarity was found to be impaired in KO organoids, resulting in a distribution of CFTR channels on both the luminal and basal side of the cells and impaired swelling upon forskolin treatment.

Conclusion: Taken together, ONECUT1 seems to play a vital role in pancreatic organogenesis and the development of ductal as well as endocrine pancreatic cells.

Disclosure: no conflict of interest.

P0800

MODELLING PANCREATIC FACETS OF JOHANSON-BLIZZARD SYNDROME IN A DISH

M. Breunig¹, J. Krumm², B. Kuster², T. Seufferlein¹, M. Hohwieler¹, M. Zenker³, A. Kleger⁴

¹Universitätsklinikum Ulm, Innere Medizin I, Ulm, Germany,

²Technical University of Munich (TUM), Chair of Proteomics

and Bioanalytics, Freising, Germany, ³Otto-von Guericke

University, Institute of Human Genetics, Magdeburg, Germany,

⁴Universitätsklinik Ulm, Internal Medicine 1, Ulm, Germany

Contact E-Mail Address: markus.breunig@uni-ulm.de

Introduction: Johanson-Blizzard syndrome (JBS) is a rare genetic disorder with autosomal recessive inheritance. The condition is characterized by congenital exocrine pancreatic insufficiency, aplasia of the nasal wings, and multiple other symptoms of varying severity. We could previously identify mutations in the UBR1 gene encoding one of several E3 ubiquitin ligases of the N-end rule pathway as the cause of the disease.

Aims & Methods: As mouse models incompletely recapitulate the phenotype of the disease, we employ pluripotent stem cells (PSCs) to investigate pancreatic facets of JBS. We have implemented two independent but complimentary PSC models by editing human embryonic stem cells via CRISPR/Cas9 and by generating induced PSCs from two patients sharing a severe pancreatic phenotype.

Results: Stepwise pancreatic lineage differentiation of UBR1 mutant PSCs did not reveal an early developmental defect in agreement with a normal pancreatic anlage in JBS patients. Global quantitative proteomics, however, revealed a stage-specific upregulation of a set of proteins in UBR1 ablated cells.

Specifically, a list of candidate proteins with described roles in cellular homeostasis were significantly upregulated. Upon repair of one allele of iPSCs from one patient the deregulation of such proteins could be successfully rescued *in vitro*. Whether these proteins are direct UBR1 substrates and contribute 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.

P0801

PROINFLAMMATORY CYTOKINES MAY HELP TO IDENTIFY EXOCRINE PANCREATIC INSUFFICIENCY PATIENTS IN A DIARRHEA-PREDOMINANT IBS- POPULATION

J.I. Olmos¹, M.M. Piskorz², N. Litwin³, M. Puga-Tejada⁴, T.N. Uehara², H. Hashimoto², A. Tevez², E. Gonzalez-Ballera¹, J. Olmos⁵

¹Hospital de Clinicas Universidad de Buenos Aires, Gastroenterology, Buenos Aires, Argentina, ²Hospital de Clinicas Universidad de Buenos Aires, Neurogastroenterology, Buenos Aires, Argentina, ³Litwin Laboratorio Bioquimico, Buenos Aires, Argentina, ⁴Instituto Ecuatoriano de Enfermedades Digestivas, Endoscopy And Gastroenterology, Guayaquil, Ecuador, ⁵Hospital de Clinicas Universidad de Buenos Aires, Neurogastroenterology, Caba, Argentina

Contact E-Mail Address: juan.ignacio.olmos@gmail.com

Introduction: Background: Irritable Bowel Syndrome (IBS) is one of the most frequent disorders in clinical practice with a mean 7.6-10.8% world-wide-prevalence and is associated with mild inflammatory response. There are studies that demonstrate the relationship between pancreatitis and systemic proinflammatory cytokines

Aims & Methods: Aim: We aimed to explore if there is any difference in the cytokines levels in EPI vs IBS-D patients.

Methods: An exploratory, nested-case-control study of patients aged over 18 years presenting to tertiary hospital outpatient with Rome IV criteria for IBS-D. From those, cases with faecal elastase <100 ug/g were considered as EPI patients, thus ≥200 ug/g as IBS. Due to the expected larger control group than cases, a control sample was selected by randomization before performing cytokines.

Gordis's rule of 4 controls per case was applied. Cytokines were described in median (interquartile range, IQR) and compared cases and controls with the Wilcoxon test. An overall agreement sub-analysis was performed for cytokines with significant median differences among study groups.

Diagnostic odds ratio (OR) was estimated through binary logistic regression if necessary, and adjusted to BMI with multivariate analysis. Data analysis was performed in Rv.4.0 (R Foundation for Statistical Computing; Vienna, Austria).

A total of 27 serum markers (Bio- Plex Pro human cytokine 27-plex Assay, Bio- Rad Lab., Inc.) was measured in all patients (FGF basic, Eotaxin, G-CSF, GM-CSF, IFN-γ, IL-1β, IL-1ra, IL-2, IL-4, IL-5, IL-6, IL-7, IL-8, IL-9, IL-10, IL-12 (p70), IL-13, IL-15, IL-17A, IP-10, MCP-1 (MCAF), MIP-1α, MIP-1β, PDGF-BB, RANTES, TNF-α, VEG).

Results: 25 patients were included, 5 EPI (mean age 67 (66-71) years, females 60%) and 20 IBS (mean age 57 (42-70) years, females 70%) (**table 1**). EPI patients showed a significant increase in monocyte chemoattractant protein 1 (MCP-1) (Median 289 pg/ml [219-385] vs 187 pg/ml [124-224], p= 0.049).

With an optimal cut-off of ≥218.87 pg/ml, MCP-1 differentiated EPI from IBS non-EPI patients with a sensibility, specificity, positive, negative predictive value and observed agreement of 80% (4/5; 28-99%), 75% (15/20; 51-91%), 44% (4/9; 14-79%), 94% (15/16; 70-100%) and 76% (19/25; 55-91%), respectively.

ROC curve reached an area under the curve of 0.79. MCP-1(MCAF) ≥218.87 reached an OR 12.0 (95% CI 1.074 - 134.11; P=.04); and OR 19.281 (95% CI 1.728 - Inf; P=.037) when adjusted to BMI. None of the other cytokines from the 27-panel kit showed significant difference between both groups.

Conclusion: Patients with EPI showed a significant increase in MCP-1 pro-inflammatory cytokine compared with controls in an IBS-D population; this cytokine is associated with several inflammatory diseases, including

pancreatitis. With an optimal cut-off of ≥218.87, MCP-1 differentiated EPI from IBS non-EPI patients. Further studies may demonstrate the usefulness of this cytokine to identify EPI in patients whom fulfill Rome IV criteria for IBS-D.

Disclosure: Nothing to disclose.

P0802

PPDPF IMPACTS PANCREATIC DIFFERENTIATION OF HUMAN PLURIPOTENT STEM CELL DERIVED PANCREATIC PROGENITORS

M. Breunig¹, M. Hohwieler¹, T. Seufferlein¹, S. Liebau², A. Kleger¹

¹Universitätsklinikum Ulm, Innere Medizin I, Ulm, Germany,

²Eberhard Karls University Tübingen, Institute of Neuroanatomy & Developmental Biology (INDB), Tübingen, Germany

Contact E-Mail Address: markus.breunig@uni-ulm.de

Introduction: Given their capability to differentiate into each cell type of the adult human body, human embryonic stem cells (hESCs) provide a unique platform for developmental studies. The generation of pancreatic progenitor (PP) cells from pluripotent stem cells follows the sequential induction of virtually pure definitive endoderm (DE), foregut endoderm (GTE), and pancreatic endoderm (PE).

Aims & Methods: In the current study, we implemented this culture system to understand the role of pancreatic progenitor differentiation and proliferation factor (PPDPF), an up to know nearly uncharacterized protein. A double nicking CrisprCas9 approach was used to ablate PPDPF in hESCs.

Results: Flow cytometry, immunofluorescence, qPCR, and RNA-seq experiments revealed an important role of PPDPF in facilitating a pancreatic fate. Such developmental function was accompanied by a decrease in apoptosis at the pancreatic endoderm in PPDPF deficient cells. In addition, we identified with KCTD12 and MAGED1 novel interaction partners of PPDPF and investigated the expression of PPDPF in normal and human pancreatic cancer tissue.

Conclusion: Thus, we report a novel signalling molecule playing a critical role during human pancreas development and identified a putative regulatory mechanism based on a pluripotent stem cell differentiation platform.

Disclosure: Nothing to disclose.

P0803

THE EFFECT AND MECHANISM OF LPS AND ASCITIC FLUID OF SEVERE ACUTE PANCREATITIS ON INTESTINAL BARRIER FUNCTION IN VITRO

Y. Song¹, F. Zhou¹, Y. Xie¹, X. Zhou¹

¹First Affiliated Hospital of Nanchang University, Nanchang, China

Contact E-Mail Address: songyanpingbg@163.com

Introduction: Severe acute pancreatitis (SAP) progresses rapidly and is often associated with systemic inflammatory response syndrome (SIRS) and persistent multiple organ failure (MOF), with a mortality of up to 40%. The disruption of intestinal barrier function in the early stage of SAP is the main reason for aggravating systemic inflammatory response and leading to poor progression.

The regulation of TLRs signal pathway in intestinal mucosa plays an important role in defending against the invasion of intestinal pathogens and maintaining the homeostasis of intestinal epithelial immune system. Studies have confirmed that the overactivation of TLRs signaling pathway occurs in multiple systems of the body during SAP, which is closely related to intestinal barrier dysfunction. In addition, inhibition TLRs signaling pathway can improve intestinal function and alleviate SAP.

Our previous study found that ascites fluid (AF) from SAP patients significantly upregulated TLR4 in macrophages and the downstream molecule MyD88, mediating NF- κ B activation and promoting the release of pro-inflammatory cytokines. Therefore, LPS and AF may be involved in the occurrence of intestinal barrier dysfunction by regulating the activation of TLRs signaling pathway in intestinal mucosa.

Therefore, the purpose of this study is to explore the causes and mechanisms of SAP intestinal barrier dysfunction based on TLRs signaling pathway. This study will help to find a new direction of intestinal barrier function protection and provide a new research idea for the treatment of severe acute pancreatitis.

Aims & Methods: The disruption of intestinal barrier function in the early stage of Severe acute pancreatitis (SAP) resulted in translocation of bacteria and lipopolysaccharide (LPS), which in turn aggravates systemic inflammatory responses and leads to poor progression. The Toll-like receptor (TLRs) signaling pathway is overactivated in many systems and organs throughout the body during SAP, which is closely related to intestinal barrier dysfunction.

The purpose of this study was to investigate the effects of ascites and LPS on intestinal epithelial cell barrier function in SAP patients through TLRs signal and the mechanism of action. And the monolayer intestinal epithelial cell barrier model was constructed by Caco-2 and IEC-6, and then the effects of LPS or SAP ascites on intestinal epithelial cell barrier function and TLRs signaling pathway were observed. SIGIRR knockdown Caco-2 cell line was constructed to verify the negative regulation of SIGIRR on TLRs signaling pathway.

Results: The integrity of intestinal epithelial cell barrier and paracellular permeability were disrupted after LPS and SAP ascites treatment. The expression of tight junction protein was significantly down-regulated. Intestinal barrier dysfunction was more severe in the hypertriglyceridemia ascites group.

In addition, we also found that intestinal epithelial cells not only showed overactivation of TLRs signaling pathway, but also significantly down-regulated SIGIRR expression. SIGIRR knockdown was also associated with a significant increase in expression of the TLRs signaling pathway.

Conclusion: Both LPS and SAP ascites can cause intestinal barrier dysfunction, in which HTG-AF is more toxic than B-AF. Excessive activation of TLRs signaling pathways may be one of the mechanisms by which LPS and SAP ascites destroy the barrier function of intestinal epithelial cells. The excessive activation of TLRs signals in intestinal epithelial cells may be related to the inhibition of the negative regulator SIGIRR.

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Disclosure: Nothing to disclose.

P0804

TBX3 SHOWS SWITCHING EXPRESSION PATTERNS IN THE EMBRYONIC PANCREAS AND FINE-TUNES REGENERATION FROM ACUTE PANCREATITIS

M.K. Melzer¹, S. Schirge², J. Gout³, F. Arnold⁴, M. Breunig⁵, C. Bolenz⁶, T. Seufferlein⁷, L. Perkhofers⁵, A. Kleger⁸

¹Ulm University, Internal Medicine I/Urology, Ulm,

Germany, ²Helmholtz Zentrum München, Munich, Germany,

³Universitätsklinikum Ulm, Internal Medicine I, Ulm, Germany,

⁴University Hospital Ulm, Internal Medicine I, Ulm, Germany, ⁵Ulm

University, Internal Medicine I, Ulm, Germany, ⁶Ulm University,

Urology, Ulm, Germany, ⁷Universitätsklinikum Ulm - Klinik für

Innere Medizin I, Klinik für Innere Medizin I, Ulm, Germany,

⁸Universitätsklinik Ulm, Internal Medicine 1, Ulm, Germany

Contact E-Mail Address: markus.breunig@uni-ulm.de

Introduction: Genetic programs from early development are crucial for organ regeneration. Re-activation of such programs can be observed in pancreatic acinar cells during reconstitution from injury. *T-Box Transcription Factor 3 (Tbx3)* facilitates somatic reprogramming and is involved in self-renewal.

Aims & Methods: Therefore, we hypothesize that *Tbx3* is expressed during regeneration from acute pancreatitis. Furthermore, we speculate that *Tbx3* is involved in embryonic development of the pancreas.

Results: Analysis of publicly available single-cell transcriptomic datasets revealed expression patterns of *Tbx3* during different milestones of murine embryonic development in various cellular compartments of the pancreas. Correlation of the expression with an *in vitro* directed differentiation of human pluripotent stem cells toward the pancreatic lineage confirmed a high *TBX3* expression during lineage commitment compared to other *T-box* transcription factors. Protein expression of *Tbx3* was confirmed by immunofluorescence studies on embryonic mice from a *Tbx3-Venus* reporter mouse strain.

Here, we clearly demonstrate that *Tbx3* expression is:

- i. Augmented at different stages during embryonic development of the pancreas on protein levels,
- ii. Switches expression patterns from mesenchymal to epithelial expression and;
- iii. Is restricted in adult pancreata to stellate cells.

However, pancreas specific deletion of *Tbx3* already at embryonic stage using a *p48-Cre* mouse resulted only in mild phenotypic alterations in the adult pancreas compared to wildtype counterparts. Higher numbers of alpha cells were detected in *Tbx3-KO* mice. However, additional depletion in the mesenchymal compartment by an *Nkx3-2-Crere* recombinase did only lead to few phenotypic alterations.

Interestingly, induction of experimental acute pancreatitis by caerulein led to an upregulation of *Tbx3* expression during the regeneration phase in wildtype mice. Concordant with our hypothesis, we observed a delayed pancreatic regeneration after caerulein-induced acute pancreatitis in *p48-Cre* depleted homozygous *Tbx3* knockout mice, resulting in a higher rate of acinar-to-ductal-metaplasia, accumulation of fibrosis and excessive proliferation in *Tbx3-KO* mice.

Conclusion: Taken together, we observed differential *Tbx3* expression patterns during embryonic development and regeneration from acute pancreatitis. A knockout of *Tbx3* leads to delayed organ regeneration and excessive proliferation after induced damage. This may indicate that *Tbx3* favors tissue development and repair through regulation of stem cell compartments and fine-tuning of genetic programs from embryonic development.

Disclosure: Nothing to disclose.

P0805

PREDICTIVE MODEL OF PERSISTENT CHOLEDOCOLITIASIS IN PATIENTS WITH ACUTE BILIARY PANCREATITIS

A. Mínguez Sabater¹, P. Ladrón Abia¹, S. Martínez Delgado¹, A. Del Val¹, P. Nos Mateu¹, C. Soutullo¹, E. de-Madaria²

¹Hospital Universitario y Politécnico La Fe, Valencia, Spain,

²Hospital General Universitario de Alicante, Gastroenterology, Alicante, Spain

Contact E-Mail Address: alejandrosab11@gmail.com

Introduction: Acute biliary pancreatitis (ABP) involves inflammation of the pancreatic gland due to the presence of choledocholithiasis (CLT) that normally spontaneously expels into the duodenum. Persistent biliary lithiasis (PBL) in the common bile duct (CBD) increases the probability of both biliary pain, biliary infection, and recurrence of ABP.

The objective of this study was to determine the efficacy of a predictive model of PBL based on epidemiological, analytical and ultrasound data in patients with ABP.

Aims & Methods: A retrospective observational cohort study included patients 18 years of age or older, admitted for ABP (defined according to the revised Atlanta classification) in our center, between the years 2013-2018. Epidemiological, analytical, imaging, and endoscopic variables were collected. The final diagnosis of PBL was made by magnetic resonance imaging cholangiography (C-MRI), endoscopic ultrasonography (EUS), or endoscopic retrograde cholangiopancreatography (ERCP).

Comparative analyses were performed between patients with the presence and absence of PBL. Subsequently, a multivariate logistic regression analysis was performed to develop a predictive model of PBL.

Results: 204 patients with ABP were included. 65.7% women, mean age 73 years. PBL was detected in 49 patients (24%). 145 patients (71.07%) underwent only C-MRI; 44 patients (21.56%) underwent C-MRI and ERCP; 1 patient (0.49%) underwent EUS and ERCP and 14 patients (6.86%) underwent ERCP only.

The variables that showed the greatest association with the presence of PBL were dilation of the common bile duct (CBD) in emergency ultrasound ($p < 0.001$; OR = 27; 95% CI: 5.8-185.5), GGT in the analysis at 72h ($p = 0.008$; OR = 3.4; 95% CI: 1.5-8.9); the presence of biliary sludge in the gallbladder, which protected against PBL ($p = 0.008$; OR = 0.03; 95% CI: 0.001-0.3).

The predictive model showed an unvalidated AUC of 0.902 (95% CI: 0.837-0.967) and a validated AUC of 0.858 for the detection of PBL in patients with ABP. A nomogram was subsequently developed with the results of the model.

Conclusion: The predictive model obtained, with simple variables to determine, had a high efficacy in the detection of PBL in patients with ABP, so it could be used in clinical practice.

Disclosure: Nothing to disclose.

P0806

LOW BODY MASS INDEX INCREASES THE RISK OF ACUTE PANCREATITIS IN TYPE 2 DIABETES: A NATIONWIDE COHORT STUDY

Y.H. Choi¹, K.-d. Han², I.R. Cho³, I.-S. Lee⁴, J.-K. Ryu⁵, Y.-T. Kim³, K.H. Chung⁶, S.H. Lee⁷

¹College of Medicine, The Catholic University of Korea, Internal Medicine, Seoul, Korea (Republic of), ²Soongsil University, Seoul, Korea (Republic of), ³Seoul National University Hospital, Seoul, Korea (Republic of), ⁴Catholic University of Korea College of Medicine, Internal Medicine, Seoul, Korea (Republic of), ⁵Seoul National University Hospital, Internal Medicine, Seoul, Korea (Republic of), ⁶Eulji Hospital, Eulji University College of Medicine, Internal Medicine, Seoul, Korea (Republic of), ⁷Seoul National University College of Medicine / Seoul National University Hospital, Internal Medicine and Liver Research Institute, Seoul, Korea (Republic of)

Contact E-Mail Address: crzyzs@naver.com

Introduction: Type 2 diabetes is known as a risk factor for acute pancreatitis, but the risk of acute pancreatitis according to glycemic status and body mass index (BMI) has remained unknown.

Aims & Methods: We aim to investigate the risk of acute pancreatitis according to BMI and glycemic status in patients with type 2 diabetes. We included 3,912,496 subjects from the Korean National Health Insurance System cohort who underwent the National Health Screening program in 2009. Each subject's clinical course was examined through follow-ups until December 2018.

BMI and glycemic status were each categorized into five groups. Hazard ratios (HRs) of acute pancreatitis according to BMI and glycemic status were calculated using the Cox proportional-hazards model with the adjustment of clinical factors.

Results: The adjusted HRs of acute pancreatitis were the highest in the underweight group (BMI < 18.5) in all five glycemic status categories. The HR of acute pancreatitis in the underweight group increased as the glycemic status worsened, excluding the category of diabetes for more than five years (HR 1.381 for normal fasting glucose; 1.805 for impaired fasting glucose; 2.332 for new-onset diabetes; 4.51 for diabetes duration < 5 years; 4.135 for diabetes duration ≥ 5 years). Sustained underweight group also showed the highest HR in those with and without type 2 diabetes (HR 1.674 for non-diabetes and 1.311 for diabetes).

Conclusion: We found that the risk of acute pancreatitis was further increased in the underweight group, depending on the glycemic status and duration of type 2 diabetes.

Disclosure: Nothing to disclose.

P0807

ACUTE PANCREATITIS INCREASES THE RISK OF GASTROINTESTINAL CANCER IN TYPE 2 DIABETIC PATIENTS: A KOREAN NATIONWIDE COHORT STUDY

J.H. Choi¹, W.H. Paik², D.-K. Jang³, K. Min Kyu¹, J.-K. Ryu¹, Y.-T. Kim², K.-d. Han⁴, S.H. Lee¹

¹Seoul National University Hospital, Internal Medicine, Seoul, Korea (Republic of), ²Seoul National University Hospital, Dept. of Internal Medicine, Seoul, Korea (Republic of), ³Seoul National University, College of Medicine, Seoul, Korea (Republic of), ⁴Soongsil University, Dept. of Statistics and Actuarial Science, Seoul, Korea (Republic of)

Contact E-Mail Address: pseudo.jh@gmail.com

Introduction: Patients with history of acute pancreatitis (AP) or diabetes have an increased risk of pancreatic cancer. However, the association between AP and other gastrointestinal cancers in diabetic patients is currently not well understood. Thus, the objective of this nationwide cohort study was to investigate the association between AP and gastrointestinal cancers in type 2 diabetic patients.

Aims & Methods: Data from the Korean National Health Insurance Service database were analyzed. Participants with diabetes who underwent a general health examination between 2009 and 2012 were followed up for cancer development until December 2018. They were divided into two groups according to AP history. The primary outcome was the occurrence of gastrointestinal cancer.

Results: A total of 2,263,184 patients were included in the final analysis. Of them, 2,390 patients were assigned into the AP group. Patients in the AP group were found to have a significant higher risk for gastrointestinal cancer except for esophageal cancer as follows: gastric cancer (aHR = 1.637, 95% CI: 1.323–2.025), colorectal cancer (aHR = 2.183, 95% CI: 1.899–2.51), liver cancer (aHR = 2.216, 95% CI: 1.874–2.621), pancreatic cancer (aHR = 4.558, 95% CI: 4.078–5.095), bile duct cancer (aHR = 3.996, 95% CI: 3.091–5.269), and gallbladder cancer (aHR = 2.445, 95% CI: 1.459–4.099).

Conclusion: The history of AP particularly increases the risk of gastrointestinal cancer in diabetic patients. Thus, it is necessary to investigate the history of AP in diabetic patients and more actively recommend screening for gastrointestinal cancers in such patients.

Disclosure: Nothing to disclose.

P0808

RECANALIZATION IN SPLANCHNIC VEIN THROMBOSIS ASSOCIATED TO ACUTE PANCREATITIS

C. Ramos Belinchón¹, A. Baines García¹, J.A. Pajares Diaz¹, A.I. Hernando Alonso¹, R.J. Martínez², J. Miranda Bautista¹, V. Flores Fernández¹

¹Hospital General Universitario Gregorio Marañón, Gastroenterology and Hepatology, Madrid, Spain, ²Hospital General de Alicante, Gastroenterology, Alicante, Spain

Contact E-Mail Address: clararamosbel@gmail.com

Introduction: One of the complications of acute pancreatitis (AP) is the development of portosplenomesenteric venous thrombosis(1). In various published studies, its incidence varies between 1% and 24%, and may be associated with multiple complications such as liver failure, intestinal ischemia, and gastrointestinal bleeding from gastroesophageal varices(2–5).

The use of anticoagulation seems reasonable, although the evidence on its efficacy and safety is scarce.

Aims & Methods: The objective of this study is to determine the rate of recanalization of splanchnic thrombosis in patients with AP, as well as the associated factors.

Single-center, observational, retrospective study conducted at the Hospital General Universitario Gregorio Marañón (HGUGM) in Madrid. All patients diagnosed with AP and splanchnic thrombosis between January 2015 and December 2019 were included. Patients with chronic pancreatitis, previously diagnosed portal hypertension or invasive malignant disease were excluded.

Results: In the HGUGM, 1213 patients with AP were treated over 5 years and 30 splanchnic thrombosis meeting the study criteria (2.47%) were diagnosed. Of the 30 patients with thrombosis, more than half had splenic vein thrombosis (n=17). Almost all patients (96.7%) received anticoagulation. Recanalization was confirmed in 19 (63.3%) patients after one year from the diagnosis.

Factors associated with recanalization were studied and an association was identified with the history of previous acute pancreatitis (36.4% vs 5.3%; p=0.047) and with the presence of occlusive thrombosis (45.5% vs 5.3%, p=0.016). In the multivariate analysis, the presence of occlusive thrombosis was associated with a lower risk of recanalization (OR, 0.06; 95% CI, 0.004–0.87). 16.7% (n=5) had at least one bleeding complication that required red blood cell transfusion. 10% (n=3) died in the following 12 months.

Conclusion: Splanchnic thrombosis associated with acute pancreatitis is a relatively common complication with high rates of bleeding and mortality. In our study, practically all thrombosis were anticoagulated, recanalization was achieved in more than half, and occlusive thrombosis was identified as a factor associated with less recanalization.

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Disclosure: Nothing to disclose

P0809 WITHDRAWN

P0810 WITHDRAWN

P0811

ENDOSCOPIC PANCREATIC SPHINCTEROTOMY IN PATIENTS WITH IPMN-RELATED RECURRENT PANCREATITIS: A SINGLE CENTER EXPERIENCE

T. Schepis¹, A. Tringali¹, F. D'Aversa², P. Familiari¹, V. Perri¹, I. Boskoski¹, E.C. Nista³, G. Costamagna¹

¹Fondazione Policlinico Universitario A. Gemelli IRCCS, Digestive Endoscopy Unit, Roma, Italy, ²Pia Fondazione Cardinale Panico, Medicine Department, Tricase, Italy, ³Fondazione Policlinico Universitario A. Gemelli IRCCS, Medical and Surgical Science Department, Rome, Italy

Contact E-Mail Address: tommaso.schepis@gmail.com

Introduction: Intraductal Papillary Mucinous Neoplasms (IPMNs) are a mucin producing subtype of pancreatic cysts arising from the pancreatic duct system. The tick mucous produced by IPMNs can cause an obstruction of the main pancreatic duct leading to recurrent acute pancreatitis (RAP). Endoscopic pancreatic sphincterotomy (EPS) has been described as an alternative minimal invasive procedure to decompress the pancreatic ductal system and reduce the recurrence of ARP. The aim of this study is to assess the safety and effectiveness of ESP in reducing the episodes of RAP in patients with IPMNs related RAP.

Aims & Methods: Patients with IPMNs induced RAP treated with ESP from January 2004 to December 2020 were retrospectively collected. Clinical and technical data were recorded (demographics, type of IPMN, number of AP episodes, type of EPS, adverse events). A clinical follow-up was performed to assess the number of episodes of AP occurred after the EPS.

Results: 25 patients were included (Table 1). The mean follow-up from ESP period was 93.4 months (SD± 56.6). The mean number of AP before and after EPS were respectively 3.29 (SD ± 1.04) and 0.51 (SD ± 0.71) ($p < .00001$ paired samples t-test). A complete response (no further episodes of AP) and a partial response (>50% reduction of AP episodes) were obtained in 64% and 88% of the cases, respectively. One post-EPS bleeding and one minor-papilla stenosis were reported and were endoscopically managed. One patient underwent pancreatic resection for the occurrence of high-risk stigmata.

Demographics:

No. of patients treated, n	25
Age (years), mean ± SD	59.6 ± 15
Sex (men), n (%)	9 (45%)

Type of IPMN:

Main duct-IPMN, n (%)	6 (24%)
Side Branches-IPMN, n (%)	17 (68%)
Mixed type-IPMN, n (%)	2 (8%)

Endoscopic procedure:

Major Papilla Sphincterotomy, n (%)	20 (80%)
Minor Papilla Sphincterotomy, n (%)	5 (20%)
Nose-Pancreatic Drainage, n (%)	21 (84%)
Pancreatic stent, n (%)	4 (16%)

Procedure related adverse events:

Sphincterotomy stenosis (treated with re- sphincterotomy, no further episodes of AP)	1
Post-sphincterotomy bleeding (treated with adrenaline injection and endoclip)	1

IPMNs: Intraductal Papillary Mucinous Neoplasms; MD-IPMN: Main Duct-Intraductal Papillary Mucinous Neoplasm; SB-IPMN: Side Branches-Intraductal Papillary Mucinous Neoplasm; MT-IPMN: Mixed-Type-Intraductal Papillary Mucinous Neoplasm; AP: acute pancreatitis; SD: standard deviation.

Table 1. Demographic and technical data of endoscopic pancreatic sphincterotomy in 25 patients with IPMNs induced RAP.

Conclusion: The correlation between IPMN-related AP and an increased risk of high-grade dysplasia or invasive carcinoma is controversial. Although the major international guidelines consider IPMN related AP a relative indication for pancreatic surgery, pancreatic resection is still today

burdened by high morbidity and mortality and endoscopy may represent a less invasive approach to manage the recurrence of AP.

Few studies evaluated the role of ERCP in IPMN-related ARP. Bernardoni et al. reported a significant reduction in AP episodes after EPS (3.5 ± 2.32 vs. 0.56 ± 1.03 , $P < 0.0001$) in 16 patients with IPMN-related ARP, without IPMN progression and only mild adverse events were reported.

Gonzalez et al. in a multicenter retrospective study involving 21 patients with symptomatic BD-IPMN (including both ARP and pancreas related abdominal pain) treated with EPS reported a complete response in 71% of the cases and a partial response in 81% (with a better response in patients with ARP -90%- than those with pancreas related abdominal pain - 50%-). The present experience confirms that EPS is safe and effective in the management of IPMN-related ARP including BD-IPMN, MD-IPMN and MT-IPMN. After a long-term follow-up (mean 93.4 months), a statistically significant reduction of AP episodes was documented with a complete response and a partial response in 64% and 88% of the cases respectively with only mild adverse events.

The main limitations of the present study are the retrospective design, the limited number of patients enrolled, and the absence of a control group, prospective trials are needed to confirm these data.

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P0812

ACUTE PANCREATITIS IN PATIENTS AFTER LIVER TRANSPLANTATION

A. Hujova¹, P. Macinga¹, J. Jarosova², P. Taimr¹, J. Spicak¹, J. Fronek³, T. Hucl⁴

¹Institute for Clinical and Experimental Medicine, Department of Gastroenterology and Hepatology, Prague, Czech Republic,

²Institute of Clinical and Experimental Medicine, Department of Gastroenterology and Hepatology, Prague, Czech Republic,

³Institute for Clinical and Experimental Medicine, Department of Transplant Surgery, Prague, Czech Republic, ⁴Institute for Clinical and Experimental Medicine (IKEM), Department of Gastroenterology and Hepatology, Prague, Czech Republic

Contact E-Mail Address: alzbeta.hujova@ikem.cz

Introduction: Acute pancreatitis (AP) is a relatively rare but serious complication that can occur after organ transplantation.

Aims & Methods: The aim of this study was to evaluate the incidence, potential risk factors and course of AP in patients following liver transplantation at a single large-volume transplant centre.

Results: Out of a total of 1850 transplanted patients, 49 (2.8%) were diagnosed with AP. Of this group, 37 (75.5%) exhibited a mild form of AP and 12 (24.5%) a severe form of AP.

The mortality rate was 10% overall and 42% in the group of patients with severe AP. An early form of AP (<30 days from transplantation) occurred in 13 patients (26.5%), most of whom presented with severe AP (10 patients, 76.9%); 4 patients died (40%). A late form of AP was diagnosed in 36 patients (73.5%), most of whom exhibited mild AP (34 patients, 94.4%); one of two patients with severe AP died.

The most common AP aetiologies were post-ERCP (38.8%), idiopathic (34.7%) and post-operative (18.4%). Chronic HBV infection proved a risk factor for the development of AP (p=0.01).

	With acute pancreatitis		Mortality	Without acute pancreatitis	
	n	%	%	n	%
Total	49	2,6	10,2	1801	97,4
Age (average)	53			49,5	
Men	30	61,2	10	1078	58,3
Women	19	38,8	10,5	772	41,7
Severe AP	12	24,5	42		
Mild AP	37	75,5	0		
Early AP	13	26,5	31		
Late AP	36	73,5	3		

Table. Characteristics of patients after liver transplantation in relation to acute pancreatitis (AP)

Conclusion: AP in liver transplant recipients was more frequent and more severe than in the general population. This unfavourable course was associated with the occurrence of AP in the early post-transplant period. Liver transplantation due to complications of HBV infection proved a risk factor for the development of AP.

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- Disclosure:** Nothing to disclose.

P0813

ENDOSCOPIC MINOR PAPILLA SPHINCTEROTOMY IN PATIENTS WITH PANCREAS DIVISUM AND ACUTE RECURRENT PANCREATITIS: A METANALYSIS

T. Schepis¹, A. Tringali¹, P.C. Pafundi², P. Familiari¹, I. Boskoski¹, V. Perri¹, G. Costamagna¹

¹Fondazione Policlinico Universitario A. Gemelli IRCCS, Digestive Endoscopy Unit, Rome, Italy, ²Facility of Epidemiology and Biostatistics, Gemelli Generator, Fondazione Policlinico Universitario A. Gemelli IRCCS, Rome, Italy

Contact E-Mail Address: tommaso.schepis@gmail.com

Introduction: Pancreas divisum (PD) is a common congenital variant of the pancreatic ductal system and a potential cause of acute recurrent pancreatitis (ARP). Endoscopic minor papilla sphincterotomy (MiES) is the most common procedure performed in the management of PD-related ARP.

The aim of this study is to perform a meta-analysis estimating the efficacy and the safety of MiES in the management of patients with PD-related ARP.

Aims & Methods: A systematic review of the literature was performed with the purpose of finding papers focusing on MiES performed in patients with *Pancreas Divisum* (PD) suffering from Acute Recurrent Pancreatitis (ARP) through January 2022. The electronic databases searched included MEDLINE (PubMed) and Scopus (Science Direct).

The studies were reviewed and selected according to inclusion and exclusion criteria. Evaluation of Heterogeneity and publication bias was performed, and a random effect model was used to estimate the effect size of each study. Design, analysis, and report of findings were performed according to the most recent PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) guidelines.

Results: 113 articles were selected and reviewed, 13 met the inclusion criteria. All the studies were retrospective with a mean follow-up duration of 45.9 months. A total of 323 patients with PD-related ARP treated with MiES were included in the meta-analysis. The clinical success rate of MiES (defined as no further episodes of ARP, reduction of episodes of ARP, or improvement in QoL) was of 77% (95%CI: 72% – 81%; p=0.30).

The common fixed effects model disclosed a 25.5% overall complications rate (95%CI: 19.3% – 32.8%; p=0.42): acute pancreatitis in 14.3% (95%CI: 9.7% – 20.6%; p=0.36), bleeding in 5.6% (95%CI: 2.9% – 10.4%; p=0.98), and other AEs in 5.6% (95%CI: 2.9% – 10.4%; p=0.67).

Conclusion: MiES is a safe and effective treatment in the management of PD-related ARP. The retrospective nature of the studies selected is the main limitations of this metanalysis. Prospective trials are needed to confirm these data.

Disclosure: Nothing to disclose.

P0814

EXPLORING THE OPTIMAL TIMING OF PERFORMING ENDOSCOPIC ULTRASOUND AFTER AN EPISODE OF ACUTE IDIOPATHIC PANCREATITIS

W. Sbeit¹, A. Shahin¹, T. Khoury¹

¹Galilee Medical Center, Department of Gastroenterology, Naharia, Israel

Contact E-Mail Address: tawfik.khoury.83@gmail.com

Introduction: Patients with acute idiopathic pancreatitis (AIP) should undergo further imaging tests such as endoscopic ultrasound (EUS) for further investigation. The time interval from the episode of AIP and the timing of EUS is still controversial.

Aims & Methods: We aimed to explore the optimal for performing EUS and to reveal parameters that might predict longer interval needed for performing EUS. We performed a single-center retrospective study at Galilee Medical Center, at which we included all patients who underwent EUS for further investigation of AIP.

Results: Overall, we included 51 patients. The average age of all patients was 54.2 ± 17.6 years (range 22-69 years), and more than half of the study cohort were males (56.9%). Classifying patients to inflamed vs. normal pancreatic tissue on EUS, we found that among patients with normal pancreatic tissue, the EUS was performed up to 44.7 ± 28.3 days from discharge, while it was higher for patients with inflamed pancreatic tissue of 48.1 ± 22.3 days.

On descriptive analysis, we found only the radiological average severity score according to Balthazar was to be significantly associated with inflamed pancreatic tissue on EUS, as it was 2.4 ± 0.74 vs. 1.5 ± 1.3 in the normal pancreatic tissue group ($P=0.03$). There was no difference in the Bed-side index for severity in acute pancreatitis (BISAP) score and there was no difference in the average American Society of Anaesthesiologist physical status (ASA) score between the two groups. Notably, 26.3% of patients had inflamed pancreatic tissue when performing EUS at 4 weeks, as compared to 15.8% who had inflamed pancreatic tissue at EUS at $>4 \leq 6$ weeks.

Conclusion: Radiological severity score was the most important in determining the time interval of performing EUS after an episode of AIP. Six-weeks interval is seeming to be needed among patients with higher Balthazar score.

Disclosure: Nothing to disclose.

P0815 WITHDRAWN

P0816

STUDY OF BILIARY MICROLITHIASIS IN THE CAUSATION OF ACUTE AND RECURRENT PANCREATITIS IN CHILDREN

S. Kumar¹, S.K. Yachha¹, M. Sarma¹, R.N. Rao², U. Poddar¹, A. Srivastava¹

¹Sanjay Gandhi Postgraduate Institute of Medical Sciences, Pediatric Gastroenterology, Lucknow, India, ²Sanjay Gandhi Postgraduate Institute of Medical Sciences, Pathology, Lucknow, India

Contact E-Mail Address: drsumitkgmu@gmail.com

Introduction: About one-third of children with acute and acute recurrent pancreatitis (AP/ARP) remain idiopathic and may progress to chronic pancreatitis. In adults, bile microlithiasis contributes to 7-79% of AP/ARP¹. However corresponding pediatric literature is lacking.

Aims & Methods: To study the occurrence of biliary microlithiasis in children with AP/ARP and to establish the causal relationship between them.

Consecutive children from 8-18 years with AP/ARP of idiopathic etiology were included over 2 years study period from November 2017 to October 2019.

Duodenal bile was collected by putting a naso-duodenal catheter under continuous cholecystokinin infusion. 10mL of the collected bile was centrifuged and examined under polarized microscope. Pellet obtained after centrifugation will be immediately observed at 37°C under a polarizing microscope (40X) fitted with a heating stage for the presence of cholesterol monohydrate crystals (CMC) and calcium bilirubinate granules (CBG). Cholesterol monohydrate crystals (CMC) will be identified as birefringent, rhomboid shaped crystals. The presence of brick-red, non-birefringent aggregates of any size will be recorded as calcium bilirubinate granules (CBG). Presence of any number of CMC or >5 CBG on at least 1 slide was considered positive. At least 3 slides will be examined. An average of the number of crystals found in 3 slide examined will be taken for the purpose of grading of abundance. Grading of the abundance will be done as follows Few: <10 /per slide, Moderate: 2-10per high-power field Abundant >10 per high-power field or clumps.

Patients found positive for the presence of microliths were started on ursodeoxycholic acid (UDCA) followed by a repeat bile microscopic examination after 6 months along with the assessment of symptoms.

Results: A total of 33 bile microscopic examinations were carried out in 29 children (22 male) with a median age of 14 (range, 8-17) years. Six children had AP and 23 were diagnosed as ARP. CMC were seen in 5 (17%) patients (AP=2, ARP=3). None of our patients was found to have CBG. All 5 children with CMC were started on UDCA therapy. Four of them underwent repeat bile microscopic examination after 6 months which was normal. None of the 5 children on UDCA treatment had any further episodes of AP over a median follow-up of 16 (4-22) months. There were no complications in any case while performing the bile collection.

Conclusion: A small (17%) but substantial proportion of children with idiopathic AP/ARP was found to have biliary microlithiasis. Resolution of microlithiasis and no recurrence of AP on UDCA therapy may substantiate biliary microlithiasis as a cause of AP/ARP in children.

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P0817

CONSENSUS DEFINITION OF MICROLITHIASIS AND SLUDGE AS A CAUSE OF PANCREATITIS: RESULTS OF A SYSTEMATIC REVIEW, EXPERT SURVEY AND CONSENSUS CONFERENCE

S. Sirtl¹, M. Zorniak¹, G. Beyer¹, J. Schirra¹, C. Schulz¹, U.M. Mahajan¹, M.M. Lerch², J. Mayerle¹, LMU Microlithiasis Expert Survey Team
¹LMU University Hospital, Department of Medicine II, Munich, Germany, ²LMU University Hospital, Munich, Germany

Contact E-Mail Address: simon.sirtl@med.uni-muenchen.de

Introduction: In up to 20% the etiology of acute pancreatitis (AP) remains elusive after routine work-up. Nevertheless, a biliary etiology warrants treatment to prevent recurrence. According to international guidelines EUS is recommended to exclude occult microlithiasis/biliary sludge as cause of pancreatitis. In a systematic literature review we analysed definitions of biliary sludge and microlithiasis.

In an expert survey we aimed for a consensus definition allowing to prospectively determine the risk of biliary pancreatitis from sludge and/or microlithiasis.

Aims & Methods: Following the PRISMA guideline and derived from a systematic review of the literature an online-survey (36 questions: clinical cases, definition, treatment strategy) was developed and sent to 30 HBP and EUS experts from 11 countries and 4 continents to coin definitions agreed on by audience voting (EPC 2021).

Results: The literature review demonstrated that in 13% of original articles and 19.2 % of reviews, microlithiasis and biliary sludge are used as synonyms and in the survey 41.7 % experts described the term “biliary sludge” and “biliary microlithiasis” as identical finding, illustrating the clinical dilemma. As result of the survey three definitions were proposed, agreed and confirmed.

1. The term “biliary sludge” can be used both to diagnose findings in the bile duct as well as the gallbladder.

2. Discrete, hyperechoic material inside the gallbladder or the bile duct, without acoustic shadowing, which sediments in the most dependent part of the gallbladder represents biliary sludge.

3. The term “biliary microlithiasis” should be used exclusively for cases in which EUS examination of the biliary tree reveals presence of stones bigger than 3 and less than 5 mm (in diameter).

Conclusion: We propose for the first time a definition of the localization, sonomorphology and size of biliary sludge as well as microlithiasis. Its relevance for risk assessment of pancreatitis and treatment recommendation needs testing in prospective studies.

Disclosure: Nothing to disclose.

P0818

ACUTE PANCREATITIS FOLLOWING PANCREATICOUDENECTOMY: A PROSPECTIVE STUDY OF DIFFUSION-WEIGHTED MAGNETIC RESONANCE IMAGING, SERUM BIOMARKERS, AND CLINICAL FEATURES

E. Bannone¹, G. Marchegiani¹, G. Zamboni², B.M. Maris³, L. Costa², G. Procida¹, P.G. Vacca¹, E. de-Madaria⁴, R. Salvia¹, C. Bassi¹

¹University of Verona, General and Pancreatic Surgery - The Pancreas Institute, Verona, Italy, ²University of Verona, Diagnostic and Public Health, Verona, Italy, ³University of Verona, Department of Computer Science, Verona, Italy, ⁴Hospital General Universitario de Alicante - Gastroenterology, Hospital General Universitario de Ali, Gastroenterology, Alicante, Spain

Contact E-Mail Address: bannone.elisa@gmail.com

Introduction: Post pancreatectomy acute pancreatitis (PPAP) is difficult to diagnose and poorly characterized in its early phases yet represents the ideal target for novel therapeutic opportunities.

Aims & Methods: This study aims to systematically investigate the early radiologic, biochemical, and clinical features of PPAP.

This is a prospective observational study of patients undergoing pancreaticoduodenectomy from September 2019 to January 2021. Diffusion-weighted (DW) magnetic resonance imaging (MRI) was performed on post-operative day (POD) 3. Serum pancreatic amylase and lipase were daily assessed until POD 5. Postoperative serum hyperamylasemia (POH) and PPAP (grade B-C) were defined based on the International Study Group for Pancreatic Surgery (ISGPS) definition.

Results: A total of 65 patients were enrolled according to the sample size calculation. Patients with POH and PPAP had significantly lower values of apparent diffusion coefficient(ADC) at DW-MRI but no macroscopic features consistent with acute pancreatitis (AP).

Subsequently, 21 patients (32.3%) underwent computed tomography imaging for clinical worsening, and six had radiologic features of AP. All these latter patients had POH and worse postoperative outcomes (p<0.05) in terms of local (postoperative pancreatic fistula: 83%) and systemic mor-

bidity (Clavien Dindo $\geq$ grade IIIb: 67%). The POH incidence was 21.5% (n=14), while PPAP occurred in 6 patients (9.2%), with 4 grade B (6.1%) and 2 grade C (3%).

Conclusion: PPAP is characterized by early biochemical alterations. Macroscopic radiologic features appear later and correlate with worse clinical scenarios. This paper paves the ground for the inclusion of PPAP in the spectrum of its medical counterpart, promoting future trials on its prediction, prevention and treatment.

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P0819

ASGE SOP 2019 CHOLEDOCHOLITHIASIS CRITERIA ARE NOT RELIABLE IN PATIENTS WITH ACUTE BILIARY PANCREATITIS: A SINGLE CENTER EXPERIENCE

Ž.P. Černe¹, D. Drobne²

¹Medical Faculty, University of Ljubljana, Ljubljana, Slovenia, ²University Medical Centre Ljubljana Slovenia, Department of Gastroenterology and Hepatology, Ljubljana, Slovenia

Contact E-Mail Address: david.drobne@gmail.com

Introduction: American Society for Gastrointestinal Endoscopy (ASGE) Standard of Practice (SOP) Guideline 2019 removed gallstone pancreatitis as a criterion for early endoscopic retrograde cholangiopancreatography (ERCP). However, most clinicians still assess the risk of choledocholithiasis in patients with acute pancreatitis by using ASGE 2019 criteria although these criteria were not tested specifically in patients with acute pancreatitis.

Aims & Methods: In this retrospective study we aimed to identify clinical predictors of choledocholithiasis in patients with acute biliary pancreatitis. We also studied the reliability of high and intermediate risk ASGE 2019 predictors of choledocholithiasis in patients with acute biliary pancreatitis.

In our hospital, which is a tertiary referral center, all patients with acute biliary pancreatitis (except those with confirmed stones in common bile duct (CBD) with transabdominal US or clinical cholangitis) have performed endoscopic ultrasound (EUS) to confirm or exclude choledocholithiasis before potential ERCP within 24 hours of admission or planned cholecystectomy.

Here we studied whether EUS could be avoided in some patients with acute biliary pancreatitis by using ASGE 2019 high or intermediate risk predictors for choledocholithiasis. We thus calculated the proportion of

patients with presence or absence specific ASGE 2019 predictor (dilated CBD on transabdominal US, bilirubin level at the time of EUS, increased liver biochemistry, patient's age) according to the EUS result (CBD stone confirmed vs. excluded).

Furthermore, we also studied the potential predictive value of improvement of bilirubin and liver biochemistry from the time of admission until the EUS was actually performed.

Results: In total we included 73 consecutive patients who were admitted to our hospital due to acute biliary pancreatitis in year 2021 and had performed EUS. EUS was performed at a median of 1 day after admission (interquartile range 0-2 days). EUS confirmed choledocholithiasis in 15/73 (21%) patients. Among 8 patients with an ASGE high risk criterion (bilirubin >4 mg/dL + CBD dilatation as assessed by transabdominal US) only 3/8 (37.5%) had confirmed choledocholithiasis by EUS.

Intermediate risk ASGE criteria performed similarly with choledocholithiasis confirmed in 15/60 (25%), 8/42 (19%), 5/16 (31%) ($p=0.59$) patients with abnormal liver biochemical tests, age > 55 years or dilated CBD by transabdominal US, respectively. Different bilirubin levels were not reliable predictors of choledocholithiasis as patients with low (<1.81 mg/dL), intermediate (1.81-4 mg/dL) and high (>4 mg/dL) bilirubin had similar proportions of EUS-confirmed choledocholithiasis (4/22 (18%), 5/24 (21%), 6/22 (27%), respectively ($p=0.76$). Also, drop of bilirubin by 50% from admission until EUS examination was not predictive of choledocholithiasis vs. no choledocholithiasis (26% vs 33%, $p=0.69$).

Conclusion: In this retrospective cohort of patients with acute biliary pancreatitis ASGE 2019 and biochemical criteria were not reliable tool for prediction of choledocholithiasis. Our findings suggest that EUS should be performed in all patients with acute biliary pancreatitis before ERCP or cholecystectomy.

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P0820

ARTERIAL BLEEDING COMPLICATING ACUTE NECROTIZING PANCREATITIS: RISK FACTORS AND PREDICTIVE FEATURES

A. Guilloux¹, M. Ronot², A. Jemal Turki³, M. Gasperment⁴, P. Lévy⁴, L. De Mestier¹, F. Maire¹, B. Jais⁵, V. Rebours⁶, **D. Lorenzo⁵**
¹Hôpital Beaujon, Dept. of Gastroenterology and Pancreatology, Clichy la Garenne, France, ²Université Paris, Unit for Training and Research in Medicine, Paris, France, ³Hôpital Beaujon, Dept. of Radiology, Clichy la Garenne, France, ⁴Université Denis Diderot Hopital Beaujon, Service de Pancreatologie, Service de Gastroenterologie-Pancreatologie, Clichy Cedex, France, ⁵Hôpital Beaujon, Dept. of Endoscopy, Clichy la Garenne, France, ⁶Hopital Beaujon, Pancreatology and Digestive Oncology Dept., Clichy, France

Contact E-Mail Address: diane.lorenzo@gmail.com

Introduction: Acute necrotizing pancreatitis (ANP) is a common pathology, associated with significant morbidity and mortality. The most common complications are related to the pancreatic necrosis (infection, organ compression). For several years, these complications have been managed

a "step-up" strategy, which involves endoscopic and/or radiological drainage, and only if unsuccessful: surgical necrosectomy. Bleeding complications from all causes are also frequent (10 to 29% of ANP) and severe (mortality 31 to 52%). No recent studies have investigated the specific bleeding complicating ANP caused by arterial rupture and their mechanism. The objective of our study is to highlight the risk factors for arterial bleeding complicating acute ANP at the time of the "step-up" management.

Aims & Methods: Main aim was to identify risk factors for arterial bleeding in patients with acute necrotizing pancreatitis (ANP).

This retrospective single-center case-control study have included patients with ANP (2017-2019) in a referral center. All patients diagnosed with AP and a CTSI severity score ≥ 4 for whom clinical and radiological data were available were included. Cases and controls were patients respectively with and without arterial bleeding. Clinical, laboratory, imaging, and follow-up data were collected. Two radiologists retrospectively reviewed CT-scans to identify culprit arteries, vascular lesions, presence and location of drains. A Cox-Mantel model was adjusted to identify risk factors for bleeding.

Results: A total of 148 patients (101 [68%] men, mean 54 ± 14.6 yrs) was included. Twenty-eight (19%) patients experienced bleedings after a mean 66 ± 50 days of ANP course. Warning signs (abdominal pain, deglobulization) preceded bleeding in 8/28 (29%) cases. The main culprit arteries were the gastroduodenal ($n=12$, 40%) and splenic arteries ($n=11$, 37%). Vascular anomalies concerned 26/28 (93%) patients in cases and 9/106 (8%, isolated narrowing artery in 2/3 of cases) in controls ($p<0.001$). In cases, vascular anomalies included pseudoaneurysms ($n=12$, 41%), arterial irregularities ($n=11$, 37%), narrowing ($n=5$, 17%) and interruption ($n=3$, 10%); 23% of patients presented several lesions. At least one was present on the previous recent CTscan in 11/21 (52%) cases.

An artery was in contact with a drain (radiological drain or endoscopic stent) in 9/28 (32%) cases and 12/120 (10%) controls ($p=0.01$). Multivariate analysis identified anticoagulation (OR=6.9, 95%CI 2.3-20.8), $p=0.001$) and a drain in contact with an artery (OR=3.9 95%CI 1.14 -13.3, $p=0.025$) as predictors of bleeding.

Embolization was performed in 24 (86%) cases. Bleeding recurred in 7 (33%) cases. Admission in ICU and mortality rates were significantly higher in cases compared with controls (93% vs. 58%, $p<0.001$, and 29% vs. 6%, log-rank $p=0.001$).

Conclusion: Arterial bleeding occurs in one out of five patients with acute necrotizing pancreatitis. Vascular anomalies are frequent, and are not limited to pseudoaneurysms. Curative anticoagulation appears as the main risk factor for bleeding.

Disclosure: Nothing to disclose.

P0821

THE ROLE OF TOTAL BILIRUBIN IN PREDICTING SEVERE ACUTE PANCREATITIS

F. Valverde-López¹, P. Abellán-Alfocea¹, M.C. Fernández-Cano¹, M. Librero Jiménez¹, J.G. Martínez-Cara¹, E. Redondo-Cerezo¹
¹Virgen de las Nieves University Hospital, Gastroenterology and Hepatology, Granada, Spain

Contact E-Mail Address: fcovalverde89@gmail.com

Introduction: Jaundice can lead to poor prognosis in acute pancreatitis but whether mild elevations in total bilirubin (TB) can be related to severe acute pancreatitis has been scarcely studied.

Aims & Methods: The aim of our prospective study is to assess if mild elevations of TB are related to poor outcomes in acute pancreatitis. Patients admitted to our tertiary center for acute pancreatitis were included. Blood samples with markers routinely used in acute pancreatitis, including TB,

were taken on admission. Patients were divided into three groups: normal bilirubin (TB < 1.5mg/dL), mild hyperbilirubinemia (1.5 - 3mg/dL) and jaundice (> 3mg/dL). Patients were followed until discharge or death and poor outcomes such as severe acute pancreatitis based on Atlanta 2012 classification, death, ICU admission, as well as time to resuming oral feeding and length of stay were collected.

Results: 223 patients were recruited. 110 were men (49%), 22 (9.8%) had severe acute pancreatitis, 15 (6.7%) were admitted to ICU and 13 (5.8%) died. Patients with at least mild elevations in TB showed significantly higher rates of death, ICU admission and severe acute pancreatitis although no differences were found in length of stay or time to initiating oral feeding (Table 1). Among patients with elevated TB, no differences were found in severe acute pancreatitis or death between mild hyperbilirubinemia and jaundice ($p = 0.54$, $p = 0.82$) but patients with jaundice had higher rates of ICU admission ($p = 0.04$)

Total Bilirubin on admission	Total	Normal (0-1.5mg/dL)	Mild Hyperbilirubinemia (1.5-3mg/dL)	Jaundice (> 3mg/dL)	P
N (%)	223	123 (55.1)	56 (25.1)	44 (19.7)	-
Severe acute pancreatitis	22 (9.8)	7 (5.6)	8 (14.3)	7 (15.9)	0.02
Death	13 (5.8)	1 (0.01)	8 (14.3)	4 (9)	0.006
ICU admission	15 (6.7)	2 (1.6)	4 (7.1)	9 (20.5)	<0.001
Time to initiating oral feeding, days. Mean (SD)	2.6 (1.9)	2.6 (2)	2.2 (1.3)	2.9 (1.9)	N.S
Length of stay, days. Mean (SD)	9.6 (12.3)	9.9 (14.7)	8.4 (9.5)	10.3 (6.6)	N.S

Table 1.

Conclusion: Patients with mild elevations in TB over 1.5mg/dL have higher rates of death, severe acute pancreatitis and ICU admission. Few differences were found between patients with the defined thresholds of hyperbilirubinemia, although we observed a higher rate of ICU admissions in patients with clinically evident jaundice (TB > 3mg/dL).

Thus, even mild increases of TB on admission should be taken into account in the initial assessment of patients with acute pancreatitis and further studies should be performed to find the mechanisms that lead to worse prognosis in these patients for the identification of potential early therapies.

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Disclosure: Nothing to disclose.

P0822

THE EFFECT OF IMMUNE ENHANCEMENT WITH TA1 ON THE INCIDENCE OF INFECTED PANCREATIC NECROSIS IN ACUTE NECROTIZING PANCREATITIS PATIENTS MAY BE DEPENDENT ON LYMPHOCYTE COUNT: A POSTHOC ANALYSIS OF A MULTICENTER RANDOMIZED TRIAL

W. Mao^{1,2}, J. Zhou^{1,2}, W. Li^{2,1}, L. Ke^{2,1}, Chinese Acute Pancreatitis Clinical Trials Group

¹Nanjing Medical University, Nanjing, China, ²Nanjing University, Nanjing, China

Contact E-Mail Address: wjm9485@163.com

Introduction: Though the primary analysis of the TRACE trial (a trial that investigated the effect of immune enhancement with Thymosin alpha 1 (Ta1) on the incidence of infected pancreatic necrosis (IPN) in patients with acute necrotizing pancreatitis (ANP)) demonstrated a negative result,

given that T cell is the pivotal effector cell during the pharmacological action of Ta1, the lymphocyte count at randomization may impact the effects of Ta1.

Aims & Methods: We aimed to investigate the effect of Ta1 on the incidence of IPN across subgroups of patients with or without baseline lymphopenia. Patients enrolled in the TRACE trial were included and who discontinued the Ta1 regimen prematurely and received less than 14 doses were excluded. The development of 90-day IPN was chosen as the primary outcome, and subgroup analyses were conducted based on three different definitions of lymphopenia or severe lymphopenia. The subgroup treatment interaction was investigated using a Cox proportional hazard model, and logistic regression models with broken-line relationships were used to determine the optimal baseline lymphocyte count interval where Ta1 treatment could exert the maximum effect in reducing the risk of IPN. **Results:** Table 1. Subgroup Analysis of Day-90 infected pancreatic necrosis. *p* value is from treatment × subgroup interaction term obtained from Cox proportional hazards model that controlled for treatment and subgroup main effects.

A total of 502 patients were enrolled in this study (248 in the Ta1 group and 254 in the placebo group). Patients with non-lymphopenia (defined as lymphocyte count at enrollment $\geq 0.8 \times 10^9/L$) (290/502) responded to the Ta1 treatment significantly differently than patients with lymphopenia (212/502) (RR, 2.55; 95% CI, 1.32–4.93; $p = 0.005$), while the other two subgroups showed no significant interaction.

Among those with a baseline lymphocyte count $\geq 0.8 \times 10^9/L$, the probability of developing IPN during the 90-day follow-up was significantly reduced with Ta1 treatment (19/138 (13.8%) vs. 40/152 (26.3%), Log-Rank $p = 0.009$), which could be partly explained by the elevated lymphocyte count at day 7 after randomization according to the ANCOVA analysis.

The results of the fitted logistic regression model showed that the estimated optimal interval was between 0.792 and 2.002 for baseline lymphocyte count, among which Ta1 could exert an effect in preventing IPN.

Day-90 infected pancreatic necrosis	Placebo (N=254)	Thymosin Ta1 (N=248)	Interaction RR (95%CI)	Interaction p
Severe lymphopenia at enrollment (lymphocyte count < $0.5 \times 10^9/L$)			1.65 (0.74-3.70)	0.220
Present, % (n/N)	9/30 (30.0%)	20/25 (40.0%)		
Not present, % (n/N)	56/224 (25.0%)	45/223 (20.2%)		
Lymphopenia at enrollment (lymphocyte count < $0.8 \times 10^9/L$)			2.55 (1.32-4.93)	0.005
Present, % (n/N)	25/102 (24.5%)	36/110 (32.7%)		
Not present, % (n/N)	40/152 (26.3%)	19/138 (13.8%)		
Lymphopenia at enrollment (lymphocyte count < $1.0 \times 10^9/L$)			1.56 (0.77-3.17)	0.216
Present, % (n/N)	42/151 (27.8%)	41/149 (27.5%)		
Not present, % (n/N)	23/103 (22.3%)	14/99 (14.1%)		

Table 1.

Conclusion: Ta1 may reduce IPN in ANP patients without lymphopenia. A new trial is needed to confirm our findings.

Disclosure: The authors have no conflicts of interest to declare.

P0823

COMPARATIVE EFFECTS OF INTRAVENOUS DICLOFENAC AND BUPRENORPHINE FOR PAIN RELIEF IN PATIENTS WITH ACUTE PANCREATITIS: A RANDOMIZED CONTROLLED STUDY

M. Saini¹, J. Samanta², R. Kochhar¹, G. Muktesh¹

¹Post Graduate Institute of Medical Education and Research, Gastroenterology, Chandigarh, India, ²Post Graduate Institute of Medical Education and Research, Gastroenterology, Kolkata, India

Contact E-Mail Address: mayanksaini870@gmail.com

Introduction: Acute pancreatitis (AP) is an acute inflammatory condition characterized by acute necrosis and inflammatory changes of the pancreas. Pain in AP is the most distressing symptom which brings the patient to the hospital. Both opioids and non-steroidal anti-inflammatory drugs (NSAIDs) have been used. However, evidence-based recommendations for analgesic of choice in AP is lacking. This study was aimed to compare the efficacy of diclofenac, an NSAIDs with Buprenorphine, an opioid for pain relief in AP.

Aims & Methods: In this double-blinded randomized controlled trial, patients presenting to a tertiary care centre in India, within 5 days of the onset of pain in AP were randomized to receive either diclofenac (75 mg q 8h IV) or buprenorphine (0.3 mg q 8h IV) for a total duration of 40 hours. Fentanyl, as a rescue analgesic was given via a patient-controlled analgesia (PCA) pump with a lockout interval of 15 minutes. Patients could use the PCA pump for a duration of 72 hours from enrolment.

Records were maintained of the PCA pump demands and the drug delivery with regards to:

1. Number of fentanyl-effective and ineffective demands;
2. Pain Free interval;
3. Dose of fentanyl delivered.

Visual Analogue Score (VAS) was recorded at baseline and subsequently at 4-hour intervals to assess the pain intensity. Pain relief was also measured objectively by the number of demands and the dose of fentanyl as a rescue analgesic and the pain free interval and by comparison of the VAS scores. Secondary outcomes included adverse events of the drugs.

Results: A total of 40 patients of AP (19 in Diclofenac group and 21 in Buprenorphine group) were recruited in the study. Buprenorphine group required significantly lesser dose of fentanyl as compared to the Diclofenac group (120 µg vs 720 µg; P<0.001) (Table 1).

The total number of effective and ineffective demands for the rescue analgesic were significantly fewer in the Buprenorphine group than Diclofenac group (7 vs 46; P<0.001). Buprenorphine arm had a significantly greater pain free interval compared to the Diclofenac arm (20 hours vs 8 hours; P<0.001). The VAS score recorded at each time point was significantly lower in the Buprenorphine arm except at baseline and at 4 hours, which were comparable between the two groups. Pain relief in terms of VAS score reduction was significantly more in the Buprenorphine group as compared to Diclofenac group at 24 hours (76% vs 5%, P<0.001), 48 hours (68.4% vs 27.2%; P=0.011), and 72 hours (79.1% vs 36.2%; P<0.001). Both drugs were comparable in terms of their safety profile.

Total (3 days)	Diclofenac arm (n=19)	Buprenorphine arm (n=21)	p value
Fentanyl Dose (ug)	720 (100-2180)	120 (20-960)	<0.001
Effective demands	36 (5-109)	6 (1-48)	<0.001
Ineffective demands	5 (0-69)	0 (0-4)	<0.001
Total demands	46 (7-178)	7 (1-50)	<0.001
Pain free interval (hours)	8 (0-20)	20 (0-60)	<0.001

Table 1. Comparison between Diclofenac and Buprenorphine groups in terms of dose of Fentanyl, effective and ineffective demands and pain free interval.

Conclusion: Buprenorphine, an opioid was found to be more effective than Diclofenac, an NSAID, for pain management in AP. Buprenorphine had lower rescue analgesic requirement, greater pain free interval and more significant reduction of pain scores.

Trial Reg no: CTRI/2020/07/034974

Disclosure: This abstract has also been selected for oral presentation in Digestive Disease week (DDW) to be held in May 2022. However, it remains doubtful if the presentation will go ahead in view of visa issues in the US consulate.

P0824

THE EFFECT OF FATTY PANCREAS ON ACUTE PANCREATITIS SEVERITY

T. Khoury¹, A. Shahin², W. Sbeit²

¹Galilee Medical Center, Department of Gastroenterology, Naharia, Israel, ²Galilee Medical Center, Gastroenterology, Naharia, Israel

Contact E-Mail Address: tawfik.khoury.83@gmail.com

Introduction: The burden of obesity is increasing, representing a risk factor for numerous diseases. In 2016, more than 1.9 billion adults were overweight; of them over 650 million were obese.

Overall, 13% of the world's adult population is obese. Among the associated findings with obesity, is fatty pancreas or Non-alcoholic fatty pancreas disease, and is usually an incidental radiological finding. A recent systematic review with meta-analysis and meta-regression have showed that NAFLD prevalence approaches 33%.

Recent studies have shown the association of fatty pancreas with pancreatic cancer, pancreatic mucinous cystic lesions and with a predisposition for acute pancreatitis, however, no studies have evaluated whether fatty pancreas led to more severe acute pancreatitis.

Aims & Methods: To explore the effect of fatty pancreas on acute pancreatitis severity. We performed a cross sectional, retrospective study, using the databases of Galilee Medical Center. All patients who were hospitalized with documented acute pancreatitis confirmed by fulfilling at least 2 out of 3 criteria including: clinical (typical upper abdominal pain), laboratory (serum amylase or lipase more than 3 times the upper limit of normal values) and imaging (computed tomography (CT), magnetic resonance imaging (MRI) or ultrasonography (US)) criteria from 2010 until 2021 were included.

Acute pancreatitis severity was determined by Systemic inflammatory response syndrome (SIRS) score, according to "International Association of Pancreatology (IAP)/American Pancreatic Association (APA)" recommendation, at admission. Fatty pancreas was determined by two independent blinded radiologists.

Results: Overall, 411 patients were included. Among them, 42 patients (10.2%, group A) had fatty pancreas on imaging, as compared to 369 patients (89.9%, group B) who did not have. The average age in group A was 58.3 years, vs. 56.5 years in group B (P=0.25).

Expectedly, the rate of obesity and fatty liver was significantly higher in group A, as compared to group B (69.4% vs. 47.5%, P=0.006) and (85.7% vs. 34.1%, P<0.0001), respectively. The Baltzhar score in group A vs. group B was 1.4 vs. 1.2 (P=0.2).

Notably, the rate of positive SIRS (fulfilling 2 out of four parameters including: 1. Temperature < 36°C or >38°C,

2. Heart rate >90/min, (

3. Respiratory rate >20/min, and;

4. White blood cells < 4 x 10⁹/L, > 12 x 10⁹ or 10% bands) was significantly higher in group A as compared to group B (23.8% vs. 11.4%, P=0.01), respectively.

Regression analysis showed fatty pancreas significantly increases the risk of severe pancreatitis (OR 2.43, 95% CI 1.12-5.30, P=0.02).

Conclusion: Fatty pancreas represents a significant factor for severe acute pancreatitis as assessed by the clinical SIRS score. Recognizing this association is of paramount importance for clinicians, to urge patients for lifestyle modification and weight loss.

Disclosure: Nothing to disclose

P0825

THE INCIDENCE OF RECURRENT ACUTE PANCREATITIS AND CHRONIC PANCREATITIS AFTER ACUTE PANCREATITIS. A SYSTEMATIC REVIEW AND META-ANALYSIS

E.-B. Gagy^{1,2}, B. Teutsch^{1,3}, D.S. Veres^{1,4}, D. Palinkas^{5,1}, N. Vörhendi³, P. Hegyi^{1,3,6}, K. Márta^{3,6,1}, P.J. Hegyi^{3,6,1}, K. Ocskay^{3,1}, B. Eross^{3,1,6}

¹Centre for Translational Medicine, Semmelweis University, Budapest, Hungary, ²Selye János Doctoral College for Advanced Studies, Semmelweis University, Budapest, Hungary, ³Institute for Translational Medicine, Medical School, University of Pécs, Pécs, Hungary, ⁴Department of Biophysics and Radiation Biology, Semmelweis University, Budapest, Hungary, ⁵Military Hospital – State Health Centre, Budapest, Hungary, ⁶Division of Pancreatic Diseases, Heart and Vascular Center, Semmelweis University, Budapest, Hungary

Contact E-Mail Address: endre.gg@gmail.com

Introduction: The incidence of acute pancreatitis (AP) ranges from 13 to 45 per 100,000 per year. Its continued recurrence can lead to chronic pancreatitis (CP), which is currently an incurable disease. However, the incidence of recurrent acute pancreatitis (RAP) after first AP and CP after AP is still unknown.

Aims & Methods: Our systematic review and meta-analysis aimed to assess the incidence of RAP after first AP and the incidence of CP after different episodes of AP. Our protocol was prospectively registered on PROSPERO (CRD42021283252). The systematic search was conducted in three major databases (MEDLINE, CENTRAL, EMBASE) on the 18th of October, 2021.

All articles that reported on the follow-up of patients diagnosed with acute pancreatitis (defined by the Revised Atlanta Classification) were eligible. Our outcomes, the incidence of RAP and CP was assessed after the first episode of AP, while CP was evaluated after one RAP episode as well. A random-effect model was used to calculate the pooled incidence rates with 95% confidence intervals (CI). Heterogeneity was analyzed with the I^2 and the Cochrane Q tests. The risk of bias assessment was carried out with the Joanna Briggs Institute Critical Appraisal tool.

Results: Out of the 9382 articles, 20 were eligible for the quantitative synthesis. The incidence rate of RAP in patients after the first episode of AP was 0.059 person-year (CI: 0.04 to 0.086; $I^2=95\%$, CI: 0.915 - 0.966). The incidence rate of CP after the first episode of AP was 0.013 person-year (CI: 0.009 to 0.02; $I^2=80\%$, CI: 0.563 - 0.907) while after the first RAP was 0.039 person-year (CI: 0.024 to 0.064, $I^2=83\%$, CI: 0.48 - 0.944). The risk of bias was low in the majority of the included studies.

Conclusion: Acute pancreatitis progression affects a high proportion of patients. While RAP can develop in the first year in around 4-8.6% and CP in 0.9-2% of patients after the first episode of AP, the risk of CP is even higher, 2.4-6.4%, when the patient already suffered from a RAP episode.

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Disclosure: Nothing to disclose.

P0826

THE DEGREE OF OBESITY HAS A SERIOUS DETRIMENTAL EFFECT ON THE COURSE OF ACUTE PANCREATITIS AND THE DEVELOPMENT OF COMORBIDITIES: ANALYSIS OF AN INTERNATIONAL PROSPECTIVE COHORT OF 2244 CASES

A. Szentesi^{1,2}, Z. Sipos¹, N. Farkas^{1,3}, Á. Vincze⁴, J. Bajor⁴, P. Sarlós⁴, S. Gódi⁴, B.C. Németh⁵, L. Czako⁵, B. Kui⁵, F. Izbéki⁶, L. Gajdán⁶, V. Dunás-Varga⁶, M. Papp⁷, J. Hamvas⁸, M. Varga⁹, I. Török¹⁰, J. Novák¹¹, A. Mickevicius¹², A. Párniczky^{13,14}, M. Földi^{2,13}, M. Imrei^{1,14}, B. Erőss^{14,15}, P.J. Hegyi¹⁵, S. Váncsa^{1,14}, P. Hegyi^{1,14,15}

¹University of Pécs, Medical School, Institute for Translational Medicine, Pécs, Hungary, ²University of Szeged, Doctoral School of Clinical Medicine, Szeged, Hungary, ³University of Pécs, Medical School, Institute of Bioanalysis, Pécs, Hungary, ⁴University of Pécs, Medical School, First Department of Medicine, Division of Gastroenterology, Pécs, Hungary, ⁵University of Szeged, Department of Medicine, Szeged, Hungary, ⁶Szent György Teaching Hospital of County Fejér, Székesfehérvár, Hungary, ⁷University of Debrecen, Division of Gastroenterology, Department of Internal Medicine, Debrecen, Hungary, ⁸Péterfy Hospital, Budapest, Hungary, ⁹BMKK Dr Rethy Pal Hospital, Department of Gastroenterology, Békéscsaba, Hungary, ¹⁰County Emergency Clinical Hospital of Târgu Mures - Gastroenterology Clinic and University of Medicine, Pharmacy, Sciences and Technology "George Emil Palade, Targu Mures, Romania, ¹¹Pándy Kálmán Hospital of Békés County, Gyula, Hungary, ¹²Vilnius University Hospital Santaros Clinics, Vilnius, Lithuania, ¹³Heim Pál National Pediatric Institute, Budapest, Hungary, ¹⁴Semmelweis University, Centre for Translational Medicine, Budapest, Hungary, ¹⁵Semmelweis University, Division of Pancreatic Diseases, Heart and Vascular Centre, Budapest, Hungary

Contact E-Mail Address: szentesiai@gmail.com

Introduction: Acute pancreatitis (AP) is a potentially severe or even fatal gastrointestinal disease requiring hospitalization. Obesity is a major risk factor for several chronic comorbidities and is associated with worse outcome in acute inflammatory conditions.

Aims & Methods: Our objective was to investigate the characteristics and role of obesity in the course and outcome of acute pancreatitis.

Clinical data of 2461 AP cases were collected in the Acute Pancreatitis Registry run by the Hungarian Pancreatic Study Group. Data on body mass index (BMI) were available in 2244 cases. Patient groups were formed based on BMI categories according to the World Health Organization definitions. Anamnestic, admission and outcome parameters were analysed. Depending on the type of variables, Pearson's Chi-squared test, Kruskal-Wallis rank sum test, univariate linear regression and binary logistic regression model was used.

Results: In our cohort 2.8% of the patients were underweight, 30% normal weight, 35% were in the pre-obesity, 20% in the obesity class I, 8.2% in the obesity class II and 3.7% in the obesity class III groups. While female patients had a 43% and male had a 57% share in the total cohort, there was a 56% female share in the underweight, 41% in the normal, 39% in the pre-obesity and 47%, 48% and 48% in the obesity class I, II and III patient groups, respectively.

Compared to the normal BMI group, there are less alcohol consumption and smoking in the patient groups with higher than normal BMI. Odds ratio (OR) for comorbidities are higher in the underweight (OR=2.00; p=0.40), pre-obesity (OR=1.28; p=0.039) and in obesity class I, II and III groups (OR=2.00, 2.11 and 4.63, respectively; p<0.001 in all three). In the pre-obesity and obesity class I, II and III groups, the odds for diabetes (OR=1.61, OR=2.71, OR=4.32 and OR=6.15; p=0.002, p<0.001, p<0.001,

$p < 0.001$, respectively) hypertension (OR=1.76, OR=3.23, OR=3.00 and OR=4.39, respectively; $p < 0.001$ in all four groups), liver steatosis (OR=1.7, OR=2.76, OR=2.93 and OR=7.05, respectively; $p < 0.001$ in all four groups) and hyperlipidemia (OR=1.72, OR=1.64, OR=1.62 and OR=3.38; $p = 0.002$, $p = 0.010$, $p = 0.049$ and $p < 0.001$, respectively) increases substantially according to the degree of obesity.

Among on admission laboratory parameters, significantly higher glutamate-oxalacetate-transaminase (GOT) and gamma-glutamyltransferase (GGT) and lower estimated glomerular filtration rate (eGFR) were measured and calculated in the higher than normal BMI groups.

Higher prevalence of systemic complications were registered in the pre-obesity, obesity class I, II and III groups (OR=1.61, OR=2.51, OR=2.85, OR=3.53; $p = 0.032$, $p < 0.001$, $p < 0.001$, $p < 0.001$, respectively). The odds for renal failure were higher in all four groups compared to the normal BMI group (OR=2.66, OR=5.64, OR=5.34, OR=7.74; $p = 0.017$, $p < 0.001$, $p < 0.001$, $p < 0.001$), while only in obesity class I, II and III groups had higher odds for respiratory failure (OR=2.30, OR=3.37, OR=2.79; $p = 0.002$, $p < 0.001$, $p = 0.016$) and heart failure (OR=2.89, OR=5.53, OR=6.16; $p = 0.025$, $p < 0.001$, $p = 0.002$). The three obesity groups had higher odds for severe acute pancreatitis as well (OR=3.73, OR=4.24, OR=3.39; $p < 0.001$, $p < 0.001$, $p = 0.008$, respectively).

Conclusion: Not only obesity, but also the degree of obesity has a significant role in the development of complications of pancreatitis and other comorbidities. Gradual weight loss can also have a significant positive effect and should be included in patient reports and education.

Disclosure: Nothing to disclose.

P0827

EFFECT OF CHOLECYSTECTOMY ON PREVENTING RECURRENCE OF ACUTE PANCREATITIS

G. Seven¹, G. Musayeva², A. Tüzün Ince¹, E. Keskin², H. Senturk¹

¹Bezmialem Vakıf University, Gastroenterology, Istanbul, Turkey,

²Bezmialem Vakıf University, Internal Medicine, Istanbul, Turkey

Contact E-Mail Address: gulserenseven@yahoo.com

Introduction: Current guidelines recommend cholecystectomy in patients with acute biliary pancreatitis (ABP) to prevent recurrence (1). Some studies suggest that a significant portion of patients with idiopathic acute pancreatitis (IAP) results from occult biliary disease and cholecystectomy, after an episode of IAP, reduces the risk of recurrent pancreatitis (2, 3). However, in these studies, the work-up for potential biliary cause is not extensive and do not include endoscopic ultrasound (EUS), which can detect a biliary disease up to one-third of patients with IAP. In this study, we aimed to ascertain whether cholecystectomy can prevent pancreatitis recurrence in patients with ABP and IAP.

Aims & Methods: Adult patients (over 18 years) with first episode of acute pancreatitis (AP) who admitted to inpatient clinic between January 1, 2015 and December 31, 2021 at a tertiary referral center were retrospectively reviewed. Medical records were scrutinized and relevant data extracted. In addition, a questionnaire either by mail or telephone was used. Patients with biliary and idiopathic AP were included in the analysis. Patients with chronic pancreatitis, previous pancreatic surgery, pancreatic cancer, and other etiologies were excluded.

Primary outcome was recurrence rate. The diagnosis of IAP was confirmed by exclusion of all known etiological factors for AP using extensive work-up, including EUS and/or magnetic resonance cholangiopancreatography (MRCP).

Results: A total of 500 patients with first episode of AP (300 patients with ABP and 200 patients with IAP) were identified. The mean age was 58 years and 267 women, 233 men. The patients were divided into three different

groups: Group 1; patients who had their first pancreatitis attack after cholecystectomy, Group 2; patients who had their gallbladder in situ during the first attack and followed by cholecystectomy and Group 3; patients who had their gallbladder in situ during the first attack but did not have cholecystectomy.

The number of patients with recurrence after the first episode of AP were not statistically different in whole study group (25%, 19% and 15%, respectively, $P = 0.176$). In the subgroup of patients with ABP, the recurrence was higher in group 1 as compared with group 2 and 3 (39%, 19% and 14%, respectively, $P = 0.018$).

On the other hand, in the subgroup of patients with IAP, there was no significant difference among the groups in terms of recurrence (15%, 18%, and 17%, respectively, $P = 0.999$). When patients with in situ gallbladder during their first attack were compared according to their cholecystectomy history (group 2 vs. group 3), no significant difference was found in neither the ABP nor the IAP subgroups (19% vs 14% and 18% vs. 17%, respectively, $P > 0.05$). In addition, the effect of endoscopic retrograde cholangiopancreatography (ERCP) on recurrence of pancreatitis was evaluated. In subgroup of ABP, ERCP was effective for reducing the recurrence in group 2 ($P = 0.008$), while it was not found statistically significant in group 1 and 3. In subgroup of IAP, it ERCP did not reduce the recurrence in any groups.

Conclusion: In ABP, the recurrence is high in patients who have their first pancreatitis attack after cholecystectomy. Cholecystectomy alone is not effective preventing recurrence in patients with gallbladder in situ during the first episode; however, the risk can be decreased with adding ERCP to cholecystectomy. On the other hand, cholecystectomy is not effective in reducing the recurrence in patients with IAP.

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Disclosure: Nothing to disclose.

P0828

A 2-YEAR FOLLOW-UP OF ACUTE PANCREATITIS: PRELIMINARY RESULTS OF THE GOULASH-PLUS STUDY OF ENDOCRINE AND EXOCRINE INSUFFICIENCY

A. Mikó¹, M. Verbó¹, B. Biro¹, P. Sarlós², Á. Vincze², N. Gede¹, A. Kovács³, S. Sztrikovics³, É. Müller³, B. Bódis², L. Gajdán⁴, F. Izbéki⁵, P. Hegyi^{6,7}, Hungarian Pancreatic Studygroup
¹University of Pécs, Medical School, Institute For Translational Medicine, Pécs, Hungary, ²University of Pécs, 1st Department of Medicine, Pécs, Hungary, ³University of Pécs, Department of Medical Imaging, Pécs, Hungary, ⁴Szent György Teaching Hospital of County Fejér, 1st Department of Internal Medicine, Székesfehérvár, Hungary, ⁵Saint George University Hospital, 1st Department of Medicine, Szekesfehervar, Hungary, ⁶University of Pecs, Centre for Translational Medicine, Pecs, Hungary, ⁷Semmelweis University, Centre for Translational Medicine, Budapest, Hungary

Contact E-Mail Address: miko.szandi@gmail.com

Introduction: Acute pancreatitis (AP) can lead to late complications, such as recurrent acute pancreatitis (RAP) and chronic pancreatitis (CP). Diabetes mellitus (DM) and exocrine insufficiency (PEI) is often detected after AP.

Aims & Methods: Our aim is to analyse the rate of DM and PEI after AP. GOULASH-PLUS is a 6-year observational study of AP, of which data of 224 patients from the first and 112 from the second year follow-up were analyzed. Each year oral glucose tolerance test (OGTT) was performed to detect newly DM, and a stool elastase test to measure PEI. Patients were grouped based on pre-existing CP, severity and RAP.

Results: Newly diagnosed DM was 25% (n=4) in the CP and 16% (n=28) in the non-CP group in the first year. These were 45% (n=5) and 8% (n=7) in the second year respectively. In the non-CP group, likely a higher rate of newly DM could be shown in severe AP than mild AP (15% vs 30%) in the first year.

PEI was newly diagnosed in 44% (n=8) in the pre-CP group and 10% (n=19) in the non-CP group in first year and it was 27% (n=3) and 5,5% (n=5) in the second year respectively. In the non-CP group the rate of PEI was likely higher in the patients who suffered from 2 or more RAP than without RAP (37% vs 7%), and for the second year more patients developed PEI, who suffered from moderate or severe AP, than mild AP (32% vs 40 vs 10%).

Conclusion: In our study population during the 2-year follow-up newly DM and PEI was prone to be detected more frequently in patients with moderate to severe AP. PEI also tended to occur more often after more AP attacks. In patients with preexistent CP both DM and PEI occurred more often. It is important to follow-up patients after AP.

Disclosure: Nothing to disclose.

P0829

COMPLIANCE WITH EVIDENCE-BASED CLINICAL GUIDELINES IN THE MANAGEMENT OF ACUTE BILIARY PANCREATITIS: THE MANCTRA-1 INTERNATIONAL COHORT STUDY

G. Pellino¹, Manctra-1 Collaborative Group
¹Università degli Studi della Campania "Luigi Vanvitelli", Department of Advanced Medical and Surgical Sciences, Naples, Italy

Contact E-Mail Address: gipe1984@gmail.com

Introduction: Despite advancements in treatment, acute pancreatitis (AP) is still associated with considerable adverse outcomes, with published overall mortality reaching up to 2% in Western countries and 7.5% in Asia.

Many scientific societies have issued practice guidelines and consensus statements over the past decades to guide surgeons and physicians in managing the disease. However, reports about the real-world implementation of evidence-based recommendations coming from AP guidelines are scant, and the impact of evidence-based guidelines on daily clinical practice has not been adequately investigated globally.

Aims & Methods: This study aimed to evaluate, on a patient-data basis, the contemporary practice patterns of management of biliary AP and to compare these practices with the recommendations by the most updated guidelines.

All consecutive patients admitted to any of the 150 participating general surgery (GS), hepatopancreatobiliary surgery (HPB), internal medicine (IM) and gastroenterology (GA) departments with a diagnosis of biliary AP between 01/01/2019 and 31/12/2020 were included in the study. Categorical data were reported as percentages representing the proportion of all study patients or different and well-defined cohorts for each variable.

Continuous data were expressed as mean and standard deviation. Differences between the compliance obtained in the four different subgroups were compared using the Mann-Whitney U, Student's t, ANOVA or Kruskal-Wallis tests for continuous data, and the Chi-square test or the Fisher's exact test for categorical data.

Results: Complete data were available for 5275 patients. The most commonly discordant gaps between daily clinical practice and recommendations included the optimal timing for the first CT scan (6.1%, $\chi^2 6.71, P=0.081$), the use of prophylactic antibiotics (44.2%, $\chi^2 221.05, P<0.00001$), CT-guided FNA aspiration to drive antibiotic therapy (33.6%, $\chi^2 15.15, P=0.001$), early enteral feeding (33.2%, $\chi^2 11.51, P=0.009$), and the implementation of early cholecystectomy strategies (29%, $\chi^2 354.64, P<0.00001$), with wide variability based on the admitting speciality.

Conclusion: The compliance with guidelines highlighted by this study was poor. A transfer of knowledge strategy is required to increase compliance with guideline recommendations.

Disclosure: Nothing to disclose.

P0830

ON ADMISSION RISK FACTORS AND PREDICTORS OF NON-MILD DISEASE COURSE OF PAEDIATRIC ACUTE PANCREATITIS: A SYSTEMATIC REVIEW AND META-ANALYSIS

M.F. Juhász^{1,2}, Z. Sipos², K. Ocskay², A. Nagy¹, A. Párniczky^{1,2}
¹Heim Pál National Pediatric Institute, Budapest, Hungary, ²University of Pécs, Medical School, Institute for Translational Medicine, Pécs, Hungary

Contact E-Mail Address: flixjuhsz@gmail.com

Introduction: Paediatric acute pancreatitis (PAP) has an increasing incidence and is now estimated to be almost as common as in adults. 20-30% of PAP patients will have a non-mild disease course, characterised by organ failure, local or systemic complications. There is still no consensus regarding on-admission severity prediction in these patients.

Aims & Methods: Our aim was to conduct the first systematic review and meta-analysis of available predictive score systems and parameters and differences between on-admission parameters between PAP severity groups.

We conducted a systematic search on the 14th February, 2022 in MEDLINE, Embase and CENTRAL. We performed random-effects meta-analysis of on-admission differences between mild and non-mild PAP in laboratory parameters, PAP aetiology, demographic factors, etc. calculating risk ratios (RR) or mean differences (MD) with 95% confidence intervals (CI) and visualized the results on forest plots. For the meta-analysis of the performance of predictive score systems, we generated hierarchical summary

receiver operating characteristic curves using a bivariate model. Chi-squared tests were performed and I^2 values calculated to assess statistical heterogeneity.

Results: 45 studies – mostly retrospective cohorts – were eligible for inclusion. Among predictive score systems examined by at least 5 studies, the modified Glasgow scale had the highest specificity (91.5% for values 3), and the Pediatric Acute Pancreatitis Severity score the highest sensitivity (63.1% for values 3). The performance of other proposed score systems and values were summarized. Traumatic (RR: 1.70 95% CI: 1.09–2.67) and drug-induced (RR: 1.33 95% CI: 0.98–1.87) aetiologies were associated with a higher rate of non-mild PAP, while anatomical (RR: 0.6195% CI: 0.38–0.96) and biliary (RR: 0.72 95% CI: 0.53–0.99) tended to be less severe.

Conclusion: Many predictive score systems were proposed to assess the possibility of non-mild PAP course. While the most common ones provide good specificity, they all have subpar sensitivity. Our systematic review provides a rigorous overview of predictive options assessed thus far, that can serve as a basis of future improvement of scores via the addition of parameters with a better observed sensitivity: eg. lipase exceeding 7-times the upper threshold, hemoglobin, etc. Aetiological factors, although they can predispose to a more severe disease, are also not included in any of the available scores.

Disclosure: Nothing to disclose

P0831

SEVERITY OF ACUTE PANCREATITIS IS GREATLY ASSOCIATED WITH THE RISK OF DEVELOPING NEW-ONSET DIABETES OR DYSGLYCAEMIA AFTER INFLAMMATION: A META-ANALYSIS OF 72,813 PATIENTS

O.J. Zahariev^{1,2}, S. Bunduc^{3,2,1,4}, A. Kovács^{2,5}, D. Demeter^{2,6}, L. Havelda^{2,1}, D. Veres^{2,7}, N. Hosszúfalusi^{2,5}, F.M. Juhász^{2,8,9}, P. Hegyi^{2,1,10,8}

¹Semmelweis University, Heart and Vascular Center, Division of Pancreatic Diseases, Budapest, Hungary, ²Semmelweis University, Centre for Translational Medicine, Budapest, Hungary, ³Carol Davila University of Medicine and Pharmacy, Bucharest, Romania, ⁴Fundeni Clinical Institute, Bucharest, Romania, ⁵Semmelweis University, Department of Internal Medicine and Hematology, Budapest, Hungary, ⁶Hungarian Army Medical Center, Budapest, Hungary, ⁷Semmelweis University, Department of Biophysics and Radiation Biology, Budapest, Hungary, ⁸University of Pécs, Institute for Translational Medicine, Medical School, Pécs, Hungary, ⁹Heim Pál National Pediatric Institute, Budapest, Hungary, ¹⁰University of Pécs, János Szentágothai Research Center, Pécs, Hungary

Contact E-Mail Address: olga.zahariev@gmail.com

Introduction: Within 5 years after an episode of acute pancreatitis (AP), one in four people develop diabetes (1), whereas three in five people develop dysglycaemia (2). However, little is known about the risk factors that may play a role in the development of diabetes.

Aims & Methods: Identifying risk and prognostic factors for developing diabetes or dysglycaemia after AP.

We performed a systematic review and meta-analysis of the association between the factors at the time of the index AP and new-onset diabetes or dysglycemia (prediabetes and/or diabetes). The search was carried out in 3 databases on 2021.11.18. The protocol was registered with PROSPERO (CRD42021281983) and follows the PRISMA guideline. For the meta-analysis, we used a random-effects model (DerSimonian-Laird) to calculate pooled odds ratios (OR) with 95% confidence intervals (CI).

Results: We identified 52 studies totalling 72,813 participants of whom 5,483 developed diabetes/dysglycaemia. Severe AP is associated with a significantly higher odds of new-onset diabetes (OR 2.06; 95% CI 1.17–

3.62) than mild and moderate disease. Having severe or moderate AP is associated with a significantly higher OR for new-onset diabetes (OR 3.13; 95% CI 1.31–7.47) than mild AP. The association is more pronounced for dysglycaemia in severe (OR 3.16; 95% CI 1.13–8.83) and severe or moderate disease progression (OR 4.75; 95% CI 2.07–10.90). Other factors significantly associated with increased diabetes and dysglycaemia development odds are necrosis development, infected necrosis, pseudocyst formation and alcohol aetiology.

No significant increase in odds of diabetes/dysglycaemia was found in case of: male sex, smoking, dyslipidaemia, obesity and liver disease as comorbidities, hypertriglyceridemia or biliary AP as aetiology, AP recurrence, organ failure development, biliary or pancreatic surgical interventions. Patients with idiopathic etiology had a significantly reduced odds (OR 0.61; CI 0.44; 0.85) of developing diabetes or dysglycaemia compared to other aetiologies.

Conclusion: Severe and moderate AP, local complications, alcoholic aetiology and necrosectomy are linked to a higher risk of developing diabetes and dysglycaemia. While all AP patients should be monitored for dysglycaemia development, a stricter follow-up is warranted for patients with these factors. This will facilitate early lifestyle and pharmacological interventions and reduce disease burden.

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Disclosure: Nothing to disclose.

P0832

GUT MICROBIOTA COMPOSITION IS SIGNIFICANTLY ALTERED IN PATIENTS WITH CHRONIC PANCREATITIS

P. Macinga¹, L. Bajer¹, N. Galanova², M. Kostovcik², K. Kostovcikova², M. Cahova³, I. Modos⁴, P. Drastich¹, J. Spicak¹, T. Hucl¹

¹Institute For Clinical And Experimental Medicine, Department Of Gastroenterology And Hepatology, Prague, Czech Republic,

²Institute of Microbiology of the Czech Academy of Sciences, Prague, Czech Republic, ³Institute For Clinical And Experimental Medicine, Center of Experimental Medicine, Prague, Czech Republic, ⁴Institute For Clinical And Experimental Medicine, Information Technology Department, Prague, Czech Republic

Contact E-Mail Address: peter.macinga@ikem.cz

Introduction: Gut microbiota represents an emerging worldwide research area. Novel findings suggest that pancreatic disorders might be modulated by gut microbiota composition. Gut microbiome alteration in patients with chronic pancreatitis (CP) was depicted in only a very few studies, with conflicting results.

Aims & Methods: Our study aimed to characterize gut bacterial microbiota composition in patients with CP. Stool samples were collected and relevant clinical data were obtained from 92 study participants, 51 patients with CP of different origins (28 alcoholic, 15 idiopathic, 3 autoimmune, 5 familial), and 41 healthy controls (C). The V3 and V4 regions of the 16S ribosomal RNA gene were sequenced on the Illumina MiSeq platform.

Results: We found that alpha diversity was comparable in CP and C groups albeit it tended to be lower in CP subjects. For visualization of the similarity or dissimilarity of subjects, we used Principal Component Analysis (PCA) and we showed that CP patients tend to separate from control. Multivariable statistics (PERMANOVA) revealed significant differences in β -diversity

at the levels of phylum ($p=0.035$), order ($p=0.023$), family ($p=0.013$) and genus ($p<0.001$). Using univariable differential abundance analysis (Mann-Whitney-Wilcoxon test) followed by effect size analysis (Cliff's delta), we identified 9 phyla with significantly different abundance between groups ($FDR\leq 0.1$). Albeit this selection encompasses 7 very low abundant phyla ($< 0.01\%$), it also involves the most abundant phylum *Firmicutes* (median abundance C vs PC 32 vs 26%) and less abundant but clinically important phylum *Proteobacteria* (median abundance C vs PC 0.1 vs 2.5%).

Using the same approach, we identified 18 genera significantly differently abundant between groups. Interestingly, among genera enriched in CP, *Eggerthella*, *Lachnoclostridium*, *Escherichia*, *Shigella* or *Enterococcus* are mucin degraders that may promote gut barrier damage and trigger systemic inflammatory responses. In contrast, fecal microbiome of CP patients was depleted with short-chain fatty acid producers (*Christensenellaceae_R.7_group*, *Lachnospiraceae_NK4A136_group*, *Coproccoccus*, *Clostridia_UCG.014* or *Erysipelotrichaceae_UCG.003*).

Conclusion: Our results indicate that fecal microbiota is significantly altered in patients suffering from chronic pancreatitis and it is shifted towards a pro-inflammatory setting associated with a compromised intestinal barrier function.

Disclosure: Nothing to disclose.

P0833

MITOFUSIN 2 REGULATES THE NICOTINE INDUCED ACTIVATION OF PANCREATIC STELLATE CELL VIA PI3K/AKT/MTOR SIGNALING PATHWAY

R. Xue¹

¹Beijing Cancer Hospital, Department of Gastroenterology, Beijing, China

Contact E-Mail Address: xueran2@sina.com

Introduction: Nicotine is the major component of cigarette smoke which can facilitate pancreatic fibrosis. Pancreatic stellate cells (PSCs) have a vital role in pancreatic fibrosis. ROS are upstream in the activation of PSCs. MFN2 (mitofusin 2) is required for mitochondrial fusion and for mitochondria-endoplasmic reticulum interaction.

Aims & Methods: This study was aimed to analyze the function and mechanism of Mfn2 in the nicotine induced activation of PSCs. Isolated primary PSCs from C57BL/6 mice were treated with lentivirus-Mfn2 and si-Mfn2, as well as Rosup and PI3K/AKT/mTOR specific inhibitors. The effects of Mfn2 on the activation of PSCs, autophagy, collagen deposition and oxidative stress were analyzed via western blotting, immunofluorescence staining, reactive oxygen species (ROS) assay.

Results: Nicotine increased collagen deposition and activation of PSCs. Expression of α -SMA, LC3II, Beclin1 levels were significantly reduced in si-Mfn2 groups under nicotine treatment. Meanwhile, compared with the control group, there was also a significantly increased for the expression of p-PI3K, p-AKT and p-mTOR levels in si-Mfn2 groups. A significant decrease in ROS positive cells were observed after si-Mfn2 groups under nicotine treatment.

Conclusion: Our finding suggests that Mfn2 improves the activation of nicotine induced PSCs by the PI3K/AKT/mTOR signaling pathway. Mfn2 may act as a therapeutic target in PSC-related pathologies and/or anti-fibrotic approaches.

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P0834

INHIBITION OF ORAI1 PROTECTS THE PANCREATIC TISSUE AND REDUCES THE PROGRESSION OF FIBROSIS IN CHRONIC PANCREATITIS

V. Szabó^{1,2,3,4}, P. Pallagi^{3,1,2}, N. Csákány-Papp^{1,4,2}, M. Görög^{2,1}, B. Tél^{1,5,2}, B. Jójárt^{2,3,1,4}, A. Varga^{2,3,1}, T. Madacsy^{1,2,3}, P. Hegyi⁶, J. Maléth^{2,3,1}

¹University of Szeged, Albert Szent-Györgyi Medical School, Department of Internal Medicine, Szeged, Hungary, ²University of Szeged, HAS-USZ Momentum Epithelial Cell Signaling and Secretion Research Group, Szeged, Hungary, ³University of Szeged, HCEMM-USZ, Molecular Gastroenterology Research Group, Szeged, Hungary, ⁴University of Szeged, Albert Szent-Györgyi Medical School, Doctoral School of Theoretical Medicine, Szeged, Hungary, ⁵Semmelweis University, 1st Department of Paediatrics, Budapest, Hungary, ⁶University of Pecs, Centre for Translational Medicine, Pecs, Hungary

Contact E-Mail Address: szaboviktoria1104@gmail.com

Introduction: Chronic pancreatitis (CP) is a progressive inflammatory disease characterized by irreversible functional and structural pancreatic damage leading to malabsorption, debilitating pain and a significant decrease in the life quality of CP patients. Moreover, CP is the strongest identified risk factor for pancreatic cancer. Clinical treatment of CP is based on surgical and endoscopic interventions accompanied by life-long conservative therapy such as pancreatic enzyme replacement, pain management and nutrition.

As different cell types of the exocrine pancreas – acinar, ductal and stellate cells – contribute to the tissue damage an effective, long-term treatment must act on drug targets, which simultaneously affect these cells. In acute pancreatitis (AP), inhibition of the plasma membrane Ca^{2+} channel ORAI1 decreased the severity of AP and protected acinar and ductal cell functions emphasizing ORAI1 as universal drug target in all cell types.

Aims & Methods: The purpose of this study was to investigate the utility of ORAI1 inhibition to decrease the severity of CP. Therefore, in wild type FVB/N mice, CP was induced by repeated administration of caerulein for two weeks (50 μ g/kg), followed by the administration of a selective ORAI1 inhibitor (CM5480; 20 mg/kg) on the last five days and histological parameters, fibrosis, pancreas weight/body weight ratio, hydroxyproline (HyP) content were quantified. Acinar and ductal functions were assessed with functional and morphological assays. Pancreatic stellate cells (PSC) were isolated and investigated in *in vitro* experiments.

Results: Our experiments revealed a marked decrease of SARAF – an endoplasmic reticulum resident protein, which inhibit ORAI1 activity – in pancreatic acinar cells from mouse and human CP tissue leading to over-activation of ORAI1 mediated extracellular Ca^{2+} influx. On the other hand, inhibition of ORAI1 significantly impaired tissue damage during experimental CP in mice, whereas the extent of fibrosis and immune cell infiltration were markedly decreased. In addition, a significant improvement of pancreatic acinar and ductal functions was observed in CM5480 treated mice.

Finally, ORAI1 inhibition decreased the activation of PSCs *in vitro* and *in vivo*, reduced the migration, whereas the proliferation was impaired due a cell cycle arrest and accumulation of the PSCs in the S phase.

Conclusion: In conclusion we established that overactivation of ORAI1 is a crucial pathogenetic event in the development of CP. Moreover, our results highlight ORAI1 inhibition as a novel universal therapeutic target in the treatment of CP. The translation of these observation shall be possible in the near future as selective ORAI1 inhibitors are currently in clinical trials to treat AP.

Disclosure: The selective ORAI1 inhibitor CM5480 was provided by CalciMedica.

P0835

EXOCRINE PANCREATIC FUNCTION IN PATIENTS AFTER MILD OR MODERATE COVID-19 DISEASE

I. Biriuchenko¹, O. Barabanchyk², V. Korendovych³, V. Bulda², N. Korendovych⁴

¹National Medical University, Internal Medicine, Kyiv, Ukraine,

²Taras Shevchenko National University of Kyiv, Internal Medicine,

Kyiv, Ukraine, ³Zhytomyr Regional Hospital, Gastroenterology,

Zhytomyr, Ukraine, ⁴Zhytomyr Regional Hospital, Internal

Medicine, Zhytomyr, Ukraine

Contact E-Mail Address: doctor.gastro@yahoo.com

Introduction: Due to the recent study [1] pancreatic exocrine cells express SARS-CoV-2 entry factors angiotensin-converting enzyme 2 (ACE2) and the transmembrane serine protease 2 (TMPRSS2) that confirms the possibility of the exocrine part of the pancreas to be susceptible to SARS-CoV-2 infection.

Although COVID-19 may present with acute pancreatic disorder in up to 32.5% cases [2], the question whether pancreas is involved in cases without clinical presentation is still unknown.

Aims & Methods: Our aim was to assess exocrine pancreatic function in patients after mild or moderate COVID-19 disease.

Adult patients after SARS-CoV-2 infection (PCR-confirmed) who were referred for outpatient GI-consultation by a family doctor in the period from December 2020 till December 2021 were included. The exclusion criteria were:

1. Severe or critical COVID-19 disease that required ICU hospitalization or oxygen support,
2. Any signs of active pancreatic inflammation during SARS-CoV-2 infection,
3. Previously diagnosed congenital or acquired pancreatic disorder,
4. Other chronic conditions that could influence on the level of faecal elastase-1 (eg. IBD, IBS, SIBO, chronic kidney disease etc.),
5. Other disorders that could explain GI symptoms.

Pancreatic exocrine insufficiency (PEI) was assessed determining the level of faecal elastase-1 (FE1) and using 13C-mixed triglyceride breath test (13C-MTGT). The results of FE1 test were interpreted as following: 200–500 µg/g - normal values; 100–200 µg/g - mild to moderate insufficiency; <100 µg/g - severe insufficiency. For 13C-MTGT the percentage cumulative dose recovered (PCDR) of 13C excretion at 360 min was calculated.

Results: After fulfilling the exclusion criteria, 68 adult patients (18–46 years, males-31) were included into the analysis. In most cases patients had complaints of upper abdominal pain, dyspeptic symptoms, bloating and stool changes (type 5–6 due to Bristol scale) that occurred for the first time after COVID-19. In 19 patients the FE1 levels corresponded to a moderate pancreatic insufficiency, and in 6 patients to a severe one.

The second FE1 test was done in 25 patients in one month after treatment with pancrelipase (the appropriate dose for each patient was calculated based on Cystic Fibrosis Foundation guidelines).

Five patients out of 25 still had decreased FE1 values that corresponded to a mild (3 patients) and a moderate (2 patients) pancreatic insufficiency. The PEI in those five patients was double checked using 13C-MTGT. Three subjects out of five had lower PCDR than normal.

Conclusion: Our data possibly indicate on the viral islet damage even in those patients who present with mild or no SARS-CoV-2 symptoms suggesting the risk of the development of long term post-COVID-19 pancreatic complications.

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P0836

BACTERIAL METABOLISM AND EXTERNAL SECRETORY INSUFFICIENCY PANCREAS

M. Adkhamova¹, R. Mirzaeva¹, D. Karimova²

¹Tashkent Medical Academy, Department of Gastroenterology,

Tashkent, Uzbekistan, ²Tashkent Medical Academy, GL Endoscopy,

Tashkent, Uzbekistan

Contact E-Mail Address: adkhamova0511@mail.ru

Introduction: Exocrine pancreatic insufficiency (EPI) leads to indigestion in the intestinal lumen. Undigested fats, proteins, and other food ingredients entering the lumen of the large intestine (LI) can significantly change its ecology and functional activity.

Aims & Methods: Evaluation of the characteristics of bacterial metabolism in the TC in patients with chronic pancreatitis (CP) with EPI. The study included 42 CP patients: 27 men and 15 women, mean age of 51.9±10.3 years. All of them completed the determination of fecal elastase enzyme immunoassay, hydrogen breath test with lactulose and determination of short-chain fatty acids (SCFA) in coprofiltrates by the method of gas-liquid chromatography. All studies were carried out before the start of a course of treatment in a hospital.

Results: According to the results of assessing the value of fecal elastase, EPI was detected in 62% of patients. This allowed us to divide the study participants into 2 groups: 1st – without EPI (n=16), and 2nd – with EPI (n=26). The study of the metabolic activity of the MC microflora showed that in patients with CP there is an increase in the enzymatic activity of the MC microflora compared to normal values (N) according to concentrations of fecal SCFA: sum of SCFA of the 1st group.

12.3±3.6 mg/g vs N 10.6±2.5 mg/g; p=0.048, and the presence of EPI further enhanced bacterial metabolism in TC. At the same time, changes were also observed in the spectrum metabolites: against the background of a decrease in the absolute and relative concentrations of acetate (C2) in almost all patients showed a significant increase in the proportions of propionate (C3) and butyrate (C4).

Availability of EPI in the participants of the 2nd group could be an additional factor in the development of the syndrome of excessive bacterial growth in the small intestine in some patients, although high hydrogen test rates (20–67 ppm; cf. 39.4±1.8 ppm) were noted only in 46% of the examined patients. The fact of increasing concentrations of C4 indicated an increase in the activity of fecal microflora producing butyrate and hydrogen.

Conclusion: All patients with CP have increased metabolic activity of the microflora of the TC with a change in structure of the main metabolites, more pronounced with the presence of EPI, which may be indirect evidence of the presence of bacterial overgrowth syndrome in CP patients with EPI.

Disclosure: Nothing to disclose.

P0837

SHEAR-WAVE VERSUS STRAIN ELASTOGRAPHY IN ENDOSCOPIC ULTRASOUND FOR THE DIAGNOSIS OF CHRONIC PANCREATITIS

Y. Yamashita¹, H. Yamazaki¹, Y. Kawaji¹, K. Hatamaru¹, T. Tamura¹, I. Masahiro¹, R. Ashida¹, M. Kitano¹

¹Wakayama Medical University, 2nd Dept. of Internal Medicine, Wakayama, Japan

Contact E-Mail Address: yasunobu@wakayama-med.ac.jp

Introduction: Endoscopic ultrasound (EUS) elastography is a non-invasive diagnostic method for evaluating tissue elasticity. The aims of this study were to compare shear-wave elastography (SWE) and conventional strain elastography (SE) in determination of the diagnosis and degree of chronic pancreatitis (CP).

Aims & Methods: Forty-nine patients who underwent computed tomography (CT), EUS-SWE, EUS-SE, and pancreatic exocrine function testing between January 2019 and January 2022 were prospectively evaluated. CP was diagnosed according to Japan Pancreatic Society criteria (JPSC) 2019, Rosemont criteria (RC), CT findings, and pancreatic exocrine dysfunction. The cut-off values, sensitivity, and specificity for CP diagnosed according to the four criteria were calculated for EUS-SWE and EUS-SE. Relationships between values measured by either of the EUS elastography methods and the number of EUS features were also assessed.

Results: EUS-SWE values were positively correlated with the severity grades of RC and JPSC, but EUS-SE values were not. EUS-SWE was significantly better than EUS-SE for diagnosing CP defined according to CT findings (area under the receiver operating characteristics curve [AUROC]: 0.77 vs. 0.61, $P < 0.001$), RC (AUROC: 0.85 vs. 0.56, $P < 0.001$), JPSC 2019 (AUROC: 0.83 vs. 0.53, $P < 0.001$), and exocrine dysfunction (AUROC: 0.78 vs. 0.61, $P < 0.001$). EUS-SWE values were positively correlated with the number of EUS features, but EUS-SE values were not.

Conclusion: EUS-SWE provides objective assessment for diagnosing and assessing the degree of CP defined according to the criteria of CT findings, RC, JPSC, or exocrine dysfunction, and it can be considered an alternative diagnostic tool to EUS-SE.

Disclosure: Nothing to disclose.

P0838

EUS-GUIDED DRAINAGE OF PANCREATIC WALLED-OFF NECROSIS WITH LUMEN-APPPOSING METAL STENT AND DOUBLE-PIGTAIL PLASTIC STENTS: COMPARISON OF EFFICACY AND SAFETY

H. Haitao¹, W. Gu¹, H. Khizar², Z. Xiaofeng¹, Y. Jianfeng¹

¹Hangzhou First People Hospital, Department of Gastroenterology, Hangzhou, China, ²Zhejiang Chinese Medical University, international education college, Hangzhou, China

Contact E-Mail Address: yjf3303@zju.edu.cn

Introduction: The aim of this study is to evaluate the efficacy and safety of EUS-guided drainage with lumen-apposing metal stent (LAMS) and double-pigtail plastic stent (DPPS) for the treatment of walled-off necrosis (WON).

Aims & Methods: This prospective cohort study included 52 consecutive patients with pancreatic WON admitted to Hangzhou First People's Hospital from December 2018 to June 2021. The patients were divided into two groups based on the types of stents used: the LAMS group ($n = 25$) and the DPPS group ($n = 27$).

Technical success (successful stent placement), operation time, clinical success (WON resolution), the number of endoscopic transluminal necrosectomy (ETN) and adverse events were compared between the two groups.

Results: All 52 patients were successfully stented, indicating a technical success rate of 100% in both groups, while the operation time in LAMS group was less than that in DPPS group (26(19.5-39.8) vs 45 (25.5-55.8) min, $P = 0.02$). The clinical success rate in LAMS group was higher than that in DPPS group (76% (19/25) vs. 37% (10/27), $P = 0.005$. ETN was performed 2.5 (1.0, 5.0) times in LAMS group.

Adverse events were experienced by 28.0% (7/25) of the LAMS group and 14.8% (4/27) of the PS group ($P = 0.245$). LAMS group were associated with similar bleeding (8.0% vs. 7.4 %, $P = 0.936$) compared to DPPS group.

Conclusion: LAMS with ETN was more effective than DPPS in treatment with EUS-guided drainage for pancreatic walled-off necrosis, but did not increase the incidence of bleeding and adverse events.

Disclosure: Nothing to disclose.

P0839

SOFT SELF-EXPANDING METAL STENT TO TREAT PAINFUL PANCREATIC DUCT STRICTURES IN PATIENTS WITH CHRONIC PANCREATITIS: A MULTICENTER TRIAL

S. Sherman¹, R. Kozarek², G. Costamagna³, D.N. Reddy⁴, P. Tarnasky⁵, R.J. Shah⁶, A. Slivka⁷, E. Fogel¹, J. Watkins¹, M. Delhay⁸, S.S. Irani³, A. Tringali³, S. Lakhtakia⁴, P. Kedia⁵, S. Edmundowicz⁶, J. Peetermans⁹, M. Rousseau⁹, J. Deviere⁸

¹Indiana University, Indianapolis, Indiana, United States,

²Virginia Mason Medical Center, Seattle, United States,

³Fondazione Policlinico Universitario Agostino Gemelli, Digestive Endoscopy Unit, Rome, Italy, ⁴Asian Inst. of Gastroenterology

- Gastroenterology, Asian Inst. of Gastroenterology,

Gastroenterology, Hyderabad, India, ⁵Methodist Dallas

Medical Center, Dallas, United States, ⁶University of Colorado,

Gastroenterology, Aurora, United States, ⁷University of Pittsburgh

Medical Center, Pittsburgh, United States, ⁸Erasmee University

Hospital, Gastroenterology, Bruxelles, Belgium, ⁹Boston Scientific

S.A.S., Marlborough, United States

Contact E-Mail Address: jacques.deviere@erasme.ulb.ac.be

Introduction: Fully covered self-expanding metal stents (FCSEMS) are a treatment option for patients with chronic pancreatitis (CP) who have pain associated with a dilated pancreatic duct (PD),¹ but patient selection, FCSEMS design, efficacy and safety remain uncertain compared to surgery or endotherapy using multiple plastic stents.

Aims & Methods: The aim of this study was to conduct a prospective, multicenter single-arm trial to evaluate 6-month indwell of an investigational 4-6 cm long, soft pancreatic FCSEMS (Boston Scientific Corporation, Marlborough, Massachusetts) for treatment of CP-associated pain. Adult patients with painful CP, a dominant downstream PD stricture in the head or proximal head of the pancreas and upstream PD dilation to ≥ 5 mm were enrolled, and had PD stone clearance where applicable.

The primary efficacy endpoint was self-reported pain scores assessed from baseline through 6 months after FCSEMS removal in patients with sufficiently severe and frequent pain at the time of FCSEMS placement as a first stent or in exchange of a plastic stent.

The primary safety endpoint was PD stenting-related serious adverse events (SAEs). Other outcomes were technical success, and proportions of patients with stent migration, restenting, incident secondary strictures, weight gain or improved self-reported quality of life (QOL) assessed during follow-up.

A post-hoc multivariate analysis examined factors associated with $\geq 50\%$ reduction in pain 6 months after FCSEMS removal or observation of complete distal migration (CDM) compared to baseline without a $\geq 50\%$ increase in narcotic use and without restenting.

Results: Among 67 patients (mean age 52.7±12.5 years, mean time since CP diagnosis was 6.4±6.4 years, 34 (50.7%) had plastic stent placement within 90 days of FCSEMS placement, and 46 (68.7%) were eligible for the primary efficacy endpoint analysis. Technical success was 97.0% (65/67). Results for the primary efficacy endpoint (26.1%, 12/46 patients) and primary safety endpoint (31.3%, 21/67 patients) failed to meet the a priori study hypotheses (Table). Study stent migration occurred in 47.7% (31/65) of patients.

Eleven patients had restenting during study follow-up: 7 at the time of and 4 after FCSEMS removal or observation of CDM. Clinically significant secondary strictures located at the intraductal edge of the FCSEMS were reported in 5 patients at the time of stent removal or observation of CDM; all were restented with a single plastic pancreatic stent. Twenty-four (39.3% of 61) patients had weight gain, and 43 (71.7% of 60) reported improved QOL at 6 months after FCSEMS removal or observation of CDM.

The multivariate analysis showed that at 6 months after FCSEMS removal or observation of CDM, patients receiving pancreatic enzyme replacement therapy, those taking narcotics at baseline, or those with higher baseline weight were less likely to report ≥ 50% reduction in pain compared to baseline without a ≥ 50% increase in narcotic use and without restenting.

	Rate	PG	Lower 95% CI	P value ²
Primary efficacy endpoint¹				
Pain relief	26.1% (12/46)	53.0%	14.3%	0.999
	Rate	PG	Upper 95% CI	P value ²
Primary safety endpoint				
Related SAEs	31.3% (21/67)	32.0%	43.8%	0.513

ITT intention to treat PG performance goal
¹Based on mean of VAS Pain Score and Izbicki Frequency of Pain subscore, with score ranging from 0 to 100
²P-value < 0.025 means the performance goal was met.

Conclusion: Some CP patients might benefit from 6-month FCSEMS treatment, but migrations and SAEs are common. Further study is needed to clarify optimal decompressive strategy, FCSEMS design and patient selection.

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P0840
GENETIC AND IDIOPATHIC CHRONIC PANCREATITIS DISPLAY DISTINCT CLINICAL FEATURES AT DIAGNOSIS

C. Deli¹, G. Dell'Anna¹, C. Stornello^{2,1}, G. Vanella¹, N. Bina¹, P. Zaccari¹, A. Mariani¹, G. Capurso¹, P.G. Arcidiacono¹
¹IRCCS San Raffaele Scientific Institute and University, Pancreatobiliary Endoscopy and Endosonography Division, Pancreas Translational and Clinical Research Center, Milan, Italy, ²University of Palermo- Policlinico Paolo Giaccone, Gastroenterology & Hepatology Unit, Department of Health Promotion, Mother & Child Care, Internal Medicine & Medical Specialties, PROMISE, Palermo, Italy

Contact E-Mail Address: c.deli@studenti.unisr.it
Introduction: In 10–30% of chronic pancreatitis (CP) cases without definite aetiology genetic testing is recommended. However, a large quote of CP cases remain idiopathic (ICP). Their distinctive features compared to genetic CP (GCP) or exotoxic cases (ECP) have been poorly described.
Aims & Methods: The aim of the study was to report demographics and clinical features in a consecutive cohort of CP cases according with their aetiology, focusing on these able to distinguish GCP from ICP and ECP. A retrospective analysis of a prospectively maintained database of definite/probable CP patients according to the M-ANNHEIM classification was performed. The groups were compared for continuous and categorical variables with Kruskal Wallis or Anova tests.

Results: 200 patients were examined. Aetiology was deemed exotoxic in 91 cases (45.5%), autoimmune (AIP) in 19 (9.5%), obstructive in 8 (4.0%) and due to recurrent acute pancreatitis in 11 (5.5%). The remaining 71 cases were considered for genetic testing when appropriate (onset age<40 or family history) that was performed in 49 of them, with findings of a genetic cause in 26 (13% of total; CFTR 53.8%, SPINK1 23.3%, PRSS1 15.4%, CTSC 7.7%). Thus 45 cases had ICP (22.5%) of whom 10 aged<35. Median age at diagnosis was lower in patients with GCP (27, IQR 17-36) compared to all other subgroups (55 ECP, 53 ICP; p<0.0001).
Diagnosis of painless, incidental CP was more frequent in ICP (35.6%) vs GCP (3.8%) (p=0.02). Patients with GCP presented more frequently with exocrine insufficiency (65.4% vs 40.7% in ECP and 37.8% in ICP; p=0.051) but less frequently with endocrine insufficiency (7.7% vs 40.7% in ECP and 22.2% in ICP; p=0.002).
The rate of calcifications at diagnosis was lower in ICP (24.4%) and GCP (26.9%) compared to ECP (39.6%) (p=0.014). Patients with GCP had a lower median BMI at diagnosis (21.4 vs 23.5 ECP and 24.2 ICP; p<0.0001) and were less frequently smokers (30.8% vs 94.5% of ECP and 44.4% of ICP; p<0.001).
Conclusion: While GCP displays distinct features, ICP is more frequently painless and shares some aspects both with ECP and GCP, possibly supporting a multifactorial aetiology.
Disclosure: Nothing to disclose.

P0841

ASSESSMENT OF PAIN AND QUALITY OF LIFE IN A SPANISH CHRONIC PANCREATITIS COHORT

D. Oyón^{1,2}, I. Ezcurra Acedo³, A. Campillo⁴, M. Martos⁵, C. Urteaga Casares⁶, N. Gendive⁷, C. Saldaña Dueñas⁸, I. Gorroño⁶, F. Bolado Concejo⁸

¹Hospital Universitario de Galdakao, Gastroenterology and Hepatology, Galdakao, Spain, ²Biocruces Bizkaia Health Research Institute, Barakaldo, Spain, ³Hospital García Orcoyen, Gastroenterology and Hepatology, Estella, Spain, ⁴Hospital Reina Sofía, Gastroenterology and Hepatology, Tudela, Spain, ⁵Hospital Universitario Donostia, Gastroenterology and Hepatology, San Sebastián, Spain, ⁶Hospital Universitario Araba, Gastroenterology and Hepatology, Vitoria-Gasteiz, Spain, ⁷Hospital Universitario de Cruces, Gastroenterology and Hepatology, Barakaldo, Spain, ⁸Hospital Universitario de Navarra, Gastroenterology and Hepatology, Pamplona, Spain

Contact E-Mail Address: daniyonlara7@hotmail.com

Introduction: Chronic pancreatitis (CP) is a multifactorial fibroinflammatory disease that causes permanent morphological changes to the pancreatic tissue. This may lead to abdominal pain and pancreatic insufficiency, seen as secondary diabetes and malnutrition, as well as to various complications. Therefore, this disease can impact negatively on the quality of life (QoL) and result in disabling consequences for the patients.

Aims & Methods: Aims: To evaluate abdominal pain and health related QoL in a Spanish CP cohort.

Prospective multicenter registry of CP patients from 2 regions in the north of Spain, Navarre and Basque Country (PaN-Eus) using the AEG-RedCap platform. QoL data was collected through the validated questionnaire EQ-5D-5L and the visual analogue scale (VAS). Global health auto-perception was measure with VAS and health index (HI). Data from the National Health Survey¹, a monographic report on health-related QoL in the Spanish adult population, was used in order to make comparisons between CP patients and the general population.

Results: A total of 322 patients were included. Mean age was 61.6 ($\pm$ 10.9) and 77.6% were males. The main etiology of CP was toxic in 75.5% of our patients. At the time of inclusion 75.2% had pancreatic calcifications and 71.4% had at least a moderate ductal lesion. The incidence of exocrine pancreatic insufficiency (EPI) in our cohort was 72.6% and 51.4% had diabetes mellitus (DM).

In the last year, 25.6% of patients had CP-related pain, most with an intermittent pattern (85.3%). Frequency of pain was daily in 5.4% of patients, >1 episode a week in 5.4%, >1 episode a month in 6.6% and <1 episode a month in 8.2%. Most patients treated pain with first step analgesia and only 2.8% of the total cohort were on third step analgesia treatment. The presence of pain was associated with younger age (56.8 vs 63.3 years; $p < 0.001$) and active smoking (70.4% vs 52.3%; $p = 0.008$). A tendency although not significant towards a less active alcohol consumption (38.1% vs 51.0%; $p = 0.074$) was also observed. Pain was not associated neither with the presence of IPE nor DM.

Pancreatic duct stricture (29.6% vs 14.8%, $p = 0.003$), obstructive lithiasis (19.8% vs 7.6%, $p = 0.002$), splanchic venous thrombosis ($p = 0.034$), gastric emptying difficulty (11.1% vs 3.4%; $p = 0.018$), pancreatic fistula (12.3% vs 1.2%, $p < 0.001$) and ascites/pleural effusion (7.4% vs 1.7%, $p = 0.02$) were associated with pain. A higher number of endoscopic (37.5% vs 21.3%; $p = 0.004$) and surgical (18.8% vs 7.2%, $p = 0.003$) procedures were performed in patients with pain.

212 QoL questionnaires were included. Global health auto-perception in CP measured with VAS was 69.0 (vs 77.5 in the general population), and HI was 87.8 (vs 93.7 in the general population). The presence of abdominal

pain ($p = 0.001$) and diabetes ($p = 0.001$) were associated with lower QoL indexes (lower VAS and HI). 68.9% of patients declared at least one problem in one of the 5 fields from the EQ-5D-5L. In each field, the prevalence of problems was higher in the CP cohort compared to the general population: mobility (40.6% vs 14.3%), self-care (9.9% vs 6.22%), daily activities (24.1% vs 11.1%), pain/discomfort (48.6% vs 25.5%) and anxiety/depression (32.1% vs 15.0%).

Conclusion: Pain is the main complication of CP and these patients have a reduced QoL. The presence of abdominal pain is associated with younger age, active smoking and complications related to CP. CP patients have a worsened QoL compared to the general population and it is related to the presence of DM. QoL assessment should be included in the global management of CP patients.

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Disclosure: Nothing to disclose.

P0842

EVOLUTION OF INDETERMINATE FOR CHRONIC PANCREATITIS AS DIAGNOSED ON EUS [ACCORDING TO ROSEMONT CRITERIA] IN PATIENTS OF RECURRENT ACUTE PANCREATITIS WITH 1 YEAR FOLLOW UP

A. Vaidya¹, K. Das¹, P.S. Parta¹

¹IPGME&R and SSKM Hospital, Department of Gastroenterology, Kolkata, India

Contact E-Mail Address: arunvaidyagastro@gmail.com

Introduction: Early chronic pancreatitis (CP) can present initially as Recurrent Acute Pancreatitis (RAP). In patients of RAP, outcome of Endoscopic Ultrasound (EUS) can be normal pancreas, indeterminate for CP, suggestive of CP and consistent with CP based on Rosemont criteria [1]. Till date there is no follow up study in literature on the outcome of RAP patients who are indeterminate for CP on EUS.

Aims & Methods: Our aim was to study the outcome of RAP patients with Indeterminate for CP in terms of clinical, biochemical, etiological and radiological evolution on 1 year follow up. We conducted prospective observational cohort study and included all the RAP patients above 12 years of age with normal CT Abdomen & MRCP and who fulfilled the diagnostic Rosemont criteria for Indeterminate for CP. Clinical history was noted and relevant investigations were done at enrollment.

All the patients were closely followed up in Pancreatic clinic at 3 monthly intervals. They were subjected to Ultrasound abdomen and Blood sugar profile 6 monthly. EUS was done after 12 months of baseline EUS.

Results: EUS was performed in 21 patients of RAP, out of which 14 patients were diagnosed as Indeterminate for CP and included in study. Males were 93% and females were 7% with median age of 26 years. Median duration between first documented attack of acute pancreatitis (AP) and EUS was 34 months with median of 4 attacks of AP prior to EUS. Most common etiology of RAP was idiopathic followed by ethanol & hypertriglyceridemia. History of smoking was present in 36% and Diabetes Mellitus & cholecystectomy in 7%.

Pain pattern was continuous in 28.6% and episodic in 71.4% with mean analgesics requirement was 4.5 days/month. On 1 year follow up, 43% patients remained pain free and 36% had AP attack. Mean analgesic requirement throughout the year was 1.2 days/month. Endocrine & exocrine insufficiency developed in 7% patients.

During 1 year follow up, ultrasound abdomen showed sludge in 2 patients and gall stones in 1 patient. Total 8 patients underwent follow up EUS at 1 year that revealed normal study in 1 patient, Indeterminate for CP in 2 patients, suggestive of CP in 3 patients and consistent with CP in 2 patients according to Rosemont criteria.

Conclusion: RAP presenting as Indeterminate for CP is more common in younger adults with idiopathic being most common etiology. Indeterminate for CP progress to CP in majority of patients. Close follow up & counselling regarding diet & lifestyle modifications including abstinence from smoking & alcohol can improve clinical outcome.

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Disclosure: Nothing to disclose.

P0843

DEVELOPMENT OF A NEW LATERAL FLOW ASSAY FOR THE QUANTIFICATION OF FAECAL PANCREATIC ELASTASE AT POINT OF CARE

J. Afonso¹, M. Schneider¹, D. Guschin¹, C.-B. Gerhold¹, B. Ricken¹

¹BÜHLMANN Laboratories AG, Development, Schönenbuch, Switzerland

Contact E-Mail Address: jpa@buhlmannlabs.ch

Introduction: Pancreatic exocrine insufficiency (PEI) can be defined as a reduced pancreatic enzyme activity that leads to fat malabsorption, weight loss and malnutrition-related complications(1). Direct methods to evaluate digestive function, such as the secretin stimulation test or the ¹³C-mixed triglycerides assay, as well as imaging tests are used to diagnose PEI. In addition, less invasive and indirect tests are also available.

Faecal pancreatic elastase is an ideal biomarker for the assessment of pancreatic function in patients suffering from PEI, due to its important role in the digestive process as a proteolytic enzyme and the high stability of the enzyme during intestinal transit.

Aims & Methods: The aim of this work was to develop and optimize a new rapid test for the quantification of faecal pancreatic elastase. The BÜHLMANN Quantum Blue® fPELA is a quantitative lateral flow assay.

The test was designed for the selective measurement of elastase antigen concentrations from stool extracts by a sandwich immunoassay. A monoclonal detection antibody is conjugated to gold nanoparticles. Elastase present in the sample binds to this gold conjugate. A polyclonal capture antibody, highly specific for elastase, is immobilized on the analytical membrane and captures the complex of elastase bound to the anti-elastase gold conjugate, resulting in a coloring of the test line. The remaining free anti-elastase gold conjugate binds to the control line.

The signal intensities of the test line and the control line are measured quantitatively by the Quantum Blue® Reader. Pancreatic elastase is quantified in extracts of human stool samples collected with the BÜHLMANN CALEX® Cap device.

Several analytical studies, such as sensitivity, linearity and High Dose Hook Effect (HDHE), were performed during optimization phase to evaluate the performance of the assay. Moreover, a method comparison with the commercially available high throughput turbidimetric BÜHLMANN fPELA® turbo assay was also performed.

Results: Analytical evaluation during the optimization step revealed preliminary results of the assay performance. Analytical sensitivity was determined as 12.8 µg/g LoB, 16.6 µg/g LoD and 17.2 µg/g LoQ. The preliminary linearity evaluation revealed a linear range of 10 to 472 µg/g. No HDHE

was observed in native samples up to 4'000 µg/g. Method comparison of the new lateral flow assay with BÜHLMANN fPELA® turbo assay, with 80 clinical samples, revealed good analytical agreement with a slope of 1.04 (Passing-Bablok) and a bias at cutoff (200 µg/g) of 5.6%. Relative bias (Bland-Altman) of the two assays was 6.9%. Considering the turbidimetric assay as the reference method, the sensitivity and specificity were 92% and 83%, respectively.

Conclusion: The new BÜHLMANN Quantum Blue® fPELA, a quantitative lateral flow assay, is an accurate, non-invasive and rapid test to determine pancreatic elastase levels in faecal extracts. BÜHLMANN Quantum Blue® fPELA is an attractive alternative to ELISA with a turn-around time of only 15 minutes enabling patients' management in a more patient near clinical environment.

References:

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Disclosure: BÜHLMANN Laboratories AG; Employee.

P0844

CHRONIC PANCREATITIS ASSOCIATED WITH HETEROZYGOUS CYSTIC FIBROSIS TRANSMEMBRANE CONDUCTANCE REGULATOR COMPARED WITH AN ALCOHOL-RELATED CHRONIC PANCREATITIS-19 YEARS COHORT STUDY

A.Y. Ahmed^{1,2}, J. McLaughlin², C. Fullwood¹, R. Harwood¹, A. Makin¹

¹Manchester Foundation Trust, Gastroenterology, Manchester, United Kingdom, ²The University of Manchester, Gastroenterology, Manchester, United Kingdom

Contact E-Mail Address: abubaker.ahmed@postgrad.manchester.ac.uk

Introduction: Alcohol is the most common cause of pancreatitis. Cystic Fibrosis Transmembrane Conductance Regulator (CFTR) can be linked with chronic pancreatitis also. Previously we reported a milder course of disease in patients with CFTR-related pancreatitis who have two gene mutations (compound heterozygous) compared with one gene mutation (heterozygous).

Aims & Methods: To establish whether chronic pancreatitis-associated CFTR gene mutations are related to different clinical outcomes when compared with alcohol-related chronic pancreatitis.

Retrospective cohort analysis of patients with chronic pancreatitis and CFTR gene carrier status and a same-sized sample of alcohol-related pancreatitis attending Manchester University NHS Foundation Trust Pancreatology Unit between 1999 and 2020. Data were reported using appropriate descriptive statistics with comparisons made between the two groups using t-tests or Fisher's exact test. Cox proportional hazard models were used to compare time to endocrine or exocrine deficiency.

Results: Forty-one patients were identified as heterozygous for CFTR associated with chronic pancreatitis, 41 were recruited in the alcohol-related chronic pancreatitis group via random selection from the pancreas clinic. Clinical outcomes are compared in the table.

Conclusion: Our cohort of patients with chronic pancreatitis associated with heterozygous CFTR gene mutations had significantly lower age of presentation and lower requirements for opiates compared to a randomly selected cohort of alcohol-induced pancreatitis patients.

Although not statistically significantly different, the CFTR group tended to have a lower incidence of pancreatitis-related complications compared with alcohol-related chronic pancreatitis.

This study suggests CFTR-related chronic pancreatitis may have a milder course of disease when compared with alcohol-related chronic pancreatitis and CFTR mutations should be considered in young patients presenting with chronic pancreatitis. However larger prospective studies are needed.

Disclosure: None.

	Heterozygous CFTR n=41	Alcohol related pancreatitis group n=41	p value
Gender			
Male	28(68.3%)	32(78.0%)	0.455
Female	13(31.7%)	9(22.0%)	
Age (years), mean (SD)	48.7 (11.9)	57.5 (8.4)	<0.001
Age at diagnosis (years), mean (SD)	34.8 (12.4)	48.7 (9.9)	<0.001
Presentation (%)			
Recurrent Pancreatitis	31 (75.6%)	40 (97.6%)	0.007
Acute attack of pancreatitis	9 (22.0%)	0 (0.0%)	
Unexplained weight loss	1 (2.4%)	1 (2.4%)	
Analgesia score N%			
Constant	13 (31.7%)	27 (65.9%)	0.004
Simple	24 (58.5%)	7 (17.1%)	
As needed	3 (7.3%)	7 (17.1%)	
Opioid use N%			
Opioid	16 (39.1%)	34 (82.9%)	<0.001
None-Opioid	25(61.0%)	7(17.1%)	
Endocrine insufficiency			
Time to endocrine insufficiency (months)	10 (24.4%)	16 (39.0%)	0.235
median IQR	96 (72.00, 126.50)	22.0 (0.00, 53.25)	0.056
Exocrine Insufficiency			
Time to exocrine insufficiency (months)	27 (65.9%)	30 (73.2%)	0.632
median IQR	48 (17.5, 93.0)	17 (2.5, 51.5)	0.040
Pancreatic Stones	5 (12.2%)	4 (9.8%)	1.000
Pancreatic Strictures	12 (29.3%)	18 (43.9%)	0.252
Pancreatic Pseudocysts	13 (31.7%)	23 (56.1%)	0.045
Pancreatic Necrosis	5 (12.2%)	7 (17.1%)	0.587
Endoscopic Therapy	24 (58.5%)	19 (46.3%)	0.377
Common Bile Duct Strictures	9 (22.0%)	12 (29.3%)	0.683
HPB Surgery	3 (7.3%)	8 (19.5%)	0.194
Vascular complication	10 (24.4%)	13 (31.7%)	

Table.

P0845

PANCREATIC DUCT WALL THICKENING ON ENDOSCOPIC ULTRASOUND: A NEW IMAGING FINDING IN AUTOIMMUNE PANCREATITIS

T. Hisa¹, S. Nishiyama¹, A. Kudo¹, T. Yamada¹, S. Osera¹,
H. Fukushima¹, A. Tomori¹

¹Saku Central Hospital Advanced Care Center, Department of
Gastroenterology, Saku, Japan

Contact E-Mail Address: hisa.takeshi@sakuhp.or.jp

Introduction: It is sometimes difficult to distinguish between autoimmune pancreatitis (AIP) and pancreatic neoplasm. In imaging diagnostic examination, long or multiple strictures, or segmental/focal narrowing of pancreatic duct without marked upstream dilatation in endoscopic retrograde pancreatography is important finding to diagnose as AIP. It has been speculated that the narrowing of pancreatic duct is attributed to periductal lymphoplasmacytic infiltration characteristic of histology in AIP. We reported a resected case of AIP in which branch pancreatic duct wall thickening demonstrated by endoscopic ultrasound (EUS) reflected periductal lymphoplasmacytic infiltration¹. EUS that provides high resolution image of pancreas can delineate periductal lymphoplasmacytic infiltration as pancreatic duct wall thickening.

Aims & Methods: The aim of this study is to determine whether pancreatic duct wall thickening on EUS contributes to the diagnosis of AIP. From March 2017, when we began focusing on pancreatic duct wall thickening in AIP, to April 2022, there were 21 consecutive patients diagnosed with AIP in our department. EUS was performed in all of them, and the presence of pancreatic duct wall thickening was noted on the EUS report.

Pancreatic duct wall thickening was focused on a thickened wall with symmetry, irregular luminal caliber, and a smooth hyperechoic layer covering the surface¹. The international consensus diagnostic criteria for AIP were applied. The detection rate of pancreatic duct wall thickening on EUS, characteristics according to pancreatic duct wall thickening, and the change of pancreatic duct wall thickening after steroid therapy were investigated.

Results: All patients were diagnosed with type 1 AIP (definitive type 19, probable type 2). Median age was 70 years (range: 60-82), and male was 15 patients. The median serum IgG4 level at diagnosis was 467 mg/dL (range: 147-2600). The detection rate of pancreatic duct wall thickening on EUS was 81.0% (17/21). Localization was diffuse in 12 patients and segmental/focal type in 9 patients. Other organ involvement was observed in 12 patients. There was no difference in the above factors depending on the presence or absence of pancreatic duct wall thickening. Seventeen patients underwent steroid trial. Among them, 7 patients who underwent EUS after steroid trial showed improvement in pancreatic duct wall thickening.

Conclusion: Pancreatic duct wall thickening on EUS was often seen in patients with AIP and improved with steroid therapy. This new imaging finding may be useful in the diagnosis of AIP.

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Disclosure: Nothing to disclose.

P0846

EFFICACY AND SAFETY OF LUMEN-APPPOSING METAL STENTS IN ENDOSCOPIC ULTRASOUND-GUIDED DRAINAGE OF ABDOMINAL FLUID COLLECTIONS AND THE INFLUENCE OF INSERTING A COAXIAL DOUBLE PIGTAIL PLASTIC STENT

C. Perez Estrada¹, R. Adalberto¹, C. Candelario Garrido¹,
J.M. Martín-Guerrero¹, M.C. Martínez Sierra¹, J. Ampuero Herrojo¹,
F.J. García Fernandez¹

¹Virgen del Rocío University Hospital, Seville, Spain

Contact E-Mail Address: celiapest94@gmail.com

Introduction: Transmural drainage by placing lumen-apposing metal stents (LAMS) is currently the standard of care for abdominal fluid collections (AFC) that can be approached by endoscopic ultrasound (EUS). Despite they have proved to be safe, complications such as bleeding and obstruction have been described.

Aims & Methods: The aim of the study is to assess the efficacy and safety of placing a coaxial double pigtail plastic stent (DPPS) in the EUS management of AFC.

Observational, retrospective study including 70 consecutive patients undergoing EUS-guided drainage of AFC by placing LAMS ± coaxial DPPS, between March-2017 and January-2022. Evaluation of the impact of coaxial DPPS vs non-DPPS insertion on: efficacy, number of endoscopic revisions and complication rate. Specifically, a subgroup analysis with walled-off necrosis (WON) cases was conducted.

Results: 70 patients were included with a mean age of 54.80±13.95 years-old, 74% male. 94% were pancreatic fluid collections: 64% WON and 30% pancreatic pseudocysts, with a mean size of 118.68 mm. 76 LAMS were placed with 100% of technical success. The indications for drainage were: 41% compressive symptoms and 59% infection. 2 patients had immediate adverse events (bleeding and aspiration) but none of them were fatal. The 2 groups, LAMS + initial DPPS (n = 18) and LAMS with no initial DPPS (n = 58), showed similar basal characteristics. The overall clinical success was

90% (100% in initial DPPS group; 87.3% in no initial DPPS group). Significantly less endoscopic revisions (0.93 ± 1.27 vs 3.34 ± 3.75 ; $p = 0.021$) and time to LAMS retrieval (56.32 ± 45.87 vs 125.83 ± 50.56 days; $p < 0.001$) were observed in initial DPPS group. The overall adverse event rate was also lower in DPPS group (13.3% vs 24.1%; $p = 0.367$). The following adverse events related to LAMS were described: 1 sepsis because of stent migration, 2 sepsis because of stent obstruction and 2 upper gastrointestinal bleeding. There were less readmissions in the first group (6.7% vs 14.5%; $p = 0.374$).

In WON subanalysis we described even bigger differences between the 2 groups with better outcomes in patients managed with LAMS + initial coaxial DPPS: 100 % of clinical success vs 80% ($p = 0.167$), significantly less endoscopic revisions (1.38 ± 1.50 vs 4.39 ± 3.97 ; $p = 0.042$) and time to LAMS retrieval (45.75 ± 26.46 vs 149.00 ± 34.72 days; $p < 0.001$), and shorter hospital stay after LAMS insertion (16.60 ± 10.78 vs 36.21 ± 31.18 days; $p = 0.176$).

In general, 4 patients (5.7%) required surgery and 10 (14.28%) required percutaneous drainage of the AFC after EUS approach. We registered 8 deaths but just 1 of them was related to LAMS (late massive bleeding). The 81.6% of LAMS have been removed.

Conclusion: LAMS are safe and effective in EUS-guided drainage of pancreatic fluid collections, including pancreatic pseudocysts and walled-off necrosis.

The initial insertion of a coaxial DPPS reduces the rate of adverse events, endoscopic revisions and readmissions, especially in WON cases.

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Disclosure: Nothing to disclose.

P0847

HIGHER VOLUME GROWTH RATE IS ASSOCIATED WITH DEVELOPMENT OF WORRISOME FEATURES IN PATIENTS WITH BRANCH DUCT-INTRADUCTAL PAPILLARY MUCINOUS NEOPLASMS

T. Innocenti^{1,2}, G. Danti³, E.N. Lynch^{1,2}, G. Dragoni^{1,2}, M. Gotti^{1,2}, F. Fedeli³, D. Palatresi³, M.R. Biagini^{1,2}, S. Milani^{1,2}, V. Miele³, A. Galli^{1,2}

¹University of Florence, Department of Biomedical, Experimental, and Clinical Sciences "Mario Serio", Florence, Italy, ²Careggi University Hospital, Clinical Gastroenterology Unit, Florence, Italy, ³Careggi University Hospital, Department of Services, Emergency Radiology Unit, Florence, Italy

Contact E-Mail Address: tommaso.innocenti@unifi.it

Introduction: Branch duct-intraductal papillary mucinous neoplasms (BD-IPMNs) are the most common pancreatic cystic tumours and have a low risk of malignant transformation^{1,2}.

None of the current guidelines take volume of the cysts and its evolution over time into account³⁻⁵, although it has recently been shown that it is a highly reproducible parameter with low inter-observer variability⁶.

To date, there are no studies investigating the correlation between cyst volume growth rate and the risk of malignant degeneration in patients with BD-IPMN.

Aims & Methods: We aimed to assess both diameter and volume growth rate of BD-IPMNs and evaluate their correlation with the development of malignant characteristics. We retrospectively included all adult patients with a BD-IPMN who had had at least two MRI studies or CT scans at our centre and a 12-month minimum follow-up time.

Diameters of cystic lesions were measured on three planes, while the volume was calculated by segmentation. A region of interest was manually drawn along the edge of the cyst on each consecutive slice covering the whole lesion.

Then, a three-dimensional volume of interest was obtained with the calculated value expressed in cm³. Changes in size over time, and development of worrisome features (WF) or high-risk stigmata (HRS) were evaluated.

The primary outcomes were to assess the volume growth rate of BD-IPMNs without WF or HRS at baseline and to evaluate if a higher volume growth rate correlates with the development of WF or HRS. The secondary outcomes were the following:

1. to compare the impact of measuring volume vs diameters (axial, coronal, and longitudinal diameters);
2. to evaluate the impact of measuring volume growth rate vs diameter growth rate;
3. to test the ability of first-year volume growth rate to predict the development of WF or HRS.

The local Ethical Committee approved the study on July 13th, 2021.

Results: Baseline patients characteristics are reported in Table 1.

After a 40.5-month median follow-up, 10 patients developed WF. No patients developed HRS. Cysts at baseline were larger in patients who developed WF (diameters: 19 vs 9 mm, $p = 0.0035$; 18 vs 10 mm, $p = 0.00652$; 22.5 vs 9.5 mm, $p = 0.00424$ – volume: 5.28 vs 0.45 cm³, $p = 0.00222$).

At the end of the follow-up, patients who developed WF had a median cyst volume of 10.17 cm³, with a median growth of 4.01 cm³, and both were higher than in patients who did not ($p = 0.0005$, $p < 0.00001$).

Volume growth rate was higher in patients who developed WF (1.12 vs 0 cm³/year, $p = 0.0001$); diameter growth rate was higher too, but the difference did not reach statistical significance. The first-year volume – but not diameter – growth rate was higher in patients who developed WF (0.46 vs 0 cm³/year, $p = 0.00634$).

n= 98		
Males (%)	33 (33.7)	
Females (%)	65 (66.3)	
Median age at diagnosis (IQR)	69 (63-75)	
Familial history (%)	9 (9.2)	
History of diabetes (%)	16 (16.3)	
Former or active smokers (%)	22 (22.4)	
Never smoked (%)	76 (77.6)	
Multifocal (%)	57 (58.2)	
Largest cyst localization	Head (%)	44 (44.9)
	Isthmus/body (%)	40 (40.8)
	Tail (%)	14 (14.3)

Table 1.

Conclusion: Our study proved that not only flat size but also cyst volume growth rate is related to the emergence of WF. Moreover, in our cohort, the cyst volume increase in the first year of follow-up was a better early predictor of the development of WF than diameter alone. This suggest that measuring cyst volume routinely could be a useful tool to monitor low-risk IPMNs.

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Disclosure: Nothing to disclose.

P0848

DIABETES MELLITUS AND THE RISK OF PROGRESSION OR MALIGNANCY OF PANCREATIC CYSTIC NEOPLASMS IN PATIENTS UNDERGOING SURVEILLANCE: A SYSTEMATIC REVIEW AND META-ANALYSIS

A. Sofi¹, S. Ahmad², M. Peerzada³, L. Hackett³

¹Cleveland Clinic Foundation, Digestive Diseases and Surgery Institute, Cleveland, United States, ²Mercy Hospitals, Medicine, Toledo, United States, ³Cleveland Clinic Foundation, Cleveland, United States

Contact E-Mail Address: aijazasofi@gmail.com

Introduction: Patients with pancreatic cystic neoplasms (PCN) generally undergo surveillance by cross-sectional imaging or endoscopic-ultrasound due to their pre-malignant potential. Several studies have shown association of certain clinical, morphological and cytological characteristics with high risk of malignant transformation of PCN in whom surgical

resection is indicated. Appearance of certain cyst characteristics during surveillance is associated with aggressive behavior or presence of malignancy. Patient characteristics associated with progression or induction of malignancy in PCN is unclear from current studies.

Aims & Methods: We performed this meta-analysis to determine the patient characteristics associated with progression or malignancy in patients with PCN who undergo surveillance.

We performed systematic research of several electronic databases for all the studies on surveillance of PCN which reported demographic data of patients who had progression or malignancy and controls. We included the observational studies which recorded the history of diabetes in patients at the initial diagnosis of PCN and compared the progression or malignant transformation of PCN in patients with and without diabetes during the surveillance. Studies which assessed the predictors of malignancy in a cohort of resected PCN were excluded.

We calculated Risk ratio (RR) or Hazard ratio (HR) with 95% confidence interval (CI) for each variable. Mantel-Haenszel method or Inverse-variance model was used to pool data of progression or malignant transformation into fixed or random effect model meta-analysis.

A separate analysis was performed to estimate the pooled univariable Risk Ratio (RR) and multivariable Hazard Ratio (HR) of potential risk factors. GRADE (Grading of Recommendations, Assessment, Development and Evaluation) framework was used to interpret the quality of evidence of our findings

Results: 11 observational studies, 4 assessing risk factors for malignancy (3955 patients) and 7 evaluating risk factors for progression of PCN (3144 patients) were included in the meta-analysis. Mean follow-up ranged from 23-96 months. Diabetes before surveillance was present in a total of 1033 (14.5%) patients and pooled malignant transformation or progression was seen in a total of 11.5 % patients. Diabetes mellitus was associated with higher risk for malignant transformation as well as progression of PCN (RR= 1.54, CI 1.23, 1.92).

Moderate heterogeneity was seen ($I^2 = 36\%$; $P = 0.11$). Funnel plot appeared asymmetric but Begg and Mazumdar test ($\tau = 0.145$; $p = 0.5332$) did not show evidence of publication bias. Pooled multivariable HR for association of progression in branch-duct IPMN (BD-IPMN) with DM was 1.44 (95% CI, 1.12-1.84).

Sub-analysis of studies with mean follow up of ≥ 60 months revealed significant association between DM and risk of malignant transformation of PCN with pooled RR 3.17 (CI, 1.69- 5.93). Advanced age was associated with higher risk of progression (RR= 2.78 (CI: 2.67, 2.88).

Male gender had higher risk for malignant transformation but not progression of PCN (RR= 1.33, CI: 1.07, 1.66). On GRADE framework, the level of quality of evidence was low for both progression and malignancy with diabetes because of observational nature of included studies.

Conclusion: Diabetes is associated with an increased risk of both malignancy and progression of PCN in patients who undergo surveillance. Advanced age is also associated with higher risk of progression of PCN. Males have higher risk for malignant transformation.

Disclosure: No Conflict of interest to disclose.

P0849

ADDED VALUE OF SECRETIN DURING MAGNETIC RESONANCE IMAGING TO IDENTIFY DUCTAL COMMUNICATION IN PANCREATIC CYSTIC NEOPLASMS (IMAGE-S): PROSPECTIVE STUDY

M. Gorris^{1,2}, N. van Huijgevoort^{2,1}, M.G. Besselink³, F. Struik⁴, M.R. Engelbrecht⁴, J. van Hooft⁵

¹Amsterdam UMC Location University of Amsterdam, Gastroenterology and Hepatology, Amsterdam, Netherlands,

²Amsterdam Gastroenterology Endocrinology Metabolism, Amsterdam, Netherlands, ³Amsterdam UMC Location University of Amsterdam, Surgery, Amsterdam, Netherlands, ⁴Amsterdam UMC Location University of Amsterdam, Radiology, Amsterdam, Netherlands, ⁵Leiden University Medical Center, Gastroenterology and Hepatology, Leiden, Netherlands

Contact E-Mail Address: m.gorris@amsterdamumc.nl

Introduction: The key feature of side-branch intraductal papillary mucinous neoplasms (SB-IPMN) is its connection with the pancreatic ductal system. This feature could be helpful to distinguish potentially premalignant SB-IPMN from benign lesions such as pseudocyst and serous cystic neoplasm.

However, ductal connection is often not well visible when conventional MRCP imaging techniques, which are used as golden standard to visualize ductal connection, are applied.

Therefore this study aimed to investigate if secretin-enhanced magnetic resonance cholangiopancreatography (s-MRCP) improved visualization of ductal connection in PCN.

Aims & Methods: We performed a prospective pilot study including consecutive adult patients who underwent follow-up for at least one pancreatic cyst without clear pancreatic duct (PD) connection on conventional MRCP. Patients provided informed consent to undergo additional s-MRCP with 0.2 mg/kg intravenous secretin during routine follow-up. All scans were re-read by two experienced abdominal radiologists.

Primary endpoint was clear PD connection (defined as the interpreting radiologist being more than 80% certain of PD connection). Secondary endpoints were artefacts, visibility of the ductal system and adverse events.

Results: We included 21 patients (median age 70 years [IQR 61-75 years], predominantly females [n=15, 67%], median cyst size 18 mm [IQR 13-24 mm]). Both readers reported significantly higher pancreatic ductal visibility after s-MRCP when compared to conventional MRCP (p=0.030 [Reader 1], p = 0.041 [Reader 2]).

This did however not result in improved visibility of PD connection after s-MRCP (p=0.166 for reader 1, p=0.807 for reader 2). Overall image quality and amount of artifacts were similar (p=0.090 and p=0.071 for reader 1, and p=0.084 and p=0.157 for reader 2, respectively). One patient experienced an episode of diarrhea after secretin administration.

Conclusion: The results of this pilot study showed that secretin-enhanced MRCP did increase pancreatic ductal visibility although it did not result in an increased visibility of PD connection in patients with PCN. Follow-up research should investigate if secretin-enhanced ductal visibility is of added value in more extensive MRI sequences to detect PD connection with PCN.

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P0850

CONTINUOUS SMOKING MAY PLAY A ROLE IN THE PROGRESSION FROM "TRIVIAL" (THE GOOD) BD-IPMNS TO IPMNS WITH AN INDICATION FOR SURGERY ("THE BAD") AND PANCREATIC CANCER (THE "UGLY")

G. Capurso¹, L. Apadula¹, G. Lauri¹, P. Lazzano¹, R. Ponz de Leon Pisani¹, M. Cobreros², M. Tacelli¹, L. Archibugi¹, G. Rossi¹, M.C. Petrone¹, P.G. Arcidiacono¹

¹IRCCS Ospedale San Raffaele, Pancreatobiliary Endoscopy and Endosonography Division, Milano, Italy, ²Instituto de investigación sanitaria Valdecilla (IDIVAL), Digestive Diseases Department, Santander, Spain

Contact E-Mail Address: lauri.galetano@hsr.it

Introduction: Intraductal Papillary Mucinous Neoplasms (IPMNs) are common but rarely evolve into invasive cancer (PDAC). Whether factors associated with PDAC risk have similar prevalence in IPMNs that show features considered relative or absolute surgical indication and in "trivial" IPMNs is unknown.

Aims & Methods: To investigate the prevalence of factors associated with PDAC risk in subgroups of "good" and "bad" IPMNs and PDAC.

Materials and Methods: Retrospective analysis of prospectively maintained databases of patients with IPMNs and PDAC. IPMNs with relative of absolute indication for surgery at diagnosis or within the first 48 months of follow-up ("bad IPMNs") were matched (same sex, age ± 5) 1:1 with BD-IPMNs without any surgical indication at diagnosis and during at least 48 months follow-up ("good" IPMNs) and with PDAC ("ugly") patients.

All environmental factors were recorded as present 12 months before diagnosis to avoid bias. The groups were compared for continuous and categorical variables with Kruskal Wallis or Anova tests with Bonferroni correction.

Results: 151 patients were enrolled in each group (49.6% male, median age at diagnosis 70.2, 70.3 and 69.7 for "good", "bad" and "ugly"). The 3 groups did not differ in terms of BMI, history of previous diabetes and related medications, of previous cancers or pancreatitis, chronic use of statins or aspirin.

While the rate of "ever smokers" was not different (46%, 54%, 51%) that of current smoking was progressively higher from "good" (8.8%) to "bad" (13.6%) IPMNs and PDAC (25.6%) (p<0.001). The rate of heavy smoking (>20 pack/years; 19%, 27%, 23%) and ever alcohol drinkers (47%, 49%, 42%) was similar.

A previous history of peptic ulcer was more common in PDAC (7.2%) compared to either "good" (1.3%) or "bad" (1.9%) IPMNs (p=0.012). 1st degree family history (FH) of PDAC was similar in the 3 groups (10.6%, 8.1%, 9.6%), but 2nd degree PDAC FH (4.7%, 1.3%, 8.2%) more frequent in PDAC patients, although not significant after Bonferroni correction (p=0.02). 1st degree FH of other cancers was not different.

Conclusion: Patients with both "good" or "bad" IPMNs share similar exposure with PDAC. Continuous smoking seems associated with the progression of IPMNs toward malignancy.

Disclosure: Nothing to disclose.

P0851

ARTIFICIAL INTELLIGENCE FOR AUTOMATIC DIAGNOSIS OF MUCINOUS PANCREATIC CYSTIC LESIONS IN ENDOSCOPIC ULTRASOUND: A PILOT STUDY

T. Ribeiro¹, M.J. Mascarenhas Saraiva², J. Afonso¹, S. Lopes¹, P. Moutinho-Ribeiro¹, J. Ferreira³, F. Vilas-Boas¹, G. Macedo¹
¹Centro Hospitalar Universitário de São João, Gastroenterology, Porto, Portugal, ²Centro Hospitalar São João, Gastroenterology, Porto, Portugal, ³Faculdade de Engenharia da Universidade do Porto, Porto, Portugal

Contact E-Mail Address: tiagofcribeiro@outlook.com

Introduction: Pancreatic cystic lesions (PCLs) are common findings in clinical practice with an estimated prevalence of 8% (1). These lesions have varied etiology and are associated with increased risk of pancreatic malignancy. However, this risk is almost exclusive of mucinous cystic lesions. Endoscopic ultrasound (EUS) plays a pivotal role in the diagnosis and characterization of these lesions. Nevertheless, the reported accuracy in the differentiation of mucinous from non-mucinous lesions varies significantly between studies (48-94%), with reported sensitivities and specificities as low as 36% and 45%, respectively (2).

The introduction of artificial intelligence (AI) algorithms to endoscopic practice, including EUS, has provided promising results (3). Convolutional neural networks (CNNs) are highly efficient artificial intelligence tools for image analysis.

Aims & Methods: This study aimed to develop a *deep learning* algorithm for the automatic diagnosis and differentiation of mucinous and non-mucinous PCLs using EUS images.

We developed, trained, and validated a CNN based on EUS images. Each frame was labelled as corresponding to a mucinous (intraductal papillary mucinous neoplasm or mucinous cystic neoplasm) or non-mucinous (serous cystadenoma or pseudocyst) PCL. The diagnosis of mucinous PCL was dependent on cyst fluid analysis (CEA fluid levels >192ng/mL and glucose levels <50mg/dL) and/or histopathologic analysis of intracystic biopsies or surgical specimens. The entire image dataset was split for constitution of training (80%) and validation (20%) datasets. The latter was used to evaluate the performance of the CNN. The sensitivity, specificity, positive and negative predictive values (PPV and NPV, respectively), accuracy and area under the curve were calculated.

Results: A total of 5505 images from 28 EUS exams were included (3725 of mucinous PCLs and 1780 of non-mucinous PCLs). The model had an overall accuracy of 98.5%, a sensitivity of 98.3%, a specificity of 98.9%, a PPV of 99.5% and a NPV of 96.4%. The AUC was 1.00. The image processing speed of the CNN was 191 frames/second.

Conclusion: In this pilot study we developed a deep learning algorithm for automatic differentiation of mucinous from non-mucinous PCLs using EUS images. Subsequent development of these tools may contribute to enhance the diagnostic performance of EUS in the characterization of PCLs, which may constitute a decisive step forward in improving the management of this group of patients, with potential impact in the overall patient prognosis.

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P0852

PANCREATIC RESECTIONS FOR CYSTIC NEOPLASMS: FROM SURGEON'S PRESUMPTION TO PATHOLOGIST'S REALITY

A. Burelli¹, A. Nepi¹, C. Tomelleri¹, G. Perri¹, G. Marchegiani¹, R. Salvia¹

¹Verona University Hospital, Department of General and Pancreatic Surgery, Verona, Italy

Contact E-Mail Address: anna.burelli@libero.it

Introduction: Pancreatic cystic neoplasms (PCNs) incidence is increasing and postoperative morbidity and mortality after pancreatic resections are not negligible. In the early 2000s misdiagnosis rate ranged from 20 to 30% [1, 2].

Aims & Methods: The aim of the current study was to assess the misdiagnosis and malignant/non-malignant mismatch rate in the last ten years in a tertiary referral hospital for presumed PCNs who underwent resection. All patients who underwent pancreatic resection for presumed PCNs at the Verona Pancreas Institute between January 2011 and December 2020 were included.

The retrospective analysis was focused on cyst characteristics and preoperative diagnostic workup. Rate of misdiagnosis and of non-malignant/malignant mismatch, defined as the rate of incorrect preoperative characterization of a cyst as non-malignant or malignant, were assessed.

Results: A total of 601 patients were included. Three hundred one patients (50%) underwent EUS with or without fine needle aspiration/biopsy. Most of the EUS were performed at the Verona Pancreas Institute (n= 222; 74%), a tertiary referral hospital for pancreatic diseases, while 79 (26%) in primary or secondary hospital.

Overall misdiagnosis and non-malignant/malignant mismatch rate were 19% and 30%, respectively. There were no significant differences between patients who underwent EUS compared to those who did not (misdiagnosis: 18% vs 20% p= 0.663; non-malignant/malignant mismatch 29% vs 31% p= 0.613).

The lowest misdiagnosis rate was documented for solid pseudopapillary neoplasms (7%), followed by intraductal papillary mucinous neoplasms (16%), mucinous cystic neoplasms (23%), serous cystic neoplasms (28%) and cystic neuroendocrine tumors (62%). In 54 patients the preoperative diagnosis was serous cystic neoplasm, of those seven (13%) were malignant at final pathology (four malignant IPMNs; one malignant MCN; one SPT; one cystic NET with positive lymphnodes).

Conclusion: In the last ten years in a tertiary referral center misdiagnosis rate is still around 20% and comparable to the previous decade [1].

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P0853

PANCREATIC CYST FLUID INTERLEUKIN-1 BETA (IL-1B) LEVEL IN PREDICTING THE RISK OF MALIGNANCY IN PANCREATIC CYSTS

T. Abdallah¹, S. Shalaby¹, A. Salem¹, T. Yousef¹, S. Saleh¹, H. Okasha², M. Zaghloul³, M. A. El-Nady²

¹Faculty of Medicine, Ain Shams University, Internal Medicine Department, Gastroenterology and Hepatology Unit, Cairo, Egypt,

²Faculty of Medicine, Cairo University, Internal Medicine, Cairo, Egypt, ³Faculty of Medicine, Kafrelsheikh University, Hepatology, Gastroenterology and Infectious Diseases, Kafrelsheikh, Egypt

Contact E-Mail Address: mariam_zaghloul@med.kfs.edu.eg

Introduction: Accurate diagnosis of pancreatic cystic lesions PCLs remains challenging despite advanced imaging techniques. They include a broad spectrum of pathology ranging from benign cysts to potentially malignant or malignant cystic lesions. EUS-guided fine-needle aspiration (FNA) cytology, EUS-guided fine needle-based confocal laser endomicroscopy (nCLE), and needle microforceps biopsy are currently used to differentiate mucinous and non-mucinous pancreatic cyst.

The combined use of both EUS findings with cystic fluid biomarkers along with clinical, radiologic, histologic, genetic, and molecular characteristics, would enhance the diagnostic accuracy of PCLs. Immunological responses have been demonstrated in multiple malignancies, including pancreatic adenocarcinoma. Cytokine markers of the Th1 and Th2 immune response have been shown to discriminate pancreatic cancer from chronic pancreatitis or normal pancreatic tissue in both serum and pancreatic juice samples.

Similarly, pancreatic cyst fluid cytokines may reflect the immunogenic/proinflammatory process induced by malignant transformation in PCLs. IL1b was postulated to have the ability to differentiate low from high-risk IPMN.

Aims & Methods: The aim of the current study was to determine the predictive value of cystic fluid IL-1β in detection of malignant pancreatic cystic lesions and its correlation to the different degrees of dysplasia. Between January 2018 and November 2020, 50 patients underwent EUS-guided fine needle aspiration (EUS-FNA) for cyst fluid analysis and cytology. Pancreatic fluid levels of IL-1β were measured using commercially available ELISA kits (Cat DLB-50; R&D, Minneapolis, Minn and RPN222; GE Healthcare Life Sciences, Pittsburgh, Penn).

The threshold value of IL-1β (>50 pg/mL).

The final diagnosis was established according to the histopathological diagnosis of the resected specimens in those who underwent surgery and FNA aspirate from the rest. All patients were followed for at least 6 months.

Results: Cyst fluid IL-1 β can differentiate between mucinous and non-mucinous pancreatic cysts at cutoff value >150 pg/ml; with a sensitivity and specificity of 83.33% and 53.78% respectively.

Also, it can differentiate between benign and malignant cysts at cutoff value >200 pg/ml; with a sensitivity and specificity of 84.00% and 56.00% respectively. On the other hand, it was unable to differentiate between variable degrees of dysplasia of IPMN.

	B	p value	Odds ratio (OR)	95% C.I. for OR
Age > 55 ys	3.401	0.000	30	5.294 -170.015
Size of cyst ≤ 55mm	1.992	0.007	7.333	1.716-31.343
C.F IL1b > 200 pg/ml	3.520	0.001	33.800	3.895 - 293.305
Mucin stain	3.386	0.002	29.545	3.428 - 254.667

Table. Univariate logistic regression analysis for predictors of malignancy.

Conclusion: Pancreatic cyst fluid IL-1β can be a promising biochemical cyst fluid marker to differentiate between mucinous and non-mucinous cysts as well as benign and malignant cysts. Further larger studies are needed to validate its role.

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Disclosure: We have nothing to disclose.

P0854

GASTROINTESTINAL FINDINGS IN VON HIPPEL LINDAU DISEASE: CHARACTERISTIC OF PANCREATIC CYSTS

A.E. Bardak¹, C. Yazkaç¹, Z. İstemihan², Z. İmanov², İ.V. Şenkal², K. Nuriyev², T. Kalaycı³, Ş. Avcı³, Ç. Güleç³, Z.O. Uyguner³, K. Çefle³, Ş. Palanduz³, Ş. Öztürk³, B. Çavuş², A. Çifçibaşı Örmeci², F. Akyüz², K. Demir², F. Beşişik², S. Kaymakoglu²

¹Istanbul University Istanbul Medical Faculty, Istanbul, Turkey, ²Istanbul University Istanbul Medical Faculty, Gastroenterohepatology, Istanbul, Turkey, ³Istanbul University Istanbul Medical Faculty, Genetics, Istanbul, Turkey

Contact E-Mail Address: bardakaliemre@gmail.com

Introduction: von Hippel Lindau (VHL) disease is a rare, familial autosomal dominant disease. It can progress with involvement of many organs such as cerebellum, spinal cord, kidney, epididymis, pancreas, surrenal glands. In pancreatic involvement, simple cysts, serous cystadenomas and PNETs which can have malignancy potential can be seen.

Aims & Methods: In this study, we tried to reveal the involvement patterns and pancreatic involvement characteristics of the patients that we followed up for VHL in our own series.

Results: The mean age of 7 female and 4 male VHL patients was 30 years. Disease age was determined as the youngest 3 years and the highest 22 years. Considering the organ involvement patterns of VHL patients, 7 patients had brain and spinal cord involvement and 10 patients had kidney involvement. Of the patients with kidney involvement, 2 had a history of RCC and one had a history of surgery due to angiomyolipoma. Two patients had epididymal involvement. Retinal involvement was present in 5 patients, adrenal gland involvement was detected as pheochromocytoma in 2 patients and they were operated.

When the patients were evaluated in terms of pancreatic involvement, 8 of 11 patients had pancreatic involvement. All 8 patients with pancreatic involvement had multiple cysts. Cyst sizes were measured as the smallest 15 mm and the largest 80 mm. Cyst aspiration was performed from 4 of 8 patients with pancreatic cysts, and findings consistent with serous cyst adenoma were found in all patients who underwent cyst aspiration.

Conclusion: In our patient series, we found that the pancreas was the most common site of involvement in VHL patients, in accordance with the literature. Our patients were mostly found to have multiple cysts, and those who had cyst sampling were mostly diagnosed as serous cystadenoma.

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Disclosure: Nothing to disclose.

P0855

EVALUATING THE USE OF IRREVERSIBLE ELECTROPORATION FOR PANCREATIC CANCER TREATMENT: PILOT IN VITRO STUDIES

I.A. Khawaja¹, Z.L. Rai¹, B.R. Davidson¹, P. Acedo²

¹University College London, Division of Surgery & Interventional Science, Royal Free Hospital, London, United Kingdom, ²University College London, Institute for Liver & Digestive Health, London, United Kingdom

Contact E-Mail Address: ibbikhawaja@hotmail.com

Introduction: Pancreatic cancer (PC) treatment continues to have exceedingly poor clinical outcomes, and therefore the need for novel and innovative methods to combat this disease remains a matter of urgency. Increasingly, loco-regional therapies used in conjunction with systemic chemotherapy, are being favoured in the clinical setting. Irreversible electroporation (IRE) is a non-thermal ablative therapy that has shown promise in this regard. IRE uses high voltage electrical current to destabilise cell membranes, subsequently causing cell death [1].

However, there is a lack of knowledge regarding effective treatment parameters or the signaling pathways induced by combining IRE with chemotherapy. Optimum field strength, pulse length and duration, as well as pathways of cell death induced after IRE, remain to be elucidated both in vitro, and in the clinic [2].

Aims & Methods: Even though IRE is already used in clinical practice, our research aims to establish optimum electroporation parameters and molecular mechanisms induced by IRE in pancreatic cancer models (2D and 3D) to aid with future device improvement. We also aim to identify possible chemotherapeutic agents that can be used in conjunction with IRE to potentiate its effects. Diverse PC cell lines (e.g. PANC-1, CFPAC-1) were electroporated using the Harvard Apparatus BTX electroporator generator. Key parameters such as voltage strength, pulse number, length and duration were evaluated.

Following treatment, cells were maintained in culture for up to 96-hours, to determine the effect of IRE on metabolic activity and viability using MTT, ToxiLight assays and LIVE/DEAD staining. Data was validated by flow cytometry and fluorescence microscopy. Upregulation of proteins involved in mitochondrial mediated cell death, such as caspases, were analysed using western blotting.

Results: Increasing voltage strength resulted in a reduction in cell proliferation and increased cell death, with a half maximal inhibitory voltage strength of 620V/cm 24-hours post-ablation. Similarly, increasing the pulse number also resulted in a reduction in cell proliferation and increased cell death, with 30 pulses being optimal. Increasing the pulse number to 50, resulted in almost total cell death, even at voltage strengths as low as 12V/cm.

Conclusion: Our research found that the two most important electroporation parameters in pancreatic cancer cell IRE treatment are voltage strength and pulse number. We have optimised these parameters for future research on ascertaining pathways of cell death post electroporation. Aggressive cancer cells such as PANC-1 and CFPAC-1 may have additional intra-cellular adaptations compared to normal pancreas cells making them resistant to electrical insults. Future work will investigate whether these adaptations can be overcome by combining IRE with diverse cytotoxic agents.

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P0856

COMPARISON OF PBMC FUNCTIONS AND *AHR*, *ELAVL-1* EXPRESSION IN PANCREATIC CANCER VS HEALTHY PATIENTS

A. Bartkeviciene¹, A. Jasukaitiene², J. Matthews³, A. Gulbinas⁴, Z. Dambrauskas⁴

¹Lithuanian University of Health Sciences, Institute for Digestive Research, Laboratory of Surgical Gastroenterology, Kaunas, Lithuania, ²Lithuanian University of Health Sciences, Institute for Digestive Research, Kaunas, Lithuania, ³University of Oslo, Molecular Toxicology Group, Oslo, Norway, ⁴Lithuanian University of Health Sciences, Department of Surgery, Kaunas, Lithuania

Contact E-Mail Address: antanas.gulbinas@ismuni.lt

Introduction: Pancreatic ductal adenocarcinoma (PDAC) is one of the biggest challenges in today's oncology. PDAC consists of more than 90% of all pancreatic cancer (PC) cases. The World Health Organization based on 2020 statistics, presented that PC was still one of the deadliest cancers, with a 5-year survival rate of only 8%.

After undergoing resection for stage I, an overall 5-year survival had increased to almost 40%. Despite improved survival rates after resection combined with chemotherapy or immunotherapy, success for the treatment was limited [1].

The aryl hydrocarbon receptor (*AHR*) is a ligand-dependent transcription factor that acts in an important role in cell environmental, metabolic and immune regulation. This post-transcriptional regulator could allow tumor cells to avoid immunosurveillance after programmed death 1 ligand 1 (*PD-1* / *PD-L1*) inhibitors immunotherapy. *AHR* also modulates the RNA-binding protein *ELAVL-1* signaling pathway that leads to an increased translation of target mRNAs and subsequent overexpression of cytoprotective and anti-apoptotic proteins also induce chemoresistance in PDAC cells.

We think that *AHR* and *ELAVL-1* genes expression differences in blood between some patients regulating unsuccessful response to *PD-1* / *PD-L1* immunotherapy against cancer. Normalization of combined target immunotherapeutic genes should return immune cell function and improve immunotherapeutic efficacy.

Aims & Methods: Our main task was to compare PBMCs function differences of PDAC patients and healthy donors with expression and protein syntheses in *AHR*, *PD-1*, *PD-L1* and other target genes. Main material of this research was blood from PDAC patients and healthy donors. PBMC were isolated by Ficoll-Paque gradient centrifugation.

Monocytes subtypes were defined by multiparametric flow cytometry. Expression of target genes and cytokines were evaluated by qRT-PCR. Free circulating cytokines were measured with Luminex multiplex assay. Fluorometric assays were used to measure phagocytic activity after 4-hour PBMC activation with LPS, ROS production was measured at same period effecting with TBHP, and NO production was measured after 16-hour activation with LPS. Simultaneously PBMCs metabolic activity was measured by resazurin metabolism method.

Results: The results showed that after PBMC activation ROS, NO production and phagocytic activity increased less (not significant) in pancreatic cancer patients than healthy control. Although metabolic activity increased similarly in both groups. The M1 / M2 cell ratio became lower in cancer patients. Expression of *IL-1 β* concentration was higher in PBMC from control group but circulating IL-1 β concentration was higher in cancer patients' sera.

Other concentrations of measured cytokines were higher in PDAC patients and the relationship between these genes and proteins remained similar. In comparing with healthy control, the expression of PBMC target genes *AHR*, *ELAVL-1* and *HO-1* decreased but *PD-1* expression significantly increased in cancer group.

Conclusion: This PBMC research showed functional imbalance and immunosuppression in PDAC patient group compared with healthy control. In cancer patients PBMC target genes *AHR*, *ELAVL-1*, *HO-1* and measured phagocytosis, NO and ROS production, reduced relatively but *PD-1* and cytokines concentrations increased significantly. Need more studies with higher amount of PDAC patients and analyze their functional PBMC response in contrast *AHR*, *ELAVL-1* expression differences.

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Disclosure: Nothing to disclose.

P0857

CHEMICAL ENHANCEMENT OF IRREVERSIBLE ELECTROPORATION IN PANCREATIC CANCER CELL LINES WITH CALCIUM: A PILOT STUDY

Z.L. Rai^{1,2}, I.A. Khawaja¹, B.R. Davidson^{1,2}, P.M. Acedo³

¹University College London, Division of Surgery and Interventional Sciences, London, United Kingdom, ²Royal Free Hospital NHS Trust, London, United Kingdom, ³University College London, Division of Medicine, London, United Kingdom

Contact E-Mail Address: zainab.raai.19@ucl.ac.uk

Introduction: Irreversible electroporation (IRE) is a novel loco-regional ablative therapy that is currently being investigated for the treatment of solid tumours. Whilst it has enjoyed success in the treatment of cancers such as prostate, IRE's treatment potential in more aggressive tumours like pancreatic cancer (PC) remains controversial (1).

It is thought IRE exerts its cytotoxic effect by increasing the transmembrane potential of the lipid bilayer. This results in pore formation, disrupting cellular homeostasis and causing cell death (2).

However, much remains unknown about the type of cell death that is initiated following IRE in PC and whether IRE's cytotoxic effect can be enhanced with concomitant synergistic therapies.

Calcium homeostasis has been implicated in cancer pathophysiology and studies have demonstrated the cytotoxic effect of supraphysiological doses of calcium in *in vitro* cell lines through acute ATP depletion and mitochondria mediated apoptosis (3).

Moreover, Ca²⁺ ions have been shown to impact resealing of damaged membranes (3) in addition to being a common second messenger in several intra-cellular pathways (4).

Aims & Methods: To understand the optimum electroporation voltage strengths when combined with supraphysiological calcium treatment.

2 immortalised pancreatic cancer cell lines; PANC-1 and CFPAC were used in addition to H6c7 an epithelial cell line, used as a healthy control. Cells were trypsinised to facilitate electroporation in 4mm cuvettes using BTX Electroporator generator from Harvard Apparatus. Pulse number, dura-

tion and inter-pulse length was standardised across all experiments to 30 pulses, 100ms long and 1s between pulses. Voltage strength varied between 250V/cm and 500V/cm and calcium concentrations between 25mM and 50mM. Following electroporation cells were plated in a 96-well plate and allowed to attach for 24-hours prior to exposure to Ca²⁺ for 24-hours. Cell viability assays were performed 24 and 48-hours following Ca²⁺ exposure.

Results: Combination therapy proved to be more cytotoxic compared to monotherapy with cell proliferation assays demonstrating a statistically significant reduction in proliferation ($p < 0.0001$) in combination therapy groups. Analysis between treatment groups revealed the greatest cytotoxic effect in cells treated with 250V/cm and 50mM Ca²⁺ treatment.

Conclusion: Our results indicate that combination therapy is more toxic compared to single therapy. Interestingly, cell death as measured by a bioluminescence assay, was highest in the cells treated with 250V/cm and 50mM of Ca²⁺ and significantly greater than that observed at 500V/cm. One explanation for this is that the higher voltage strength resulted in a reduction in cell attachment resulting in a reduction in the final number of Ca²⁺ treated cells.

IRE is thought to induce cell death through apoptosis; a pathway that relies significantly on Ca²⁺ signalling through changes in mitochondrial membrane potential (MMP). Future work will involve delineating the effect of single and dual therapy on MMP and mitochondria mediated apoptosis using Flow cytometry and Western Blotting.

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P0858

ROLE OF ENDOSCOPIC ULTRASOUND COMBINED WITH A NEWLY MODIFIED SCORING SYSTEM TO DETECT PANCREATIC HIGH-GRADE PRECANCEROUS LESIONS

R. Sagami^{1,2}, T. Sato¹, H. Nishikiori¹, K. Murakami²

¹Oita San-ai Medical Center, Department of Gastroenterology, Oita, Japan, ²Oita University, Department of Gastroenterology, Faculty of Medicine, Yufu, Japan

Contact E-Mail Address: sagami1985@yahoo.co.jp

Introduction: Although pancreatic cancer (PC) has an extremely poor prognosis, the five-year survival rate of patients with pancreatic high-grade precancerous lesion without invasive carcinoma (PHP; high-grade pancreatic intraepithelial neoplasia [PanIN]) and high-grade intraductal papillary mucinous neoplasm [IPMN]) is favorable. PHP diagnosis and identification of patients requiring intervention are needed. We aimed to validate a modified PC detection scoring system regarding its detection ability for PHP and PC in the general population.

Aims & Methods: We modified an existing PC detection scoring system that incorporates low-grade risk (LGR) factors (family history, presence of type 2 diabetes mellitus [DM] or worsening DM, heavy drinking, smoking,

stomach symptoms, weight loss, and pancreatic enzyme) and high-grade risk (HGR) factors (new-onset DM, familial PC, jaundice, tumor biomarkers, chronic pancreatitis, IPMN, cysts, hereditary PC syndrome, and hereditary pancreatitis). Each factor was scored as one point; LGR score ≥ 3 points and/or HGR score ≥ 1 point (positive scores) were indicative of PC.

The newly modified scoring system incorporated main pancreatic duct dilation as an HGR factor. Patients who visited the Department of Gastroenterology at our hospital between March 2018 and July 2019 with any clinical symptoms or risk factors, and were screened by their initial EUS examination were prospectively enrolled. Patients with any pancreatic diseases undergoing repeated imaging examination in the surveillance program or who were strongly suggested to have pancreatic tumors using other imaging modalities were excluded.

The primary endpoint was the diagnosis rate of PHP without an invasive carcinoma among patients with positive scores. Additionally, the effectiveness of the LGR/HGR factors and scoring system was analyzed in patients with PHP and PC, compared with those without PHP and PC.

Results: Among 544 patients with positive scores, 10 had PHP (7 high-grade PanIN and 3 high-grade IPMN). The diagnosis rates were 1.8% for PHP and 4.2% for invasive PC.

Furthermore, 311 patients with negative scores according to our system were screened during the same period, and two (0.6%) patients had unresectable PC. No adverse events due to the EUS surveillance occurred. In the diagnosis of patients with PHP, resectable PC, and all lesions (PHP and PC), although the number of LGR and HGR factors tended to increase with PC progression, none of the individual factors were significantly different between patients with PHP and those without lesions. Sensitivity for PHP patient detection via LGR score positive, HGR score positive, and both scores positive were 60%, 80%, and 100%, respectively.

Score positive patients (N=544)	Score negative patients (N=311)
High-grade precancerous lesion 1.8% (N=10)	Pancreatic cancer 0.6% (N=2)
High-grade PanIN (N=7)	Unresectable PC 0.6% (N=2)
High-grade IPMN (N=3)	
Pancreatic cancer 4.2% (N=23)	
Resectable pancreatic cancer 1.8% (N=10)	
Unresectable pancreatic cancer 2.4% (N=13)	

Conclusion: The newly modified scoring system evaluating multiple factors associated with PC could potentially identify patients with higher risk of PHP or PC.

Disclosure: Nothing to disclose.

P0859

COMBINED EUS AND ERCP REDUCES TIME TO ONSET OF TREATMENT IN PANCREATOBILIARY MALIGNANCY

J. Gauci¹, W. On¹, B. Paranandi¹, M. Huggett¹, S.M. Everett¹

¹Leeds Teaching Hospital NHS Trust, Department of Gastroenterology, Leeds, United Kingdom

Contact E-Mail Address: jamesgauci111@gmail.com

Introduction: Standard ERCP sampling techniques for pancreaticobiliary (PB) malignancy have modest yields that could lead to delay in treatment. We aimed to evaluate whether combining EUS guided tissue acquisition (EUS-TA) with ERCP versus ERCP alone at time of index procedure improved time to treatment in patients with suspected PB malignancy.

Aims & Methods: All patients without a prior pathological diagnosis who underwent index ERCP at Leeds Teaching Hospitals NHS Trust for distal biliary obstruction from January 2015 to December 2020 were included.

Time to first clinical evaluation (for outpatients) and time to initial treatment were compared between ERCP alone and ERCP combined with EUS-TA.

Results: A total of 292 patients were included; 74.7% (n=202) underwent EUS-TA/ERCP and the remainder (n=90) underwent ERCP alone. EUS-TA/ERCP yielded a positive diagnosis more frequently than ERCP alone (96.5% (n=195) vs 57.8% (n=52), $p < 0.01$).

Further procedures for tissue acquisition were required in 2.0% (n=4) of the EUS-TA/ERCP group and 17.8% (n=16) of the ERCP group. Mean time to first outpatient oncological/surgical evaluation (16.9 days vs 24.5 days ($p = 0.01$)) and times to commencement of oncological (55.1 vs 79.3 days ($p = 0.03$)) and surgical treatment (50.7 vs 72.0 days ($p = 0.13$)) were shorter in the EUS-TA/ERCP than the ERCP alone groups.

However, 33.2% (n=86/292) of patients who had a positive tissue diagnosis did not undergo further oncological/surgical treatment, of whom 70.9% (n=61/86) were from the EUS-TA/ERCP group.

Conclusion: In our cohort of patients with malignant distal biliary obstruction, a combined approach of EUS-TA/ERCP at index procedure improved diagnostic yield, reduced the need for repeat sampling procedures and was associated with reduced time to treatment. Careful case selection is required to avoid offering unnecessary EUS procedures to patients who will not benefit from further treatment.

Disclosure: Nothing to disclose.

P0860

EPIDEMIOLOGY, CLINICAL CHARACTERISTICS, PROGNOSIS, AND NOMOGRAM FOR PRIMARY PANCREATIC LYMPHOMA PATIENTS: A SEER POPULATION-BASED STUDY

Y. Liu¹, Y. Xie¹

¹First Affiliated Hospital of Nanchang University, Gastroenterology, Nanchang, China

Contact E-Mail Address: doctor_liu0218@163.com

Introduction: Primary pancreatic lymphoma (PPL) is extremely rare, usually insidious in onset, and account for 0.5% or less of pancreatic tumors [1; 2].

There are different definitions available for PPL throughout the past decade [3; 4].

More recently, diagnostic criteria developed by the World Health Organization (WHO) are summarized as follow:

1. The pancreas is the primary lesion of PPL;
2. When the presence of lymph node and distant metastases, the main clinical presentation should involve the pancreas [5]. Diffuse large B-cell lymphoma (DLBCL) is one of the most common types of PPL [6; 7]. Other subtypes of lymphomas, comprising of follicular lymphoma (FL), non-Hodgkin lymphoma (NHL), Burkitt lymphoma (BL), Hodgkin lymphoma (HL), T cell lymphoma (TCL), and Not Otherwise Specified (NOS), etc.

Aims & Methods: Primary pancreatic lymphoma (PPL) is a rare type of digestive lymphoma of which the epidemiology, clinical features, and prognosis of survival are limitedly reported.

Therefore, this study aimed to evaluate the epidemiological characteristics of PPL and establish efficient nomograms to predict patient survival. Patients diagnosed with PPL were extracted from the Surveillance Epidemiology and End Results (SEER) program from 1983 to 2015.

The incidence rates of PPL were calculated from 1975 to 2018. The Joinpoint regression analysis to assess the temporal trends. Independent predictive factors for overall survival (OS) and disease-specific survival (DSS) were identified using univariate and multivariate Cox regression analyses. We constructed nomograms to predict the survival possibility of PPL patients by integrating independent clinicopathological factors.

Results: A total of 867 patients with PPL were diagnosed from 1983 to 2015. The average age was 65.7 y with a male-to-female of 1.5:1. The overall incidence of PPL was 0.44/1,000,000 from 1975 to 2018, with a significantly increasing trend reflecting an annual percentage change (APC) of 2.33 (95% CI 0.88-3.80, $P<0.05$). Multivariate Cox regression analysis indicated that age, sex, marital status, pathological classification, Ann Arbor stage, surgery, and chemotherapy were independent prognostic predictive factors for OS and DSS ($P<0.05$). Nomograms were constructed to predict the 1-, 5-, and 10-year OS and DSS. The predictive performance and compliance of the model were evaluated using the consistency index and the calibration curve.

Conclusion: PPL rarely occurs, but the incidence has been steadily increasing over the past four decades. Nomograms constructed can predict 1-, 5-, and 10-year OS and DSS. Nomograms can also distinguish high-risk PPL patients.

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Disclosure: Nothing to disclose

P0861

FOCAL PANCREATIC PARENCHYMA ATROPHY IS COMMON AND MAY HELP DETECT THE INTRADUCTAL SPREADING SUBTYPE OF PANCREATIC CARCINOMA

J. Nakahodo¹, Y. Fukumura², S.-i. Horiguchi³, K. Chiba¹, H. Tabata¹, M. Suzuki⁴, M. Kikuyama⁵, T. Iiduka¹, T. Kamisawa¹

¹Tokyo Metropolitan Cancer and Infectious Diseases Center, Komagome Hospital, Department of Gastroenterology, Tokyo, Japan, ²Juntendo University, Department of Human Pathology, Tokyo, Japan, ³Tokyo Metropolitan Cancer and Infectious Diseases Center, Komagome Hospital, Department of Pathology, Tokyo, Japan, ⁴Tokyo Metropolitan Cancer and Infectious Diseases Center, Komagome Hospital, Department of Radiology, Tokyo, Japan, ⁵Tokyo Women's Medical University, Department of Gastroenterology, Tokyo, Japan

Contact E-Mail Address: nakajun58@yahoo.co.jp

Introduction: Early detection of small pancreatic ductal adenocarcinoma (PDAC) requires pancreatic cancer screening method establishment for asymptomatic subjects. Current imaging technologies are limited in detecting small size PDACs. It is thus essential to identify the secondary changes of PDAC for early diagnosis. We have reported that a precancer-

ous lesion, high-grade pancreatic intraepithelial neoplasm, is accompanied by atrophy of the pancreatic acinar cell, which is detected as an indentation of the pancreas on imaging as focal pancreatic parenchymal atrophy (FPPA).

Aims & Methods: Radiological evidence of FPPA may consist in changes secondary to early PDAC. We aimed herein to verify the FPPA incidence via retrospective imaging analysis and clarify the clinicopathological features of PDAC with FPPA before diagnosis. Data on endoscopic ultrasonography-guided fine-needle biopsies and surgical samples in 170 patients who received imaging before their histological diagnosis of pancreatic cancer (n=1,011) between 2014 to 2019 were extracted from the pathological database of Komagome Hospital and Juntendo University Hospital. The FPPA incidence and clinicopathological features were then retrospectively evaluated.

Results: FPPA was identified in 52 of the 170 patients (31%) before PDAC diagnosis. The median duration from FPPA detection to diagnosis was 33.5 (range: 3-116) months. The atrophic region was later filled in 28 (54%) of the patients. The patients with (n=52) and without (n=118) FPPA had a tumor location in the head vs body-tail in 17/83 vs. 55/45 of cases [$P<0.001$]; a histopathological main pancreatic ductal lesion in a resected specimen in 47% vs. 23% of cases [$P=0.097$]; and positivity for malignancy at the surgical margin rate in 24% vs. 3% of cases [$P=0.031$], respectively. PDAC with FPPA, which was accompanied by malignancy at the pancreatic resection margin, stemmed from a high-grade, pancreatic, intraepithelial neoplasia.

Conclusion: FPPA occurred in 31% of the patients with PDAC and was detectable 33.5 months before diagnosis. The indentation in the FPPA area resolved before PDAC onset. Benchmarking pre-diagnosis images of the pancreas focusing on FPPA may enable prediction of PDAC occurrence. PDAC with FPPA presents widespread high-grade pancreatic intraepithelial neoplasia; thus, a wide surgical margin should be made.

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Disclosure: Nothing to disclose.

P0862

EFFECT INVESTIGATION OF LAG TIME BETWEEN THE START OF DIAGNOSTIC PROCEDURE AND TREATMENT OF PANCREATIC CANCER PATIENTS: A SYSTEMATIC REVIEW AND META-ANALYSIS

A.N. Nemeth^{1,2}, S. Bunduc^{2,1,3,4}, A.S. Bognár^{2,1}, D.S. Veress^{1,5}, B. Erőss^{1,2,6}, D. Tarján^{1,2}, D. Sőtő¹, M. Imrei^{1,7}, K. Márta^{2,1}, P. Hegyi^{2,1,6,8}

¹Semmelweis University, Center for Translational Medicine, Budapest, Hungary, ²Semmelweis University, Division of Pancreatic Diseases, Budapest, Hungary, ³Carol Davila University of Medicine and Pharmacy, Bucharest, Romania, ⁴Fundeni Clinical Institute, Bucharest, Romania, ⁵Semmelweis University, Department of Biophysics and Radiation Biology, Budapest, Hungary, ⁶University of Pécs, Institute for Translational Medicine, Medical School, Pécs, Hungary, ⁷Heim Pál National Pediatric Institute, Budapest, Hungary, ⁸University of Pécs, János Szentágothai Research Center, Pécs, Hungary

Contact E-Mail Address: nemethannus93@gmail.com

Introduction: Pancreatic cancer (PC) is highly aggressive with a 5-year mortality that almost matches the incidence. In current practice the length of diagnostic procedure can take up to 50 days. As PC is a rapidly progressing disease, this delay might strongly affect prognosis.

Aims & Methods: We investigated if the time interval from the start of diagnostic procedure to therapy initiation (DgT) or from symptoms onset to diagnosis (SDg) (early versus (vs.) late), influences the prognosis of PC patients by performing a systematic review and meta-analysis.

Our protocol was previously submitted on PROSPERO (CRD: 282619) We systematically screened Pubmed, Embase and Central from 1st of January 2005 to 16th of October, 2021. without other filters.

Eligible studies compared prognosis, reported as overall (OS) or progression-free survival (PFS) of PC patients with shorter vs longer DgT and SDg intervals at various thresholds. The random effect model yielded the pooled hazard ratios (HRs) and 95% confidence intervals (CI).

Results: Altogether 23 articles (80542 patients) out of the 21632 were eligible. DgT interval length and disease stage varied across the studies. We analyzed the association between time from DgT and OS at different thresholds including all disease stages (2 weeks: HR=0.99; 95%CI: 0.98-1.01, I²=4%, 4 weeks: HR=1.02; 95%CI: 0.97-1.07, I²=68%, 6 weeks: HR=1.00; 95%CI: 0.97-1.03; I²=54%, 8 weeks: HR=1.05; 95%CI: 0.94-1.17, I²=84%) and found no significant differences.

The results for the resectable cases were similar. There was no significant association between SDg delay at 4 week threshold and OS for various stages of PC (HR=1.00; 95%CI: 0.99-1.03), suggesting that the start of therapy is too late in these time windows.

Conclusion: The outcome of pancreatic cancer can no longer be influenced by shortening the time in therapies started later than two weeks after diagnosis. Further studies are needed to determine what the time window is in the first 14 days in which the outcome of the disease can be improved by accelerating the start of therapy.

Disclosure: Nothing to disclose.

P0863

THE DIAGNOSTIC AND PROGNOSTIC VALUE OF APELIN (APLN) AND SERUM AMYLOID A3 (SAA3) ADIPOCYTOKINE MEASUREMENT IN PATIENTS WITH PANCREATIC DUCTAL ADENOCARCINOMA (PDAC) COMPARED TO CHRONIC PANCREATITIS (CP) AND HEALTHY SUBJECTS

M. Stasiak¹, B. Włodarczyk¹, E. Malecka-Wojcieszko¹

¹Medical University of Łódź, Department of Digestive Tract Diseases, Łódź, Poland

Contact E-Mail Address: michal_jakub_stasiak@o2.pl

Introduction: Despite extensive efforts, there are still no widely accepted, sensitive and specific early detection biomarkers for pancreatic cancer. APLN and SAA3 participate in carcinogenesis of multiple solid tumours, particularly connected to metabolic alterations. Their role in PDAC is not elucidated yet.

Aims & Methods: The aim of the study was to search for the possible diagnostic and prognostic value of serum APLN and SAA3 adipocytokines measurement in patients with PDAC compared to CP.

Serum samples (5-10 ml), fasting, were collected from 65 patients, including 34 subjects with PDAC, 11 with CP and 20 from the healthy subjects (Ctrl). APLN and SAA3 levels were measured by enzyme-linked immunosorbent assay (ELISA) (Corgenix UK Ltd R&D Systems).

The results were analysed by the non-parametric Kruskal-Wallis and Mann-Whitney U test; a peak was deemed to show a statistically significant difference in group means if its p-value was < 0.01. The study protocol was approved by the Bioethics Committee at the Medical University of Łódź.

Results: The serum mean APLN concentration level was significantly higher in CP compared to PDAC patients (1391.81 +/- 454.06 pg/ml vs 782.29 +/- 542.17 pg/ml, p<0.01). On the other hand, the patients with PDAC had significantly higher mean SAA3 level than those with CP (61.51

+/- 44.44 pg/ml vs 14.00 +/- 5.79 pg/ml, p<0.01). The APLN in Ctrl was significantly lower than in both PDAC (347.58 +/- 119.14 pg/ml vs 782.29 +/- 542.17 pg/ml, p<0.01) and CP (347.58 +/- 119.14 pg/ml vs 1391.81 +/- 454.06 pg/ml).

Serum mean SAA3 concentration in Ctrl was also significantly lower than in PDAC patients (37.01 +/- 19.37 pg/ml vs 61.51 +/- 44.44 pg/ml, p<0.01) but significantly higher than in CP patients (37.01 +/- 19.37 pg/ml vs 14.00 +/- 5.79 pg/ml, p<0.01). In PDAC group without metastases (M0), mean serum level of APLN was significantly higher compared to patients with metastases (M1) (879.34 +/- 526.37 pg/ml vs 554.29 +/- 391.16 pg/ml, p<0.01).

On the other hand, mean serum SAA3 level was significantly higher in M1 group than in patients M0 (84.83 +/- 41.83 pg/ml vs 46.95 +/- 39.67 pg/ml, p<0.01). Mean APLN and SAA3 levels were not different (p>0.05) in both, PDAC and CP groups depending on accompanying obesity or diabetes.

Conclusion: APLN and SAA3 may represent the possible biomarkers for CP and PDAC. APLN, but not SAA3 expression seems to be stronger in pancreatic inflammation than in malignancy. APLN and SAA3 concentration measurement may have the prognostic value in patients with PDAC. Additionally, those proteins may be potentially useful in PDAC and CP differentiation. Further studies are necessary to find out if this biomarkers could be useful in early PDAC detection.

Disclosure: Nothing to disclose.

P0864

THE ASSOCIATION BETWEEN PROTON PUMP INHIBITORS AND PANCREATIC CANCER

W. Sbeiti¹, A. Shahin¹, T. Khoury²

¹Galilee Medical Center, Gastroenterology, Naharia, Israel,

²Galilee Medical Center, Department of Gastroenterology, Naharia, Israel

Contact E-Mail Address: tawfik.khoury.83@gmail.com

Introduction: Pancreatic cancer is among the deadliest cancer types worldwide. Their incidence is increasing. There are several risk factors for the development of pancreatic cancer, however, data regarding medications that might be associated with pancreatic cancer are lacking. Proton pump inhibitors (PPIs) are among the commonest drugs used in gastroenterology, as their use was shown to be associated with certain diseases.

Recent data have shown that the profound acid suppression caused by PPI use, leads to hypergastrinemia and disrupts the normal gut microbiome, leading to dysbiosis and bacterial overgrowth that may increase the risk of pancreato-biliary malignancies.

Aims & Methods: We aimed To retrospectively explore whether PPI use is associated with increasing prevalence of pancreato-biliary malignancies. We performed a retrospective study including all patients who were referred for EUS from 2010 till 2021. Patients were divided into two groups, the first one will include all patients with radiological and histological diagnosis of pancreatic cancer, while the other group included all other patients and were served as a control group. PPI consumption in the two groups was assessed by logistic regression model.

Results: Overall, a total of 806 patients were included in the study. Among them, 69 patients were finally diagnosed with pancreatic cancer (group A), as compared to 737 without pancreatic cancer (group B). The average age was 68.6 ± 13.2 vs. 60.6 ± 18.2, in groups A and B, respectively (P=0.0001). In group A, 33 patients (47.8%) vs. 314 patients (42.6) in group B, were males (P=0.2). the rate of smoking and diabetes were significantly higher in group A, as compared to group B (34.8% and 49.3% vs. 19.7% and 32.3%, P=0.001 and P=0.002), respectively.

On the other hand, there was no difference in the rate of hyperlipidemia and hypertension (53.6% and 53.6% vs. 45.7% and 50.7%, $P=0.1$ and $P=0.32$), respectively. The rate of personal history of cancer was higher in group A (24.6% vs. 8.2%, $P<0.0001$). Notably, the rate of PPI use was significantly higher in group A (55.1%) vs. 37.9% in group B ($P=0.002$). After regression analysis, PPI use was significantly associated with pancreatic cancer (OR 2.01, 95% CI 1.22-3.31, $P=0.005$).

Conclusion: An association of PPI use with pancreatic cancer was found. Further large nationwide studies are needed to confirm our findings

Disclosure: Nothing to disclose.

P0865

A NOVEL, MULTIPRONGED, SINGLE-PASS EUS NEEDLE FOR IMPROVED TISSUE DIAGNOSIS OF SOLID PANCREATIC LESIONS

J. Lachter¹, R. Epelbaum², J. BenArie², J. Lazarovitch², D. Diehl³, V. Kaul⁴

¹United Meuhedet HMO, Gastro, Haifa, Israel, ²Independent, Haifa, Israel, ³Geisinger, Danville, United States, ⁴Univ Rochester Med Institute, Rochester, United States

Contact E-Mail Address: Jesse.lachter@gmail.com

Introduction: Diagnosis and treatment of pancreatic ductal adenocarcinoma (PDAC) can be challenging. Dense desmoplastic stromal reaction associated with the tumor is common, and tumor cells often comprise only 20% of lesion volume. This may negatively impact diagnostic yield at endoscopic ultrasound (EUS) with fine-needle aspiration or biopsy (FNA/B).

Current commercially available EUS needles utilize a single needle for tissue sampling, typically requiring multiple passes to obtain an adequate diagnostic specimen.

Aims & Methods: Diagnosis and treatment of pancreatic ductal adenocarcinoma (PDAC) can be challenging. Dense desmoplastic stromal reaction associated with the tumor is common, and tumor cells often comprise only 20% of lesion volume. This may negatively impact diagnostic yield at endoscopic ultrasound (EUS) with fine-needle aspiration or biopsy (FNA/B). Current commercially available EUS needles utilize a single needle for tissue sampling, typically requiring multiple passes to obtain an adequate diagnostic specimen.

Methods: In 6 live pigs, EUS-FNA procedures were done by 4 endoscopists with extensive clinical experience in EUS-FNA. There were three endoscopy sessions. A sampling of different intraabdominal structures with the multipronged needle device was done, with up to 4 passes made in several organs in each pig.

Ability to sample multiple foci simultaneously was assessed, as well as the ease of use of the multipronged needle device. In addition, post-mortem analysis of the animals was done to assess potential intra-abdominal tissue injury related to the needle.

Results: The 4 endoscopists did 15 needle passes in the 6 pigs. No problems were found with the passage of the multipronged needle device down the endoscope channel, and an FNA specimen could be obtained in all attempts. Physicians felt that the device was easy to use. Post-mortem analysis of the pigs did not demonstrate unanticipated tissue injury or perforation. Using fluoroscopy, Barium was injected at the end of the procedure and it ruled out leaks indicative of perforation.

One pig was left alive for 72 hours for observation and follow-up. No complications or adverse events were recorded.

Pathological analyses showed high-quality tissue samples in all cases.

Conclusion: The multipronged needle device represents a technological innovation enabling simultaneous needle penetration into 5 foci within a target lesion under EUS guidance.

The multisite penetrations have the potential to improve diagnostic yield with fewer needle passes. Based on this live animal study, the device appears safe and performs as intended, heralding a new era in EUS guided tissue sampling.

Disclosure: Jesse Lachter is a paid consultant to Onepass Medical and to Verily LLC.

P0866

THE IMPACT OF A MULTIDISCIPLINARY TEAM APPROACH ON THE MANAGEMENT OF FOCAL PANCREATIC LESIONS: A TERTIARY SINGLE-CENTER EXPERIENCE

S. Francisse¹, P. Gkolfakis¹, M. Fernandez Y. Viesca¹, L. Mans¹, M. Pezzullo², P. Loi³, J. Navez³, J. Closset³, M. Van Wettere², M.A. Bali⁴, N. D'Haene⁵, P. Demetter⁶, L. Verset⁶, C. Bouchart⁷, A. Lemmers¹, J. Deviere¹, A. Demols¹, M. Delhaye¹, J.L. Van Laethem¹, M. Arvanitakis¹

¹ERASME University Hospital, Université Libre de Bruxelles, HUB, Department of Gastroenterology, Hepatopancreatology, and Digestive Oncology, Brussels, Belgium, ²ERASME University Hospital, Université Libre de Bruxelles, HUB, Department of Radiology, Brussels, Belgium, ³ERASME University Hospital, Université Libre de Bruxelles, HUB, Department of Digestive Surgery, Surgical Oncology, Metabolic Surgery, Hepatopancreatology, Liver and Kidney Transplantations, Brussels, Belgium, ⁴Jules Bordet Institut, Université Libre de Bruxelles, Department of Radiology, Bruxelles, Belgium, ⁵ERASME University Hospital, Université Libre de Bruxelles, HUB, Department of Pathology, Brussels, Belgium, ⁶Jules Bordet Institut, HUB, Université Libre de Bruxelles, Department of Pathology, Bruxelles, Belgium, ⁷Jules Bordet Institut, HUB, Université Libre de Bruxelles, Department of Radiation-Oncology, Bruxelles, Belgium

Contact E-Mail Address: pgolfakis@gmail.com

Introduction: Multidisciplinary team (MDT) meetings aim to optimize patients' management by eliminating errors, decreasing the time to treatment initiation, and providing better adherence to guidelines. They are associated with changes in the initial diagnosis as well as in recommended treatment plan.

The aim of this study was to evaluate the impact of a MDT approach on the management and diagnosis of focal pancreatic lesions.

Aims & Methods: All patients discussed to our institution's MDT meeting of pancreatic diseases from 1/1/2020 to 31/12/2021 with an initial diagnosis of focal (solid or cystic) pancreatic lesion were included in the study. Patients' medical records were retrospectively reviewed. The impact of MDT discussion in patients' management, defined as a modification of the initially proposed therapeutic plan after MDT discussion, as well as the criteria leading to this modification were the study's primary outcomes, where its impact on patient's diagnosis, defined as a modification of the initially proposed diagnosis, was the secondary outcome.

Categorical and continue variables are presented as value (%) and as mean $\pm$ standard deviation, respectively. Comparisons were performed using a χ^2 test or Fisher's exact test with the Yates correction or non-parametrical tests, as needed. P value < 0.05 indicated statistical significance.

Results: 522 patients [257(49.2%) females, 65 ± 13.6 years] were included in the study (896 total number of MDT referrals; mean referrals per patient: 1.68 ± 0.9). Of them, 185 (35.4%) and 337 (64.6%) patients had an initial diagnosis of a cystic and a solid lesion, respectively. The most common referral query was about the management plan ($n=349/522; 66.9\%$). Most of the patients addressed with solid lesions were referred for a management question ($n=288/337; 85.5\%$) while for cystic lesions, the most

common query was regarding both the diagnosis and the management (n=68/185;36.8%). The most commonly proposed management before the MDT discussion was radiological follow-up for patients with cystic lesions (n=53/185;28.6%) and endoscopy for patients with a solid lesion (n=93/337;27.6%; p<0.001).

Overall, the MDT discussion led to modification of the management plan in 377/522 patients (72.2%), with a statistically significant difference between cystic and solid lesions [63.2% vs 77.2%; p<0.001; OR(95%CI):0.77(0.65-0.91)]. Among patients with solid lesions, chemotherapy was the most commonly proposed treatment after MDT (n=180/337; 53.7%), while for cystic lesions radiological follow-up most commonly proposed (n=89/185; 48.1%).

Among patients where a different management plan was proposed after the MDT discussion this was mainly driven by revision of the cross-sectional radiological images [n=87; 74.4% and n=157; 60.4% for cystic and solid lesions, respectively=0.11].

Regarding diagnosis, adenocarcinoma was the most common diagnosis before MDT (n=250; 47.9%) followed by Intraductal Papillary Mucinous Neoplasms (n=108;20.7%). MDT discussion led to modification of the diagnosis in 92/522 patients (17.6%), with a statistically significant difference between solid and cystic lesions [n=26 (7.7%) vs. n=66 (35.7%); p<0.001; OR (95%CI):0.15 (0.09-0.25)]. Once again, the most common criteria leading to modification of the initial diagnosis was cross sectional imaging review (n=50/92;54.3%).

Conclusion: MDT discussion significantly impacts the management of patients with both cystic and solid pancreatic lesions leading to a modification of the initially proposed management in two thirds of them, mainly due to revision of cross-sectional imaging.

Disclosure: Nothing to disclose.

P0867

OUTCOME OF METAL VERSUS PLASTIC STENTS FOR BILIARY OBSTRUCTION IN PATIENTS WITH PANCREATIC CARCINOMA UNDERGOING NEOADJUVANT CHEMORADIOTHERAPY: META-ANALYSIS

N. Kumar¹, A. Jena¹, V. Sharma¹, S. Shukla², J. Shah¹

¹Postgraduate Institute of Medical Education and Research, Gastroenterology, Chandigarh, India, ²Command Hospital, Gastroenterology, Chandigarh, India

Contact E-Mail Address: shahjamil22@gmail.com

Introduction: Preoperative biliary drainage (PBT) may be warranted in patients with borderline resectable or locally advanced pancreatic carcinoma before neoadjuvant chemoradiotherapy (NAT) to relieve obstructive jaundice. However, it is unclear if use of self-expanding metal stent (SEMS) has any benefit over plastic stent in this setting.

Aims & Methods: We searched electronic databases from inception to February 11, 2022 to identify studies comparing SEMS and plastic stents for PBT in patients with pancreatic carcinoma undergoing NAT. Random effect models were used to determine pooled rates of recurrent biliary obstruction (RBO) and/or need for re-intervention, stent related complication and surgical outcome.

Results: A total of 10 studies (474 patients; Metal group-37.1%) were included. Pooled risk ratio of RBO and/or need for re-intervention was lower in the metal group [RR, 0.23(95% CI, 0.11-0.45, I²=60%)]. Pooled risks of stent occlusion [RR, 0.43 (95%CI, 0.24-0.80, I²=45%)] and stent related cholangitis [RR, 0.37(95%CI, 0.17-0.78, I²=1%)] were lower in metal group. However, risks of stent related cholecystitis [RR, 1.51(95%CI, 0.36-6.41, I²=0%)] and pancreatitis [RR, 1.52(95%CI, 0.07-31.84, I²=66%)] were higher in metal group. Metal group was also associated with reduced risk of delay in NAT [RR, 0.38 (95%CI, 0.18-0.80, I²= 14%)].

Pooled risk ratio of R0 resection [RR, 1.12 (95%CI, 0.86-1.46, I²= 70%)] and post-operative complications [RR, 0.83 (95%CI, 0.55-1.25, I²= 0%)] was equal amongst both groups.

Author	Type of Study	Number of Patients (Metal/Plastic)	RBO and/or need for re-intervention (Metal/Plastic)
Adams MA et al	Retrospective	9/43	5/36
Kubota K et al	Retrospective	17/21	4/18
Nakamura K et al	Retrospective	17/26	3/13
Kuwatani M et al	Retrospective	17/12	1/10
Hasegawa et al	Retrospective	27/40	4/39
Kobayashi K et al	Retrospective	21/22	1/21
Vehviläinen S et al	Retrospective	15/91	0/26

Conclusion: Metal stents are associated with reduced risk of RBO and/or need for re-intervention, reduced risk of stent occlusion and cholangitis as compared to plastic stents in patients with pancreatic carcinoma undergoing NAT.

Disclosure: Nothing to disclose.

P0868

DIAGNOSTIC ADEQUACY OF NEEDLES USED IN EUS-GUIDED TISSUE ACQUISITION OF SOLID PANCREATIC MASSES – A SYSTEMATIC REVIEW AND NETWORK META-ANALYSIS

M.A. Engh¹, B. Teutsch^{1,2}, A. Rancz¹, L. Frim², S. Váncsa^{1,2,3}, K. Márta^{1,3,2}, D.S. Veres^{1,4}, P. Hegyi^{1,3,2}, B. Eross^{3,1,5}

¹Semmelweis University, Centre for Translational Medicine, Budapest, Hungary, ²University of Pécs, Medical School, Institute of Translational Medicine, Pécs, Hungary, ³Semmelweis University, Division of Pancreatic Diseases, Heart and Vascular Center, Budapest, Hungary, ⁴Semmelweis University, Department of Biophysics and Radiation Biology, Budapest, Hungary, ⁵University of Pécs Medical School, Institute for Translational Medicine, Pécs, Hungary

Contact E-Mail Address: marieaengh@gmail.com

Introduction: Several needle designs are available in different sizes for endoscopic ultrasound (EUS)-guided tissue acquisition (TA) of solid pancreatic masses, and they offer different efficacy and safety profiles. No clear guidelines exist for the choice of needle for TA in this context.

We aimed to compare the needles in terms of efficacy (diagnostic adequacy, technical failures) and safety (adverse effects), and by means of network meta-analysis create a ranking of all available needle types.

Aims&Methods: This review was registered in Prospero (CRD42021284755). Randomized controlled trials comparing at least two needles of a specified gauge for TA of solid pancreatic masses were eligible for inclusion. MEDLINE (via PubMed), CENTRAL, Embase, Web of Science and Scopus were searched on October 15th, 2021, without filters or restrictions. Risk of bias was assessed using the Cochrane Risk of Bias tool (RoB2).

Results: 3665 records were identified, and 35 were finally included for analysis. For the outcome of histological adequacy, the 25G (p-score: 0.748) and 22G (0.746) Fork-tip performed best, the 25G (0.279) and 22G (0.264) Menghini worst. For the outcome of cytological adequacy, the best performing needles were the 22G Fork-tip (0.814) and 25G reverse-bevel (0.767), and worst were the 22G reverse-bevel (0.332) and 22G Menghini (0.175). For adverse events, the 25G reverse-bevel (0.797) and 20G forward-bevel (0.689) performed best, the 22G Franseen (0.319) and 19G Menghini (0.228) worst. For technical failures, the best performing needles were the 25G (0.845) and 22G (0.742) Franseen, the worst were the 22G

(0.199) reverse-bevel and 19G (0.060) Menghini needles. Significant results were only for technical failures: 19G Menghini needle was worse than 22G Franseen, 25G Franseen and 25G Menghini (all indirect), and 22G Menghini (indirect and direct). 22G Reverse-bevel was worse than 22G franseen (indirect) and 22G Menghini (direct).

Conclusion: Based on our results, fork-tip needles can be recommended for their higher diagnostic adequacy, but with a slightly increased risk of adverse events and technical failures. Menghini needles performed worst for nearly all outcomes. Limitations of the review are large uncertainties due to low event numbers for adverse events and technical failures, and a small number of direct comparisons.

Disclosure: Nothing to disclose.

P0869

CURRENT SMOKING IS ASSOCIATED WITH SHORTER PROGRESSION-FREE SURVIVAL IN PANCREATIC CANCER PATIENTS TREATED WITH FIRST-LINE FOLFIRINOX, BUT NOT WITH OTHER INTENSIFIED REGIMENS

P. Lazzano^{1,2}, R. Ponz de Leon Pisani¹, L. Archibugi¹, G. Dell'Anna¹, M. Falconi³, M. Reni⁴, P.G. Arcidiacono¹, G. Capurso¹

¹IRCCS Ospedale San Raffaele, Pancreato-Biliary Endoscopy and Endoscopic Ultrasound, Milan, Italy, ²Università Vita Salute San Raffaele, Milan, Italy, ³IRCCS Ospedale San Raffaele, Pancreatic Surgery Unit, Milan, Italy, ⁴IRCCS Ospedale San Raffaele, Department of Medical Oncology, Milan, Italy

Contact E-Mail Address: lazzano.pi@gmail.com

Introduction: Most patients with pancreatic ductal adenocarcinoma (PDAC) are currently treated with intensified chemotherapy regimens as first-line. Besides stage, age and Ca 19-9 levels, there is limited knowledge on "patient-related factors" that are associated with the response to such treatments. Smoking has been associated with worse response to polychemotherapy in other tumor types, but data in PDAC patients are scanty and limited to single-drug regimen with gemcitabine

Aims & Methods: The aim is to investigate the role of smoking in patients with PDAC treated with intensified polychemotherapy as first line therapy. Consecutive patients affected by PDAC were prospectively enrolled within a biobank/exposome registry at our centre at time of diagnosis. We collected demographic, risk factors (smoking, BMI, alcohol, family history, diabetes mellitus, allergies, use of drugs), stage (resectable (1), borderline resectable (2), locally advanced (3), metastatic (4) as per NCCN classification), therapy (surgery, chemotherapy) and follow-up (overall survival (OS), progression free survival (PFS) or recurrence free survival (RFS)). For the present study patients' related factors associated with PFS of patients treated with first-line polychemotherapy were investigated by means of Cox regression analysis.

Results: 143 patients were treated with first-line gemcitabine+abraxane (AG; n=63), PAXG (cisplatin, nab-paclitaxel, capecitabine, gemcitabine) (n=40) or FOLFIRINOX (n=40). In the AG group 47.6% of patients were male; mean age was 69.1 years; 14.2% of patients were stage I, 31.7% stage II, 22.2% stage III, 31.7 stage IV. In the FOLFIRINOX group 52.5% of patients were male; mean age was 60.2 years; 17.5% of patients were stage 1, 57.5% stage 2, 17.5% stage 3, 7.5% stage 4. In the PAXG group 65% of patients were male; mean age was 61.6 years; 10% of patients were stage I, 35% stage II, 27.5% stage III, 27.5% stage IV. In the whole cohort, stage was the only factor significantly associated with PFS (HR 1.3; 95% CI 1.1-1.7 for increasing stage), while the mean progression-free survival was not different in ever smokers (n=75) vs never smokers (n=66) (8.4 vs 8.9 months; p=0.73; HR: 1.2 (0.7-2); p=0.29). Similar results were obtained for current smokers in the whole cohort and in the subgroups treated with AG

and PAXG. As for patients treated with FOLFIRINOX, the mean PFS of current smokers was 7 months vs 14 of non-current smokers, with an HR of 4.3 (1.2-16; p=0.02) in a multivariate Cox regression analysis corrected for stage and age. As for other exposome variables, alcohol intake, diabetes and BMI were not associated with PFS, but for higher BMI being associated with worse PFS in the subgroup treated with AG only (HR=1.1 (1-1.3) per increasing BMI unit; p=0.01).

Conclusion: The present results point toward smoking as a factor possibly associated with worse response to first-line FOLFIRINOX, but not to AG or PAXG. Whether this is due to molecular mechanisms induced by tobacco smoking, reduced tolerance or modified pharmacokinetics requires further investigation.

Disclosure: Nothing to disclose.

P0870

SHEAR-WAVE ELASTOGRAPHY VERSUS STRAIN ELASTOGRAPHY WITH HISTOGRAM ANALYSIS IN SOLID PANCREATIC LESIONS: A PILOT STUDY

V. Rednic¹, C. Cioltean¹, R.-I. Orzan¹, C. Pojoga¹, O. Mosteanu², C. Hagiu², I. Rusu¹, A. Seicean²

¹Regional Institute of Gastroenterology-Hepatology "Prof.Dr. Octavian Fodor", Gastroenterology, Cluj-Napoca, Romania, ²UMF Cluj-Napoca Dept. of Gastroenterology, Dept. of Gastroenterology 4, Cluj-Napoca, Romania

Contact E-Mail Address: rednicvoicu@gmail.com

Introduction: Strain elastography histogram endoscopic ultrasound (SH) has been proved as a valuable supplement to endoscopic ultrasound (EUS) in assessing solid pancreatic lesions, with sensitivity of 98% and specificity of 63%. However, the value of newly available shear wave EUS elastography (EUS-SWM) has been disappointing in one retrospective study.

Aims & Methods: Aim: to assess the diagnostic value of SH and EUS-SWM in solid pancreatic lesions.

Methods: Our prospective study was started in August 2021 in one tertiary medical center and were recruited patients with solid pancreatic masses >2 cm in diameter at CT scan for EUS assessment first with strain histogram (SH) (3 measurements), followed by EUS-SWM (3 measurements with VsN > 20). Patients with inconclusive pathology results were excluded. The final diagnosis was based on surgery or EUS tissue acquisition results.

Results: 37 patients with solid pancreatic lesions were evaluated. The final diagnosis was 26 pancreatic adenocarcinomas, 2 neuroendocrine pancreatic tumours (NETs). Nine patients (24,32%) were excluded because of inconclusive biopsy results or other kind of lesions. The mean value of SH for pancreatic adenocarcinoma was 35,93 and for NETs 38,83 (p<0,05). The mean values of EUS-SWM were 45,86kPa for pancreatic adenocarcinomas and 20,59kPa (p<0,05).

Conclusion: In this prospective study we found a significant difference between SH and EUS-SWM in differentiating pancreatic adenocarcinomas and NETs. Semiquantitative assessment by strain ratio was higher in neuroendocrine tumors compared with pancreatic adenocarcinoma, which was discordant compared to the results of shear-wave. Further research is needed in this topic with a larger database in order to face the challenges in standardizing the EUS-SWM procedure in pancreatic lesions.

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Disclosure: Nothing to disclose.

P0871

IMMUNOHISTOCHEMICAL EVALUATION OF THE EXPRESSION OF SPECIFIC MEMBRANE ANTIGENS IN PATIENTS WITH PANCREATIC DUCTAL ADENOCARCINOMA UNDERGOING SURGERY

F. Vitale¹, A. Nicoletti¹, M. Paratore¹, M. Negri¹, G. Quero², A. Gasbarrini¹, L. Zileri Dal Verme¹

¹Università Cattolica del Sacro Cuore, Fondazione Policlinico Universitario "A. Gemelli" IRCCS, Internal Medicine and Gastroenterology, Rome, Italy, ²Università Cattolica del Sacro Cuore, Fondazione Policlinico Universitario "A. Gemelli" IRCCS, Digestive Surgery, Rome, Italy

Contact E-Mail Address: fede.vitale1996@gmail.com

Introduction: Pancreatic cancer is one of the most lethal malignancies in the population with a 5-year survival rate of only 8% and a poor response to oncological treatments. Hence, an early detection remains the most important prognostic criteria. However, the lack of validated disease biomarkers makes timely diagnosis challenging in most cases. Cell membrane and surface proteins play a crucial role in several routes of oncogenesis and tissue differentiation, as well as facilitating adhesion and metastasis.

Aims & Methods: This study aimed to evaluate the expression of six membrane antigens on pancreatic cancer cells (CA 19.9, MUC1, MUC4, Mesothelin, Annexin A10, and Glypican-1) and its relationship with clinical, laboratory, histological data and oncological outcomes, in terms of overall survival (OS) and disease free survival (DFS).

Surgical samples of 50 consecutive patients with pancreatic ductal adenocarcinoma (PDAC) undergoing pancreaticoduodenectomy were collected. Exclusion criteria were neoadjuvant therapy and history of other malignancies. Immunohistochemical staining for CA 19.9, MUC1, MUC4, Mesothelin, Annexin A10, and Glypican-1 using monoclonal antibodies was performed. The antigen expression was evaluated blindly by two different pathologists and classified according to Histoscore (H-score). The score was obtained considering immunostaining intensities (strong 3+, intermediate 2+, weak 1+, or no 0) and percentage of positive cells of the tumour (H-score=[0× percentage of immunonegative tumour cells]+[1× percentage of weakly stained tumour cells]+[2× percentage of intermediately stained tumour cells]+[3× percentage of strongly stained tumour cells]). The maximum possible H-score was 300. H-score for tumoral, ductal and acinar tissues was calculated. The patients were followed after surgery and clinical and laboratory data were collected.

Results: Median follow-up was 21,5 months. During the follow-up period, in 23 patients (47%) PDAC recurred, with a median DFS of 15 months, and 18 patients (36%) deceased, with a median OS of 21.5 months. Immunostaining for CA 19.9 and MUC1 showed a significantly higher expression in neoplastic tissue compared with non-tumoral ductal and acinar tissues (p<0.001). Moreover, the intensity of CA 19.9 and MUC1 staining of neoplastic tissue was very high, with mean H-score of 270 and 210 respectively. The expression of MUC4, Mesothelin, Annexin-10 and Glypican-1 were significantly different between normal and pathologic tissue (p<0.001), resulting completely absent in normal tissue and expressed in cancer cells in various percentages.

Neutrophil count > 4.8x10⁹/L and CA 19.9 H-score > 270 were found to be significantly correlated with OS (p=0.02 and p=0.05, respectively) and DFS

(p=0.04 and 0.05, respectively) in univariate analysis and, in multivariate analysis, they were confirmed to be independent predictor variables for OS.

Conclusion: CA 19.9 and MUC1 are highly expressed in PDAC cells. The histological expression of CA 19.9 may predict prognosis, in terms of OS, in patients with PDAC. MUC4, Mesothelin, Annexin-10 and Glypican-1 are selectively expressed by neoplastic tissue compared with non-tumoral pancreatic tissues and may represent a potential histological biomarker of disease.

Disclosure: Nothing to disclose.

P0872

A NOVEL TECHNOLOGY FOR MOLECULAR PROFILING OF KRAS GENE IN TUMOR SAMPLES AND LIQUID BIOPSIES IN PATIENTS WITH PANCREATIC DUCTAL ADENOCARCINOMA

B. Morão¹, B. Oliveira^{2,3}, B. Costa^{2,3}, S. Faías⁴, L. Mascarenhas^{1,5}, C. Fidalgo^{1,5}, S. Saraiva⁵, P. V. Baptista^{2,3}, R. Maio^{1,5}, A. R. Fernandes^{2,3}, M. Lopes Cravo⁵

¹Hospital Beatriz Ângelo, Gastroenterology, Loures, Portugal, ²Associate Laboratory i4HB - Institute for Health and Bioeconomy, NOVA School of Science and Technology, NOVA University Lisbon, 2819-516 Caparica, Lisboa, Portugal, ³UCIBIO - Applied Molecular Biosciences Unit, Department of Life Sciences, NOVA School of Science and Technology, NOVA University Lisbon, 2819-516 Caparica, Lisboa, Portugal, ⁴Instituto Português de Oncologia de Lisboa Francisco Gentil, Lisboa, Portugal, ⁵Hospital da Luz Lisboa, Lisboa, Portugal

Contact E-Mail Address: barbara.tsmorao@gmail.com

Introduction: The oncogenic activation of KRAS gene is the leading event in pancreatic cancer (PC), and clinical studies have highlighted the prognostic importance of detecting KRAS mutations in tumor and plasma of PC patients. The lack of sensitive and rapid methods have hampered its utilization in clinic.

Aims & Methods: To develop and validate a single-step methodology based on amplification-refractory mutation system (ARMS) coupled with high-resolution melting analyses (HRMA) to assess the 2 most frequent codon 12 KRAS mutations detected by Sanger Sequencing (SS) in tumor and liquid biopsies of patients with PC; the prognostic value of such mutations was evaluated. Prospective study including patients with PC between 2017-2022; tumor and plasma samples were collected at diagnosis. Molecular profiling of samples was made via sequence-specific PCR primers that only allow amplification of DNA harboring the specific target allele (ARMS technique), which is then corroborated by HRMA for the correct calling of the allele profile with improved sensitivity, when compared to SS. Primary endpoint was overall survival (OS).

Results: We included 41 patients (59% males, 69±9 years): most (21, 51%) had resectable disease; 4(10%) had borderline resectable, 1(2%) had locally advanced and 15(37%) had metastatic disease. Tumor KRAS mutations were detected by SS in 24(59%) patients: G12D=13(32%), G12V=11(27%), WT=17(41%). ARMS-HRMA in tumor samples was feasible in 38(93%) patients and detected all mutations detected by SS (kappa 0.215, p<0.01; 100% Se and Sp) but also in 9 additional samples who were previously WT by SS: G12D=5(33%), G12V=4(27%) G12D/G12V=1(7%), WT=5(33%). SS was feasible in 21(51%) plasma samples but only detected a G12V mutation in 1 patient. ARMS-HRMA was feasible in 31(76%) plasma samples, and besides the mutation detected by SS, 6 other mutations were detected: G12D=3(10%), G12V=3(10%), G12V/G12D=1(3%), WT=24(77%). No differences regarding metastatic disease stage (43% vs 46%, p=0.89) or CA 19.9 levels (median 385 vs 63, p=0.11) were observed

between patients with or without mutations detected in plasma by ARMS-HRMA. There was no agreement between *KRAS* genotype determined by SS in tumor and plasma samples (κ 0.106, $p=0.15$), but a significant agreement was observed (κ 0.190, $p<0.01$ - table) when using ARMS-HRMA technique.

There was no significant association between mutations detected by SS and OS, but patients with plasma *KRAS* mutation detected by ARMS/HRMA had a tendency for lower disease progression (14% vs 54%, $p=0.05$) mainly if a G12V mutation was present (WT 54% vs G12V 0% vs G12D 25%, $p=0.04$). No significant differences were observed regarding OS between plasma *KRAS* mutated and WT (median 2 vs 11 months, $p=0.11$), but patients with G12D mutations had a lower OS comparing to G12V and WT (2 vs 7 vs 11 months, $p=0.03$).

Tumor \ Plasma	WT	G12V	G12D	G12V/G12D
WT	3	0	0	0
G12V	6	2	0	0
G12D	11	0	3	0
G12V/G12D	2	0	0	1

Conclusion: ARMS-HRMA technique seems to be a fast, accurate and reliable diagnostic tool to assess *KRAS* mutations in PC tumor and plasma samples. In our cohort, tumor and mainly plasma codon 12 *KRAS* mutation in PC patients was associated with lower OS, namely G12D mutation. Future studies should assess its value in monitoring disease progression and response to therapy.

Disclosure: No conflicts.

P0873

SPORADIC AND MEN1-RELATED GASTRINOMA AND ZOLLINGER ELLISON SYNDROME: DIFFERENCES IN CLINICAL MANIFESTATION AND SEVERITY

S. Massironi¹, R.E. Rossi², C. Eller Vainicher³, F. Cavalcoli⁴, A. Zilli⁵, A. Laffusa⁶, C. Ciafardini⁷, V. Sciola⁷, P. Invernizzi⁸, M. Peracchi⁷

¹San Gerardo Hospital and University of Milano-Bicocca, Gastroenterology, Monza, Italy, ²Fondazione IRCCS Istituto Nazionale Tumori, Milan, Italy, ³Fondazione IRCC Ca' Granda Ospedale Policlinico di Milano, Endocrinology, Milan, Italy, ⁴IRCCS Istituto Nazionale Tumori Milano, Endoscopy, Milano, Italy, ⁵IRCCS Ospedale San Raffaele, Vita-Salute University, Gastroenterology and Endoscopy, Milano, Italy, ⁶Milano-Bicocca University/San Gerardo Hospital, Department of Medicine and Surgery, Gastroenterology, Monza, Italy, ⁷Fondazione IRCC Ca' Granda Ospedale Policlinico di Milano, Gastroenterology and Endoscopy, Milan, Italy, ⁸University of Milano-Bicocca, Center for Autoimmune Liver Diseases, Department of Medicine and Surgery, Monza, Italy

Contact E-Mail Address: a.laffusa@campus.unimib.it

Introduction: Zollinger-Ellison syndrome (ZES) associated with gastrinoma may be sporadic (Sp), but in 25% of the cases, ZES is part of the inherited multiple endocrine neoplasia 1 (MEN-1) syndrome. Data comparing Sp and MEN-1/ZES forms are scanty.

Aims & Methods: We aimed to identify and compare the clinical characteristics of Sp and MEN-1/ZES.

Between 1995-2020, all the consecutive patients with a diagnosis of gastrinoma/ZES were evaluated at the Department of Gastroenterology, Ospedale Policlinico, Milan, Italy.

Results: 76 MEN-1 and 320 Sp-GEP-NEN patients were evaluated. Among the MEN-1 patients, 41 were diagnosed with a GEPNEN. Among the Sp-GEP-NENs patients, 19 were diagnosed with Sp-ZES. MEN-1/ZES patients were younger than Sp-ZES (43.7 vs 53.5 ys, $p=0.035$), primary MEN-1/ZES gastrinoma was smaller than Sp-ZES (13 vs 18 mm, $p=0.03$). Liver metastases were present in 10 patients both among the Sp-ZES and the MEN-1/ZES. Only Sp-ZES developed extra-hepatic metastases ($p=0.0197$). Surgery was performed in 13 Sp-ZES and 8 MEN-1/ZES. 15 patients received somatostatin analogs (SSAs). Median OS (mOS) of the entire cohort resulted in 204 months. Median OS was higher in MEN-1/ZES than in Sp-ZES (310 vs 168 months, $p=0.0347$). At univariate logistic regression, age at ZES diagnosis ($p=0.01$, OR 1.1, CI 1.0-1.1), G3 grading ($p=0.003$, OR 21.3, CI 2.8-162.0), MEN-1/ZES ($p=0.02$, OR 0.3, CI 0.1-0.9) and diffuse extra-hepatic metastases ($p=0.001$, OR 7.2, CI 2.2-23.4) were related to OS. At multivariate analysis, none of the variables was independently associated with OS. At univariate analysis, age ($p=0.04$, OR 1.0, CI 1.0-1.1), size ($p=0.039$, OR 1.0, CI 1.0-1.1), G3 grade ($p=0.008$, OR 14.6, CI 2.0-107.6) and diffuse extra-hepatic metastases ($p=0.005$, OR 4.6, CI 1.6-13.8) were independently associated with PFS. At multivariate analysis, only diffuse extrahepatic metastases ($p=0.05$, OR 3.4, CI 1.0-11.6) resulted associated with PFS. Among patients treated with SSAs, MEN-1/ZES patients showed a better progression-free survival (PFS) with a median PFS not reached in MEN-1/ZES vs 34.5 months in Sp-ZES ($p=0.0227$ at Log-Rank-Test).

Conclusion: MEN-1/ZES patients generally show better OS and PFS compared to Sp-ZES, and a better SSAs response, even if a significant proportion of patients die from ZES in both groups.

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Disclosure: Nothing to disclose.

P0874

SINGLE CENTER 43 YEARS' EXPERIENCE OF ENUCLEATION OF PANCREATIC INSULINOMAS: EARLY- AND LONG-TERM RESULTS

A.C. Milanetto¹, G. Gabriel¹, E. De Carlo², C. Pasquali¹

¹Università degli Studi di Padova, Department of Surgery, Oncology and Gastroenterology, Padova, Italy, ²Università degli Studi di Padova, Department of Medicine, Padova, Italy

Contact E-Mail Address: acmilanetto@unipd.it

Introduction: Insulinoma is the most common functioning pancreatic neuroendocrine neoplasm, and almost all patients can be cured with surgery. Whenever possible, a parenchyma-preserving procedure is advisable to prevent early/late onset of diabetes.

Aims & Methods: The objective is to analyze the clinical outcome of patients who underwent open enucleation of insulinoma in the early post-operative period, and the long-term outcomes (pancreatic endocrine function, disease recurrence and survival).

From 1979 to 2021 we performed 88 pancreatic operations for insulinoma. Clinical data collected were retrieved. All patients were followed on an outpatient basis. Follow-up (FU) till February 2022.

Results: Out of 88 patients operated on for insulinoma, 42 were enucleations (48%). There were 29 F/ 13 M, averaging 53 years (range, 20-83); none of them had a MEN-1 syndrome. All patients presented symptomatic with evidence of organic hyperinsulinism. Average tumor size was 1.4 cm (median size 1.3 cm, range 0.7-3.0 cm); only 3 (7.1%) neoplasms were > 2.0 cm in size. Twenty-five (60%) insulinomas were located in the pancreatic head, four in the uncinate process, and 13 in the body-tail region. Five insulinomas (12%) were classified as G2, while 26 out of 42 were G1. Thirty-one patients (73%) had an uneventful postoperative course. Average hospital stay was 10.8 days. Pancreatic fistula grade B occurred in four (9.5%) patients (12% reported biochemical leaks), bleeding occurred in one patient (who needed only a blood transfusion), and one patient was reoperated for an early incisional hernia. No post-operative mortality occurred. Average FU time was 211 months, and in this 43 year-long period, ten patients died of other causes. Thirty-two (76%) patients are alive with no evidence of disease (no disease recurrence). Only three out of 42 (7%) patients developed diabetes in long-term FU of more of 17 years (average, up to 39 years).

Conclusion: Enucleation in open pancreatic surgery was performed in nearly half (48%) of patients for the treatment of insulinoma, while in literature the rate of enucleations in laparoscopic procedures do not exceed 20%. Enucleation provides an excellent long-term outcome in terms of preserving endocrine function (7% of late diabetes), and the procedure in open surgery has a low rate (< 10%) of pancreatic grade B fistulas. Enucleation should be considered as the gold standard technique with whom to compare the results of the alternative treatments.

Disclosure: Nothing to disclose.

Poster presentations

Endoscopy and imaging

Poster Presentations Endoscopy and imaging

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P0875

NURSE DELIVERED ELECTIVETHERAPEUTIC AND EMERGENCY UPPER GI ENDOSCOPY

C. Clisby¹, S. Dharmasiri¹, G. Elsayed¹, M. Sherman¹, B. Eross²,
C. Gordon¹

¹University Hospitals Dorset, Bournemouth, United Kingdom,

²University of Pecs Medical School, Institute for Translational
Medicine, Pecs, Hungary

Contact E-Mail Address: c.clisby83@gmail.com

Introduction: We describe the development of nurse delivered advanced upper GI therapeutic endoscopy service, which has ensured timely and efficient access to urgent and elective therapeutic procedures.

Aims & Methods: We utilised the HEE accelerated Clinical Endoscopist training programme to train a nurse in diagnostic upper GI endoscopy. Training commenced Apr '16 with JAG accreditation in diagnostic OGD achieved Oct '16. From '17 we began regular weekly therapeutic training lists, initially in observer role but progressing to hands on training (on top of the 4 job planned independent diagnostic lists/week + other duties). The Clinical Endoscopist attended a weekly specialist upper GI clinic with a consultant gastroenterologist, progressing to an allocated patient list after 6 months.

This training was supplemented with regular attendance at MDTs, national conferences and external courses as well as a Master's Degree in Advanced clinical practice.

Over a 4 year period, competency was attained in multimodal assessment of Barrett's oesophagus, HALO radiofrequency ablation, endoscopic mucosal resection, pneumatic dilatation of oesophageal strictures, placement of oesophageal stents, the assessment and multi-modal treatment of emergency upper GI bleeding (and delivery of daily inpatient emergency endoscopy lists), and placement of percutaneous endoscopic gastrostomy feeding tubes.

Furthermore the Clinical Endoscopist is "train the trainer's" accredited and is a now major provider of upper GI endoscopy training to SpRs and consultants in our unit.

Results: No. of independent lists delivered over the most recent 12 month period:

Therapeutic OGD 26

RFA 6

Inpatient OGD lists 94

RFA list shared with trainer 15

TOTAL: 126 independent therapeutic / inpatient lists and 15 continued training lists.

Compared to a gastroenterology consultant's endoscopy commitment, this is the equivalent of 3 endoscopy lists per week over 42 weeks i.e. approximately the total amount of endoscopy that a consultant is contracted to deliver in a year.

Procedures performed in same time period:

Number of Procedures :737

Therapeutic modalities: Number

Argon plasma coagulation (APC)	28
Variceal Banding	6
Gold Probe / electrocoagulation	12
Injection – adrenaline	13
Endoclip placement	4
Endomucosal resection (EMR) <i>supervised in room</i>	10
HALO radiofrequency ablation	16
Stricture dilatation with balloon	41
Nasojejunal tube placement	16
Oesophageal Stent placement	9

Conclusion: We have shown that with the appropriate structured training, mentoring and clinical governance, Nurse Endoscopists can successfully and safely deliver an independent upper GI therapeutic service.

Disclosure: Nothing to disclose.

P0876

THE AID OF ARTIFICIAL INTELLIGENCE (AI) IN OESOPHAGOGASTRODUODENOSCOPY (OGD) TO IMPROVE QUALITY OF THE UPPER GASTROINTESTINAL STUDY - A DESCRIPTIVE REPORT

G.Y.C. Sit¹, K.F.K. Wong¹, S.-K. Leung¹, S.M. Lam², S.Y. Wong²,
Y.Y. Lo², K.M. Yan², S.K. Tam², M.F. Wong², H.L. Chan²

¹Tuen Mun Hospital, Dept. of Surgery, Hong Kong, Hong Kong,
China (SAR), ²Combined Endoscopy Unit, Tin Shui Wai Hospital,
Hong Kong, Hong Kong, China (SAR)

Contact E-Mail Address: sgy442@ha.org.hk

Introduction: Cerebro is an artificial intelligence (AI) system that uses 29 views of 12 landmarks to enhance endoscopic coverage and increase pathology detection of the upper gastrointestinal tract. The endoscopist is encouraged to ensure complete coverage as the anatomical check-list is progressively completed. The inspection time for each site is recorded and shown in real-time to improve examination quality. The system can automatically capture photos of the landmarks and provide recommendations to improve image quality.

Aims & Methods: The objective of this report is to investigate the effect of Cerebro on the improvement of quality, and in training of young endoscopists of oesophagogastrroduodenoscopy (OGD). This is a descriptive report of OGDs performed with the application of Cerebro in Tin Shui Wai Hospital in Hong Kong in a two-month period. All procedures were performed by trained endoscopists. Commonly missed landmarks were summarised and impacts of the system were concluded.

Results: A total of 69 OGDs with Cerebro were done in our centre. The three most commonly missed views are lower gastric body (26.7%), gastric fundus-cardia (21.0%) and middle-upper gastric body (17.9%). There was an increase in the averaged views seen as time progresses with the use of Cerebro from 84.5% in the beginning to 97.3% at the end.

Conclusion: The number of missed areas from a single endoscopy is affected by the endoscopist's experience, reflected by the accuracy of the examination and total scope time. Other possible factors include system malfunction, and actions done during the procedure. Endoscopists reflected increased awareness of anatomy, more dedicated endoscopic

coverage and examination of areas under the presence of Cerebro. This provides improved quality assurance by setting benchmark in anatomical coverage, quality of images, and as a tool for training young endoscopists. **Disclosure:** Nothing to disclose.

P0877

A MULTICENTER, RANDOMIZED, DOUBLE-BLIND, CONTROLLED TRIAL OF EFFECTS OF USING INTRAVENOUS METOCLOPRAMIDE TO INCREASE MUCOSAL VISUALIZATION DURING ENDOSCOPY IN PATIENTS WITH ACUTE UPPER GASTROINTESTINAL BLEEDING

P. Manupeeraphant¹

¹*Vajira Hospital, Medicine, Bangkok, Thailand*

Contact E-Mail Address: salapao.muntou@gmail.com

Introduction: Acute upper gastrointestinal bleeding is a most common emergency condition and have high mortality if cannot achieve endoscopic management. ESGE recommend administered erythromycin intravenous before upper GI endoscopy. Erythromycin intravenous route is unavailable in Thailand. Therefore, we designed this study to evaluate the effects of metoclopramide before endoscopy in acute upper gastrointestinal bleeding.

Aims & Methods: Objective: We investigated the effects of an intravenous metoclopramide on mucosal visualization during EGD for acute upper gastrointestinal bleed in patients who were endoscopy within 24 hours after diagnosed or visited to hospital, assisted by subjective and objective criteria. The secondary endpoints including rate of repeat endoscopy, cause of upper gastrointestinal bleeding, adverse event, length of hospital stay were observed and recorded until patient discharge or death.

Methods: We designed multicenter, randomized, double-blind controlled trial included 154 patients who diagnosed acute gastrointestinal bleeding visited hospital or during admission and administered upper gastrointestinal endoscopy within 24 hours were enrolled. Participants were assigned to either metoclopramide group or placebo group by a blocked of four randomization. Modified Avgerinos Score were evaluated during endoscopy by endoscopist.

Results: There was no significant difference in baseline characteristic between 2 groups except syncope was higher in metoclopramide group. Metoclopramide was improved mucosal visualization in upper gastrointestinal bleeding within 24 hours, total score were 7.45 ± 1.08 vs 6.87 ± 1.62 ; p -value = 0.012. Successful in identifying lesion were 96.3% and 90.3% for metoclopramide and placebo. Rate of repeat endoscopy was not significant between both groups, 3.7% in metoclopramide and 8.3% in placebo; p -value = 0.217 and length of hospital stay was 5.39 ± 5.93 days vs 4.82 ± 6.06 days for metoclopramide and placebo.

We divided subgroup analysis high risk ulcer group compared results in visualization, metoclopramide no significant better mucosal visualization during endoscopy to placebo group. No neurologic and cardiogenic complication were found in this study.

Conclusion: Metoclopramide was improved visualization during endoscopy in upper gastrointestinal bleeding but was not helped to identifying causes of bleeding, intervention, length of hospital stay, and rate of gastrointestinal bleeding related death.

Disclosure: Nothing to disclose.

P0878

SINGLE CENTRE EXPERIENCE OF MANAGING BURIED PEG BUMPER USING FLAMINGO DEVICE

J. Fisher¹, I.M. Bell¹, H. Sharma¹

¹*Tunbridge Wells Hospital, Gastroenterology, Tunbridge Wells, United Kingdom*

Contact E-Mail Address: jennfisher@doctors.org.uk

Introduction: Buried bumper syndrome (BBS) occurs when the internal fixation of a percutaneous endoscopic gastrostomy (PEG) tube migrates outside of the stomach lumen along the stoma tract and becomes embedded in the gastric wall. (1)

It is a rare late complication which may result in loss of patency of the PEG, tube leakage and abdominal pain. There have been many non-surgical treatment options trialled in the past but none that have shown consistent results (2).

The Flamingo device is a novel tool specifically designed to enable endoscopic removal of buried bumpers. This would reduce the risks associated with a GA and surgical removal as well as improving patient experience. It is a sphincterotome like device connected to diathermy with a 180 degree cutting wire. The overgrown granulation tissue is cut until the bumper is exposed and can be advanced into the stomach. (3)

Aims & Methods: A retrospective data collection was performed for all patients with BBS in which the Flamingo procedure was attempted at our centre. We aimed to determine percentage success rate, average time of completion and whether a second PEG site was needed. We were also able to analyse the amount of sedation required for these procedures in comparison to GA needed for surgical removal.

Results: 12 Procedures were completed at Tunbridge Wells Hospital, a DGH, between June 2018 and October 2021. 11 of the patients were Male, 1 was female, with an age range of 41 to 88 years of age. 9 of the procedures were successful, a further 1 was successful on the second attempt and 2 needed surgical removal. The patient that needed to undergo a repeat procedure was agitated and desaturated after sedation and the procedure was abandoned. 1 patient was readmitted 4 days post procedure with sepsis secondary to cholecystitis. 1 Flamingo procedure was done under a general anaesthetic (GA). Average time of the procedure was 36mins. Average sedation use was 2mg Midazolam, (range 1-5mg) and 50mcg Fentanyl (range 25-75mcg).

Conclusion: The Flamingo device offers a reliable and reproducible non-surgical technique for the treatment of BBS. As this is a co-morbid group of patients this is particularly beneficial in avoiding the potential risks associated with GA and surgical removal. We have shown that it can be done with minimal sedation and is both safe and less resource intensive than the traditional surgical techniques. It can be done as a day case procedure and helps to avoid hospital admissions which is beneficial both for patients and hospital trusts.

The limitations of this study are the small sample size and relatively short study period.

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Disclosure: Nothing to disclose.

P0879

ALGORITHM FOR ENDOCYTOSCOPIC DIAGNOSIS OF SUPERFICIAL NON-AMPULLARY DUODENAL EPITHELIAL TUMORS USING COMPUTER ANALYSIS

M. Kubo¹, M. Higashino¹, T. Sone¹, S. Matsumoto¹, Y. Nishimura¹, M. Ono¹, K. Yamamoto², S. Ono², N. Sakamoto¹

¹Hokkaido University Faculty of Medicine and Graduate School of Medicine, Department of Gastroenterology and Hepatology, Sapporo, Japan, ²Hokkaido University Hospital, Division of Endoscopy, Sapporo, Japan

Contact E-Mail Address: kyokui080024@gmail.com

Introduction: Superficial non-ampullary duodenal epithelial tumors (SNADETs) has been increasing in recent years due to advanced endoscopic technology. Biopsy of SNADETs induced fibrosis of submucosal layer of SNADETs and makes endoscopic resection more difficult, therefore evaluation of histological atypia without biopsy is recommended. Endocytoscopy (ECS) is a novel ultra-high magnification endoscopic technique designed for gastrointestinal tract. ECS can provide up to 500x continuous zoom-focus magnification and is useful for evaluation of histological atypia. However, there have been no reports on ECS of SNADETs using computer analysis.

Aims & Methods: The aim of this study was to propose algorithm for endocytoscopic diagnosis of SNADETs based on computer analysis. This was a single-center, retrospective study. Between January 2017 and July 2021, patients who received ECS for SNADETs and who were histopathologically diagnosed by biopsy or endoscopic resection or surgery were included. ECS was performed followed white-light imaging and narrow-band imaging. For cell staining in vivo, 1% methylene blue and 0.05% crystal violet was used. All biopsy specimens and resected specimens were fixed in 10% formalin and stained with hematoxylin and eosin. Each 1 image with the most severe atypia from ECS images and histological images were selected and all images were converted to 8-bit gray scale to be computer analyzed using ImageJ v1.53c on Windows-based systems.

The number of glands per 1mm² and percentage of densely stained area with methylene blue (DSM) per one screen in ECS images were measured. Histopathological diagnoses of duodenal lesions were classified into 3 groups (C1, C3 and C4/5) according to the revised Vienna classification (VCL). A P value of <0.05 was considered statistically significant.

Results: Seventy-nine patients with suspected SNADETs were included in this study, and 9 patients were excluded because of unclear ECS images and VCL C2.

Finally, a total of 70 ECS images and histological images including 13 cases of C1, 12 cases of C3 and 45 cases of C4/5 were analyzed. The mean number of glands per 1mm² were 18.8 in C1, 60.3 in C3 and 125.0 in C4/5. There were significant differences in the mean number of glands between 3 groups (C1: C3, $P = 0.008$, C1: C4/5, $P < 0.001$, C3: C4/5, $P = 0.03$). Percentage of DSM per one screen were 6.75 in C1, 10.1 in C3 and 21.7 in C4/5. There was a significant difference in percentage of DSM per one screen between C4/5 and C1 ($P < 0.001$). Based on these results, the cutoff value

at 0.89 which was the highest AUC was calculated. Our algorithm recommends therapeutic intervention for the SNADETs as follows: the lesions in which the number of glands per 1mm² is 47 or more and percentage of DSM in one screen is 7.4% or more, the lesions in which the number of glands per 1mm² is less than 47 and percentage of DSM per screen is 20.8% or more.

Conclusion: Computer analysis of ECS images would be useful for optical biopsy of SNADETs and would provide quantitative algorithm.

Disclosure: This study was funded by JFE (The Japanese Foundation for Research and Promotion of Endoscopy) Grant. The funding source had no role in study design, data collection, data analysis, data interpretation, or writing of the report.

P0880

PREDICTORS OF SPONTANEOUS PASSAGE OF INGESTED FOREIGN BODIES IN ADULTS: A SINGLE-CENTER 13-YEAR EXPERIENCE

W. Sbeit¹, A. Shahin¹, T. Khoury¹

¹Galilee Medical Center, Department of Gastroenterology, Naharia, Israel

Contact E-Mail Address: tawfik.khoury.83@gmail.com

Introduction: Foreign body ingestion in adults is commonly encountered in clinical practice. Usually, the therapeutic approach whether to follow-up or extract is controversial.

Aims & Methods: We aimed to explore predictors for spontaneous passage of ingested foreign bodies by focusing mainly on foreign body type, location of impaction and length. We performed a retrospective single-center study over 13-years including a large number of patients. Logistic regression analysis was done to identify predictors of spontaneous passage.

Results: Overall, 365 patients with foreign bodies ingestion were included. The rate of spontaneous passage was the 53.7% in general, while the spontaneous passage rate in food impaction was 47.9%, 44.3% in sharp objects, 88.7% in blunt objects and only 22.2% among the long blunt objects (≥ 6 cm).

On regression analysis, esophageal location was associated with a higher impaction rate and lower spontaneous passage as compared to stomach, small and large intestine (OR 0.15, $P < 0.0001$, OR 0.18, $P < 0.0001$ and OR 0.02, $P = 0.0001$), respectively. Performing Receiver operating characteristics (ROC) analysis we found that the maximal length at which above it, the foreign body will fail to pass spontaneously was 3.5 cm and 3 cm in the stomach and small intestine, with area under the curve (AUC) of 0.8509 in stomach and 0.8073 in small intestine.

Conclusion: Spontaneous passage of ingested foreign body mainly depends on foreign body type, location and length. Endoscopic intervention should be considered based on these parameters.

Disclosure: Nothing to disclose.

P0881

STRATEGY OF ENDOSCOPIC TREATMENT FOR NON-AMPULLARY DUODENAL TUMORS IN OUR INSTITUTION

M. Ono¹, T. Sone¹, M. Higashino¹, S. Matsumoto¹, Y. Nishimura¹, M. Kubo¹, K. Yamamoto¹, S. Ono², N. Sakamoto¹

¹Hokkaido University Faculty of Medicine and Graduate School of Medicine, Department of Gastroenterology and Hepatology, Sapporo, Japan, ²Hokkaido University Hospital, Department of Gastroenterology, Sapporo, Japan

Contact E-Mail Address: cdf41180@par.odn.ne.jp

Introduction: There have been some reports that the number of non-ampullary duodenal tumors has been increasing in recent years, but they seem to be many problems concerning endoscopic treatment. First, the concordance rate of pathological biopsy is low between biopsies and specimens after endoscopic treatment. Next, endoscopic treatment is difficult and the rate of postoperative complications is very high.

Recently, cold polypectomy and underwater EMR (UEMR) have been reported as safe treatment options for endoscopic treatment. There have been some reports that UEMR can be safely performed even for relatively large lesions, and UEMR has therefore been introduced at our hospital.

Aims & Methods: Endoscopic treatment for duodenal tumors was retrospectively examined during the period from January 2017 to December 2021.

Results: There were 90 cases of duodenal tumors and 116 lesions during the observation period. The average age of the patients was 64.7 (44-86) years, and the male-female ratio was 63/27. There were 69 lesions (59.4%) in which biopsy was performed before endoscopic treatment.

The methods used for endoscopic treatment were EMR in 46 cases, cold polypectomy in 41 cases, UEMR in 25 cases, polypectomy in 1 case, EMR using a ligating device (EMRL) in 2 cases, and hybrid ESD in 1 case. As complications, postoperative bleeding occurred in 2 cases (in 1 case after UEMR and in 1 case after EMRL) and perforation occurred in hybrid ESD. In the 25 patients who underwent UEMR, the average tumor diameter was 10.4 mm (5-20 mm), the average procedure time was 10.4 min (4-50 min), and the endoscopic complete resection rate was 100% (25/25). The R0 resection rate was 64% (16/25), and there were 6 cases with an unknown horizontal margin and 3 cases with a positive horizontal margin, but all vertical margins were negative.

On the other hand, the average tumor diameter in the 46 patients who underwent EMR was 10.9 mm (2-30 mm), but the average resection time was 20.6 min (4-66 min), which was significantly longer than that in UEMR ($p < 0.001$). In those 46 patients, the endoscopic complete resection rate was 82.6% (38/46) and the R0 resection rate was 65.2% (30/46). There were 14 cases with an unknown horizontal margin, 1 case with a positive horizontal margin, and 4 cases with an unknown vertical margin.

Conclusion: Endoscopic treatment for non-ampullary duodenal tumors is relatively safe except for hybrid ESD cases. The procedure time for UEMR is shorter than that for EMR and the treatment results are comparable.

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Disclosure: Nothing to disclose.

P0882

ENDOSCOPIC TRANS-ORAL OUTLET REDUCTION IS EFFECTIVE FOR BILIARY REFLUX AFTER LAPAROSCOPIC ONE ANASTOMOSIS GASTRIC BYPASS

R. Reicher¹, M. Shnell¹, S. Fishman¹

¹Tel Aviv Sourasky Medical Center, Bariatric Endoscopy Service, Department of Gastroenterology and Liver Disease, Tel Aviv, Israel

Contact E-Mail Address: rellyr@tlvmc.gov.il

Introduction: Biliary reflux (BR) represents a common complication of one anastomosis gastric bypass (OAGB), with a wide side-to-side anastomosis of the gastric pouch to the bilio-pancreatic and alimentary limbs. The symptoms may be severe with substantial impact on quality of life. Moreover, BR has been implicated in pre-cancerous conditions like Barrett's esophagus and increased risk for gastric cancer after Bilroth II surgery. To date, there is no pharmacotherapy effective for BR and surgical revision is the only option for refractory patients.

Aims & Methods: Patients after OAGB suffering BR were diagnosed upon typical symptoms. Possible acid reflux was treated with high-dose PPI in all patients. After gastroscopy excluding alternative causes of symptoms and contra-indications for endoscopic trans-oral outlet reduction (TORE) the procedure was carried out. Using circumferential argon plasma coagulation and endosuturing with two Z-shaped sutures, the anastomosis was narrowed to a diameter of less than 10mm. Patients were prospectively followed.

Results: Twelve OAGB patients (M:F=2:10) underwent TORE for BR between 5/2019 and 10/2021. Mean age was 48 (24-64) and mean pre-procedure BMI was 33 (26-44). Four patients suffered in addition to BR from dumping and weight regain and 5 suffered in addition to BR from weight regain alone. Technical success rate was 100% with all patients reaching anastomosis diameter of less than 10mm. Resolution of BR symptoms was achieved in 10 out of 12 patients (83%) with a mean follow up period of 11 months (4-34). One patient required repeat TORE due to recurrence of BR symptoms after initial improvement. Mean total body weight-loss (TBWL) at 6 months was 8% (0-15%). All six patients with concomitant Dumping syndrome had BR resolution and 4/6 (67%) had resolution of their Dumping syndrome.

Severe adverse events occurred in one patient experiencing a gastric perforation that was immediately sutured endoscopically during the procedure. The patient was admitted and treated with antibiotics with no further intervention needed.

Conclusion: TORE appears to be a safe and effective treatment for BR in OAGB patients, at least in the short term. A success rate of 83% was shown, with only one serious adverse event that was treated conservatively. BR represents a common side-effect of OAGB. Definitive objective diagnosis of BR remains problematic, with a paucity of reliable tests that demonstrate BR. Clinicians must be aware of this diagnosis especially in patients with altered anatomy that predisposes to BR.

The possible role that bile exposure has in increased risk for gastric and esophageal malignancies implies that these patients should be treated and remain in some sort of surveillance, at least until further more robust data is available.

Disclosure: Nothing to disclose.

P0883

IN-VIVO DETECTION AND DIAGNOSIS OF GASTRIC PRENEOPLASTIC LESIONS BY FOURTH-GENERATION ENDOCYTOSCOPY: A PILOT STUDY

R. Vasapolli^{1,2}, L. Macke^{1,2}, N. Koch¹, L. Neuhaus¹, J. Schirra¹, J. Neumann³, J. Mayerle¹, P. Malfertheiner¹, C. Schulz^{1,2}

¹Hospital of the Ludwig Maximilians University of Munich, Department of Internal Medicine II, Munich, Germany, ²DZIF Deutsches Zentrum für Infektionsforschung, Partner Site Munich, Munich, Germany, ³Hospital of the Ludwig Maximilians University of Munich, Institute of Pathology, Munich, Germany

Contact E-Mail Address: riccardo.vasapolli@med.uni-muenchen.de

Introduction: Endocytoscopy (EC) was recently introduced as new-generation endoscopic system that provides ultra-high magnification images and enables in vivo histologic assessment after appropriate staining of nuclear and cellular structures. Gastric precancerous lesions (GPL) have been assessed by EC only in a limited number of studies. No data are available on the diagnostic utility of EC for diagnosis of GPL both in antrum and corpus.

Aims & Methods: Aim of our study was to characterize endocytoscopic features related to GPL and to assess the diagnostic performance of EC compared to standard histopathology.

A total of 80 gastric areas (36 from antrum, 44 from corpus) of 25 prospectively recruited patients (12 men, mean age 58.1 ± 14.6 years), who underwent gastroscopy with EC between November 2020 and Mai 2021 were analyzed. All endoscopies were performed by one endoscopist (A) with expertise in EC using an Olympus endocytoscope (GIF-H290EC) and crystal violet-methylene blue for double staining.

Target biopsies were obtained from each area. Histopathological diagnosis was used as gold standard. EC diagnosis was made based on a preexisting EC classification¹.

By assessing cellular and glandular structures, lumen changes and nuclear morphology lesions were classified in EC 1, normal or chronic gastritis (CG); EC 2a, atrophic gastritis (AG); EC 2b, intestinal metaplasia (IM); EC 2ab, both AG and IM; and EC 3, dysplasia and/or gastric cancer (CGA).

After independent EC diagnosis 419 high-quality EC images were selected from video-documentation by endoscopist A and used for review by 3 endoscopists (B, with minor experience in performing EC, C and D, with no experience in performing EC but trained for EC images assessment), who were blinded to endoscopic findings and histopathology. Diagnostic accuracy values and concordance rates between observers were calculated by using the κ-value.

Results: Gastric areas were histologically classified as follows: normal, 6 (7.5%); CG, 45 (56.25%); AG with IM, 14 (17.50%); IM, 11 (13.75%); GCA, 3 (3.75%).

The diagnostic performances of EC for GPL detection are summarized in Table 1.

The mean sensitivity, specificity and accuracy for EC diagnosis of GPL (EC 2a/2b/2ab + EC 3 vs. EC 1) were 88%, 93% and 91% among endoscopists A and B and 86%, 68% and 74% among endoscopists C and D, respectively. The interobserver agreement was substantial (κ-value 0.75, p < 0.001) between the two EC experts and fair (κ-value 0.29, p = 0.006) between the two non-expert endoscopists.

Table 1. Diagnostic performances of EC for GPL detection as assessed by 4 endoscopists (A-D). Values are shown as percentage with 95% confidence intervals. Abbreviations: Sen (sensitivity), Spe (specificity), Acc (accuracy), PPV (positive predictive value), NPV (negative predictive value).

EC 1	EC 2a	EC 2b	EC 2a/2b/2ab	EC 2 + EC 3
Endoscopist A	Endoscopist A	Endoscopist A	Endoscopist A	Endoscopist A
Sen 98.08 % (89.74-99.95); Spe 96.43 % (81.65-99.91); Acc 97.50 % (91.26-99.70); PPV 98.08 % (88.15-99.71); NPV 96.43 % (79.47-99.47)	Sen 64.29 % (35.14-87.24); Spe 100 % (94.56-100.00); Acc 93.75 % (86.01-97.94); PPV 100.00%; NPV 92.96 % (86.73-96.38)	Sen 84.00 % (63.92-95.46); Spe 98.18 % (90.28-99.95); Acc 93.75 % (86.01-97.94); PPV 95.45 % (74.93-99.33); NPV 93.10 % (84.60-97.07)	Sen 96.00 % (79.65-99.90); Spe 98.18 % (90.28-99.95); Acc 97.50 % (91.26-99.70); PPV 96.00 % (77.46-99.41); NPV 98.18 % (88.78-99.73)	Sen 96.55 % (82.24-99.91); Spe 98.11 % (89.93-99.95); Acc 97.56 % (91.47-99.70); PPV 96.55 % (80.05-99.49); NPV 98.11 % (88.34-99.72)
Endoscopist B	Endoscopist B	Endoscopist B	Endoscopist B	Endoscopist B
Sen 90.38 % (78.97-96.80); Spe 78.57 % (59.05-91.70); Acc 86.25 % (76.73-92.93); PPV 88.68 % (79.31-94.12); NPV 81.48 % (65.16-91.19)	Sen 35.71 % (12.76-64.86); Spe 98.48 % (91.84-99.96); Acc 87.50 % (78.21-93.84); PPV 83.33 % (38.73-97.53); NPV 87.84 % (83.00-91.44)	Sen 64.00 % (42.52-81.03); Spe 92.73 % (82.41-97.98); Acc 83.75 % (73.82-91.05); PPV 80.00 % (59.82-91.49); NPV 85.00 % (76.97-90.57)	Sen 80.00 % (59.30-93.17); Spe 90.38 % (78.97-96.80); Acc 87.01 % (77.41-93.59); PPV 80.00 % (62.95-90.40); NPV 90.38 % (81.03-95.39)	Sen 78.57 % (59.05-91.70); Spe 88.68 % (76.97-95.73); Acc 85.19 % (75.55-92.10); PPV 88.68 % (62.75-88.87); NPV 88.68 % (79.29-94.13)
Endoscopist C	Endoscopist C	Endoscopist C	Endoscopist C	Endoscopist C
Sen 61.54 % (47.02-74.70); Spe 96.43 % (81.65-99.91); Acc 73.75 % (62.71-82.96); PPV 96.97 % (82.19-99.55); NPV 57.45 % (48.72-65.73)	Sen 57.14 % (28.86-82.34); Spe 92.42 % (83.20-97.49); Acc 86.25 % (76.73-92.93); PPV 61.54 % (38.06-80.64); NPV 91.04 % (84.69-94.92)	Sen 64.00 % (42.52-82.03); Spe 80.00 % (67.03-89.57); Acc 75.00 % (64.06-84.01); PPV 59.26 % (44.27-72.70); NPV 83.02 % (74.04-89.34)	Sen 84.00 % (63.92-95.46); Spe 72.22 % (58.36-83.54); Acc 75.95 % (65.02-84.86); PPV 58.33 % (46.84-68.98); NPV 90.70 % (79.64-96.05)	Sen 96.43 % (81.65-99.91); Spe 61.54 % (47.02-74.70); Acc 73.75 % (62.71-82.96); PPV 57.45 % (48.72-65.73); NPV 96.97 % (82.19-99.55)
Endoscopist D	Endoscopist D	Endoscopist D	Endoscopist D	Endoscopist D
Sen 75.00 % (61.05-85.97); Spe 75.00 % (55.13-89.31); Acc 75.00 % (64.06-84.01); PPV 84.78 % (74.22-91.51); NPV 61.76 % (49.06-73.04)	Sen 57.14 % (28.86-82.34); Spe 80.30 % (68.68-89.07); Acc 76.25 % (65.42-85.05); PPV 38.10 % (24.03-54.49); NPV 89.83 % (82.66-94.24)	Sen 40.00 % (21.13-61.33); Spe 100.00 % (93.51-100.00); Acc 81.25 % (70.97-89.11); PPV 100.00 % (72.70-83.47)	Sen 68.00 % (46.50-85.05); Spe 78.18 % (64.99-88.19); Acc 75.00 % (64.06-84.01); PPV 58.62 % (44.53-71.43); NPV 84.31 % (74.90-90.64)	Sen 75.00 % (55.13-89.31); Spe 75.00 % (61.05-85.97); Acc 75.00 % (64.06-84.01); PPV 61.76 % (49.06-73.04); NPV 84.78 % (74.22-91.51)

Conclusion: New-generation EC has a potential to identify GPL with high diagnostic accuracy, high reliability and good reproducibility. Training and experience in performing EC affect substantially the diagnostic performances. Further studies are needed to assess the cost-effectiveness of EC and the improvement in diagnostic accuracy compared to conventional endoscopy and virtual chromoendoscopy.

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P0884

THE ASSOCIATION BETWEEN LOW BODY-MASS INDEX AND SERIOUS POST-ENDOSCOPIC ADVERSE EVENTS

N. Glaubach¹, D. Ben Hur^{1,2}, A. Korytny², Y. Isenberg³, Y. Laham⁴, R. Almog⁵, I. Chermesh², R. Weissshof², H. Bar-Yoseph^{2,4}

¹Rambam Health Care Campus, Internal Medicine H, Haifa, Israel,

²Rambam Health Care Campus, Department of Gastroenterology,

Haifa, Israel, ³Rambam Health Care Campus, Department of

Hematology, Haifa, Israel, ⁴The Ruth & Bruce Rappaport Faculty of Medicine, Technion-Israel institute of technology, Haifa, Israel,

⁵Rambam Health Care Campus, Department of Epidemiology and Biobank, Haifa, Israel

Contact E-Mail Address: netta.glaubach@gmail.com

Introduction: Low body mass index (LBMI) was associated with longer colonoscopy procedure time and procedural failure, and commonly considered to be a risk factor for post-endoscopic adverse events (AE), but evidence is lacking.

Aims & Methods: We aimed to assess the association between serious AE (SAE) and LBMI.

A single center retrospective cohort of patients with LBMI (body mass index (BMI)≤18.5) undergoing an endoscopic procedure was matched (1:2 ratio) to a comparator group (19≤BMI≤30). Matching was performed according to age, gender, inflammatory bowel disease or malignancy diagnoses, previous abdomino-pelvic surgery, anticoagulation therapy and type of endoscopic procedure.

The primary outcome was any SAE, defined as bleeding, perforation, aspiration or infection, following the procedure. The attribution between each SAE and the endoscopic procedure was determined. The Secondary outcomes included each complication alone and endoscopy-attributed SAEs. Univariate and multivariate analyses were used to compare between groups.

Results: 1986 patients were included (662 in the LBMI group). Baseline characteristics were mostly similar between the groups. The primary outcome occurred in 31/662 (4.7%) patients in the LBMI group and in 41/1324 (3.1%) patients in the comparator group (p=0.075). Among the specific secondary outcomes, infections (2.1% vs. 0.8%, p=0.009) occurred more frequently in the LBMI group. Multivariate analysis revealed an adjusted association between SAE and LBMI (OR 1.64, 95% CI 1.00-2.67), male gender, diagnosis of malignancy, advanced endoscopic procedure and an ambulatory setting.

Characteristics	OR	95%CI	P value
Low BMI	1.64	1.00, 2.67	0.048
Male gender	1.81	1.12, 2.98	0.017
Diagnosis of Malignancy	2.36	1.44, 3.87	<0.001
Advanced endoscopy*	3.75	2.16, 6.35	<0.001
Hospitalized patients	0.53	0.32, 0.91	0.017

BMI - body mass index,

*Advanced endoscopy included ERCP, DBE, EUS with intervention, PEG and big-polyp EMR.

Table. Multivariate model to predict post-endoscopy severe adverse events

The model included BMI group, gender, age (as a categorical variable), previous diagnosis of IBD, malignancy, diabetes, chronic obstructive pulmonary disease, anticoagulation therapy, endoscopy type (dichotomized as advanced and non-advanced), hospitalization status (inpatients vs. ambulatory) and matching pairs. A forward selection/backward elimination procedure was then applied to yield the final model. OR – odds ratio. CI – confidence interval.

Conclusion: Low BMI was associated with higher post-endoscopic serious adverse events. Special attention is required when performing endoscopy in this fragile patient population.

Disclosure: Nothing to disclose.

P0885

PRACTICE OF ENDOSCOPY BY SURGEONS – A WEO GLOBAL SURVEY

P.W.Y. Chiu¹, H. Thorlacius², H.C. Yip¹, S. Chan³, K. Nakajima⁴, W. Huang⁵, G. Rao⁶, S. Perretta⁷, L. Swanstrom⁷, H. Inoue⁸

¹The Chinese University of Hong Kong, Department of Surgery, Faculty of Medicine, Hong Kong, Hong Kong, China (SAR),

²Lund University Surgery, Dept. of Gastrointestinal Surgery,

Malmö, Sweden, ³The Chinese University of Hong Kong, Surgery, Hong Kong, Hong Kong, China (SAR), ⁴Osaka University

Graduate School of Medicine, Dept of Next Generation

Endoscopy Intervention, Osaka, Japan, ⁵IRCAD Taiwan, Lukang,

Taiwan, ⁶Asian Institute of Gastroenterology, Hyderabad, India,

⁷IRCAD-IHU, Surgery, Strasbourg, France, ⁸Showa University Northern Yokohama Hospital, Digestive Disease Center,

Yokohama, Japan

Contact E-Mail Address: philipchiu@surgery.cuhk.edu.hk

Introduction: The horizon of diagnostic and therapeutic endoscopy had been extending for past decade. In recent years, the practice of endoscopy has been increased among surgical societies. Numerous professional surgical societies have implemented training on flexible endoscopy for surgeons.

However, there is scarce data on the practice of endoscopy among surgeons worldwide. This is a global survey conducted among surgeons worldwide on the practice of flexible endoscopy.

Aims & Methods: This is a global survey on the practice and training on endoscopy among surgeons conducted through an electronic platform. We invited leading surgical societies worldwide to assist in disseminating the invitation to their members, including Society of American GI & Endoscopic Surgeons (SAGES), the European Association of Endoscopic Surgery (EAES), Endoscopic and Laparoscopic Surgeons of Asia (ELSA), Japan Society of Endoscopic Surgery (JSSES), Indian Association of Gastrointestinal EndoSurgeons (IAGES), etc.

The WEO committee on Surgical Endoscopy designed a set of 28 questions targeting at assessing the practice, credentialing and training of endoscopy was delivered to the delegates. A structured database was designed to collect the results from the questionnaire.

Results: The survey was conducted in April 2021, and a total of 309 participants responded to the questionnaire survey including 179 from Europe, 58 from Asia, 22 from UK and 13 from US. 57% of responders are older than 45 yrs, and 86% of them were male. 139 of them received 1 to 5 years of endoscopy training, while 40% of them confirmed performance of digestive endoscopy by surgeons in their countries. 60.2% of them claimed that surgeons were performing less than 50% of the endoscopy in their countries, while a certain proportion of emergency endoscopy would be performed by surgeons.

Moreover, there is also a need for intraoperative and postoperative endoscopy performed by surgeons. Only 29% of the respondents claimed that there is a standard training program for surgeons to perform OGD and colonoscopy, while 17% claimed to have training program for ERCP.

Less than 15% of the countries had training program for ESD, POEM, EUS and Advanced ERCP for surgeons. 60% of the respondents believed that a training program is necessary to improve on the clinical outcomes of OGD, colonoscopy and ERCP. The role of surgeons seems to be important in development of procedures including endoscopic laparoscopic collabora-

tive surgery and bariatric endoscopy. Lack of training, granting of privilege and access to appropriate equipment are main barriers for surgeons to perform endoscopy.

Conclusion: There is a trend towards increasing practice of endoscopy among surgeons worldwide. The major barriers for surgeons to perform endoscopy should be addressed by surgical societies worldwide to safeguard clinical outcomes by surgeons.

Disclosure: The conduction of this survey is supported by Surgical Endoscopy Committee of World Endoscopy Organization (WEO).

P0886

DECISION-TO-SCOPE (DTS) SCORE: A NOVEL TOOL WITH EXCELLENT ACCURACY IN PREDICTING FOREIGN BODIES IN THE UPPER GASTROINTESTINAL TRACT

V. Macedo Silva^{1,2,3}, T. Lima Capela^{1,2,3}, M. Freitas^{1,2,3}, T. Cúrdia Gonçalves^{1,2,3}, P. Boal Carvalho^{1,2,3}, B. Rosa^{1,2,3}, J. Berkeley Cotter^{1,2,3}

¹Hospital da Senhora da Oliveira, Gastroenterology Department, Guimarães, Portugal, ²Life and Health Sciences Research Institute (ICVS), School of Medicine, University of Minho, Braga, Portugal, ³ICVS/3B's, PT Government Associate Laboratory, Braga / Guimarães, Portugal

Contact E-Mail Address: tiagolimacapela@gmail.com

Introduction: Foreign body (FB) ingestion and food bolus impaction are common indications for urgent esophagogastroduodenoscopy (EGD). Nevertheless, most of the ingested FB (80 to 90%) pass spontaneously through the gastrointestinal (GI) tract. Differently from upper GI bleeding, there is no currently validated score aiming to identify "low-risk" patients in suspected FB in the upper GI tract.

Aims & Methods: We aimed to create a score able to discriminate patients who are candidates to urgent EGD in this scenario. We conducted a retrospective study of consecutive patients referred to our endoscopic unit for suspected FB in the upper GI tract between 2016 and 2021.

Every patient was previously evaluated by an otorhinolaryngology specialist. The evaluated outcome was endoscopic confirmation of a FB in the upper GI tract. Variables significantly associated with the outcome on multivariate analysis were computed into a score predicting the confirmation of FB in EGD.

Results: Our sample included 228 patients, 122 (53.5%) of them female, with a mean age of 58.0±19.7 years. From these, 97 (42.5%) had a confirmed FB in EGD. Time since ingestion < 6h (OR=4.0; *p*=0.042); absence of any meal after FB ingestion (OR=7.1; *p*=0.005); dysphagia (OR=11.8; *p*<0.001); odynophagia (OR=4.6; *p*=0.004); and drooling (OR=15.1; *p*<0.001) were independent predictors of confirmed FB on EGD.

These variables were used to compute a confirmed FB predicting score – the Decision-To-Scope (DTS) score: time since ingestion < 6h (+1pt), absence of meals (+2pts), dysphagia (+3pts), odynophagia (+1pt), and drooling (+4pts), with a maximum value of 11 pts, which had an excellent accuracy to predict the outcome (AUC=0.953; 95%CI=0.928-0.977; *p*<0.001). The optimal cut-off to identify low-risk patients was a score ≤5 (sensitivity 85% and specificity 95%).

Conclusion: More than half of the suspected FB in the upper GI tract were not confirmed by EGD. The DTS-score presented an excellent accuracy at stratifying patients' risk, and may contribute to the decision to perform urgent EGD in suspected FB in the upper GI tract.

Disclosure: Nothing to disclose.

P0887

EFFECTS OF TRANEXAMIC ACID AND ADRENALINE INJECTATES ON HISTOPATHOLOGICAL HEALING AFTER GASTRIC AND COLONIC ENDOSCOPIC SUBMUCOSAL DISSECTION IN AN IN VIVO PORCINE MODEL

A. Bermont¹, S. Matalon¹, D.L. Cohen¹, H. Shirin¹, S. Vosko¹

¹Gastroenterology and Liver Diseases Institute, Shamir Medical Centre, Be'er Ya'akov, Israel

Contact E-Mail Address: bermont@doctor.com

Introduction: Endoscopic submucosal dissection (ESD) has become a common minimally invasive therapy for resection of early colonic and gastric neoplasia, but there is limited data on the histopathological effects of the different haemostatic agents (HAs) used within the injection solution. We used an in vivo porcine model to compare the tissue effects of tranexamic acid (TXA) and adrenaline compared to controls.

Aims & Methods: Standard ESD, using a 2 mm flash-knife, was performed in three pigs. Lifting fluid was used based on a 4% succinylated gelatin solution and indigo carmine. Four resections were performed in the stomach and colon in each pig. HAs were blindly randomised to either TXA, adrenaline, or neither (control). Stomachs and colons were surgically removed after 7 days. A specialist pathologist blinded to the intervention assessed the specimens which were assigned a composite score (on a scale of 0-4) based on inflammation, necrosis, and granulation.

Results: Twenty four defects were analysed (8 per pig, median defect size 30X30 mm). For HA effects, 48 tissue sections were assessed. TXA was comparable to adrenaline and controls for deep involvement of the colon wall. However, in gastric wall specimens, TXA and adrenaline both showed less inflammation, necrosis, and better regeneration compared to controls (average scores of 3 as compared to 4).

Animal No./Tissue	Inflammation	Necrosis	Granulation Tissue	Total Score
Adrenaline/ Stomach	2	0	4	3
Adrenaline/ Colorectum	4	4	2	4
TXA/ Stomach	3	1	4	3
TXA/ Colorectum	3	2	2	3
Saline/ Stomach	4	4	1	4
Saline/ Colorectum	3	2	2	3

Table. A semi-quantitative analysis of the histopathological findings, using a scoring scale.

Conclusion: For ESD, HAs such as TXA and adrenaline added to the submucosal injectate may have protective effects on the depth and extent of injury to the underlying tissue.

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P0888

DUODENAL NEUROENDOCRINE TUMORS: SHORT AND LONG-TERM OUTCOMES OF ENDOSCOPIC SUBMUCOSAL DISSECTION PERFORMED IN THE WESTERN SETTING

S. Gupta^{1,2}, P. Kumar^{3,1}, T. O'Sullivan^{2,1}, A. Whitfield^{2,1}, O. Cronin^{2,1}, H. Wang^{2,1}, R. Chacchi Cahuin⁴, A. Murino⁴, E.J. Despott⁴, A. Lemmers⁵, M. Pioche⁶, M.J. Bourke^{1,2}

¹Westmead Hospital Sydney, Gastroenterology and Hepatology, Sydney, Australia, ²University of Sydney, Westmead Clinical School of Medicine, Sydney, Australia, ³University of Calgary, Division of Gastroenterology and Hepatology, Alberta, Canada, ⁴Royal Free Unit for Endoscopy, Royal Free Unit for Endoscopy, Department of Gastroenterology, London, United Kingdom, ⁵Hôpital Univ. Erasme, Gastroenterology Department, Bruxelles, Belgium, ⁶Hospices Civils de Lyon, Gastroenterology and Endoscopy, Lyon, France

Contact E-Mail Address: sunil.gupta@live.com.au

Introduction: Endoscopic resection (ER) is recommended for the management of duodenal neuroendocrine tumors (D-NETs) confined to the submucosal layer, without lymph node or distant metastasis. While this is accepted practice for lesions < 10mm, consensus for larger lesions remains unclear.

Although endoscopic submucosal dissection (ESD) has been proposed as the preferred ER technique for DNETs ≥ 10mm, there is limited data on efficacy and safety, particularly in the Western setting.

Aims & Methods: We performed a retrospective analysis of patients with D-NETs who underwent ESD between 2012 and 2021 in three tertiary referral centers in Australia, France and Belgium.

Results: Fourteen patients with 15 D-NETs were evaluated. The median patient age was 64 years (IQR 58-70). All D-NETs were confined to duodenal bulb. The median D-NET size was 10 mm (IQR 7-12 mm) and the median specimen size was 15 mm (IQR 15-20mm). Median procedure time was 60 minutes (IQR 25-90 minutes). The rate of *en bloc* and curative resection was 100% and 40% respectively. Intra-procedural perforation occurred in 4 cases (26.7%), all of which were treated with endoscopic closure, without long-term sequelae. There were no episodes of clinically significant bleeding or stenosis. No local recurrence, lymph node or distant metastasis was observed during a median follow up period of 16.2 months (IQR 5.9-43.2 months).

Conclusion: In experienced hands, ESD for D-NETs can achieve a 100% *en bloc* resection rate. Despite a curative rate of 40%, there were no cases of local recurrence or distant metastatic spread, indicating that ESD may be a viable option for patients with D-NETs < 20mm that are not surgical candidates.

Disclosure: Nothing to disclose.

P0889

ARTIFICIAL INTELLIGENCE ASSISTED PATTERN RECOGNITION DURING THIRD-SPACE ENDOSCOPY

M.W. Scheppach¹, R. Mendel^{2,3}, A. Probst¹, M. Meinikheim¹, D. Rauber^{2,4}, T. Rückert², C. Palm^{2,3,4}, H. Messmann¹, A. Ebigo¹

¹University of Augsburg, Gastroenterology, Augsburg, Germany, ²Ostbayerische Technische Hochschule Regensburg (OTH Regensburg), Regensburg Medical Image Computing (ReMIC), Regensburg, Germany, ³Ostbayerische Technische Hochschule (OTH Regensburg), Regensburg Center of Health Sciences and Technology (RCHST), Regensburg, Germany, ⁴Ostbayerische Technische Hochschule Regensburg (OTH Regensburg), Regensburg Center of Biomedical Engineering (RCBE), Regensburg, Germany

Contact E-Mail Address: markus.scheppach@uk-augsburg.de

Introduction: Recently, artificial intelligence (AI) tools have been developed for clinical decision support in diagnostic endoscopy, but so far no algorithm has been introduced for therapeutic interventions. Considering the elevated risk of bleeding and perforation during third-space endoscopic procedures such as ESD and POEM, there is an apparent need for innovation and research into AI guidance in order to minimize operator-dependent complications. In this study we developed a deep learning algorithm for the real-time detection and delineation of relevant structures during third space endoscopy.

Aims & Methods: We used 2465 still images from 27 full length third space endoscopic procedures (21x ESD, 6x POEM) for the training of a DeepLabv3+ neural network architecture with KSAC and a 101-layer ResNeSt backbone. The images were annotated for the categories submucosal layer, muscle layer, blood vessel, electrosurgical knife and endoscopic instrument shaft by experts in third space endoscopy. The trained algorithm was evaluated by five-fold internal cross validation and validation using a separate dataset for the parameters Intersection over union (IoU), Dice Score and pixel accuracy.

Furthermore, vessel detection on video was evaluated using 31 video clips with 52 predefined vessels from 3 separate third space endoscopic procedures (1x POEM, 1x rectal ESD, 1x esophageal ESD).

Results: For delineation performance on still images the algorithm showed values of 63%, 76% and 81% for mean IoU, mean Dice Score and pixel accuracy respectively in the internal cross validation. Tested on the separate data set, the measures were 68%, 80% and 87% for the same parameters. The mean vessel detection rate on video (VDR) was 85%. Values of 92%, 95% and 70% were calculated for VDR of POEM, esophageal ESD and rectal ESD respectively. The mean false positive rate was measured as 0.75 structures per minute. 7 out of 9 vessels, which caused intra-procedural bleeding were identified by the algorithm.

Conclusion: The trained algorithm showed promising performance for the detection and delineation of relevant tissue structures on still images and on video. In surgery, AI has been successfully applied for various tasks including image-guidance, navigation and the detection of surgical instruments ("Smart Surgery"). This new technology may improve therapeutic endoscopic procedures in the same manner ("Smart ESD").

Disclosure: Nothing to disclose.

P0890

PHYSICIAN-GUIDED PERIPROCEDURAL MANAGEMENT OF EDOXABAN THERAPY AND CLINICAL OUTCOMES IN PATIENTS UNDERGOING ENDOSCOPIC PROCEDURES: A SUB-ANALYSIS OF THE GLOBAL EMIT-AF/VTE PROGRAM

T. Vanassche¹, P. Colonna², A. Santamaria³, C. Chen⁴, S. Köhler⁵, A. Borrow⁴, C. von Heymann⁶, J. Jin⁴, M. Saxena⁷, M. Unverdorben⁴

¹University Hospitals (UZ) Leuven, Department of Cardiovascular Sciences, Leuven, Belgium, ²Polyclinic of Bari - Hospital, Department of Cardiology, Bari, Italy, ³University Hospital Vinalopo, Hematology Department, Alicante, Spain, ⁴Daiichi Sankyo Inc., Global Specialty Medical Affairs, Basking Ridge, United States, ⁵Serenis GmbH, Munich, Germany, ⁶Vivantes Klinikum im Friedrichshain, Department of Anaesthesia & Intensive Care Medicine, Emergency Medicine, and Pain Therapy, Berlin, Germany, ⁷William Harvey Research Institute, Barts Health NHS Trust, Charterhouse Square, London, United Kingdom

Contact E-Mail Address: thomas.vanassche@uzleuven.be

Introduction: Direct oral anticoagulants (DOACs) may increase the risk of major bleeding (MB) associated with endoscopic procedures. However, periprocedural interruption of anticoagulation may put patients with atrial fibrillation (AF) or venous thromboembolism (VTE) at risk of thromboembolic events. Therefore, physicians must determine an appropriate schedule for interruption.

Here we report in real-world practice the physician-guided periprocedural interruption of the DOAC edoxaban and clinical outcomes for patients with AF or VTE undergoing endoscopic procedures.

Aims & Methods: Baseline characteristics and data on periprocedural edoxaban interruption were prospectively collected from patients in Europe and South Korea/Taiwan enrolled in the Global EMIT-AF/VTE program (NCT02950168, NCT02951039). The observation window for interruption was 5 days pre- to 29 days post-procedure.

The incidences of any bleeding, MB, clinically relevant nonmajor bleeding (CRNMB), acute coronary syndrome (ACS), stroke, transient ischemic attack (TIA), systemic embolic events (SEE), and all-cause death were assessed from the procedure day to 30 days post-procedure; ratios of events per procedure were calculated. Endoscopic procedures included in this sub-analysis were not restricted to upper gastrointestinal tract endoscopies.

Results: Patients (n = 237) had a mean $\pm$ standard deviation age of 72.0 $\pm$ 8.2 years and were mostly male (60.8% [n = 144]). Of 288 endoscopic procedures (primarily gastroesophageal endoscopies [n = 140] or colonoscopies $\pm$ polypectomies [n = 112]), edoxaban was not interrupted in 84 (29.2%); interruption occurred only pre-procedurally in 91 (31.6%), only post-procedurally in 21 (7.3%), and both pre- and post-procedurally in 92 (31.9%). The median (range) periprocedural interruption duration within the observation window was 3 (1–35) days. The incidence of bleeding and thromboembolic events was ≤ 0.02 events/procedure for MB, CRNMB, ACS, stroke, TIA, and SEE (Table).

There were 5 periprocedural MB events, 1 stroke, and 1 TIA. Of 5 reported deaths, 3 (1 each: ischemic stroke, congestive heart failure, unknown) occurred during the first 3 days of edoxaban interruption; the 2 deaths that occurred >3 days after last edoxaban dose were categorized as resulting from non-cardiovascular “other” causes.

Conclusion: Physician-guided periprocedural edoxaban management was associated with short interruptions in patients with AF or VTE undergoing endoscopic procedures in routine clinical practice. The incidences of MB and thromboembolic events in this sub-analysis were consistent with previous studies of edoxaban and other DOACs.

Baseline demographics	Patients with endoscopic procedures (n = 237)	Periprocedural clinical events, n (events/procedure) [†]	Endoscopic procedures (N = 288)
BMI, kg/m ² , mean $\pm$ SD	26.6 $\pm$ 4.8	Any bleeding	15 (0.05)
Hypertension, n (%)	180 (75.9)	Major bleeding [†]	5 (0.02)
Dyslipidemia, n (%)	97 (40.9)	Clinically relevant nonmajor bleeding	3 (0.01)
Diabetes mellitus, n (%)	54 (22.8)	Acute coronary syndrome	0
Creatinine clearance, mL/min, mean $\pm$ SD	69.5 $\pm$ 29.5	Stroke	1 (0.003)
HAS-BLED, mean $\pm$ SD	1.9 $\pm$ 1.1	Transient ischemic attack	1 (0.003)
CHA ₂ DS ₂ -VAsC, mean $\pm$ SD	3.3 $\pm$ 1.5	Systemic embolic event	0
30 mg edoxaban, n (%)	72 (30.4)	All-cause death	5 (0.02)
60 mg edoxaban, n (%)	163 (68.8)		

N refers to number of procedures.

[†]Clinical events were recorded within 30 days of the procedure. [†]International Society on Thrombosis and Haemostasis definition.

CHA₂DS₂-VAsC, congestive heart failure, hypertension, age, diabetes, prior stroke/transient ischemic attack, vascular disease, and sex category; HAS-BLED, hypertension, abnormal renal and liver function, stroke, bleeding, labile international normalized ratio, elderly (age >65), prior alcohol or drug usage history.

Table.

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P0891

BURIED BUMPER SYNDROME: AN INCIDENCE STUDY AND CLINICAL CHARACTERIZATION OF A RARE COMPLICATION OF PERCUTANEOUS ENDOSCOPIC GASTROSTOMY

E. Dias¹, J. Santos-Antunes¹, A. Peixoto¹, R. Ramalho¹, G. Macedo¹

¹Centro Hospitalar Universitário de São João, Gastroenterology, Porto, Portugal

Contact E-Mail Address: diasj0310@gmail.com

Introduction: Buried bumper syndrome is a rare complication of percutaneous endoscopic gastrostomy, in which the internal fixation device migrates alongside the tract of the stoma outside the stomach, with an incidence of approximately 1%. Inability to insert, loss of patency and leakage around the tube are considered to be a typical symptomatic triad. Upper digestive endoscopy is indicated in all cases where buried bumper syndrome is suspected. Although rare, it can be complicated by gastrointestinal bleeding, perforation or abscess, and these complications can lead to fatal outcomes, underscoring the importance of an early accurate diagnosis.

Aims & Methods: The aims of this study were to evaluate the incidence of buried bumper syndrome following percutaneous endoscopic gastrostomy and describe its main clinical characteristics. We retrospectively analyzed every patient who performed percutaneous endoscopic gastrostomy between January 2016 and December 2021 and included all cases with endoscopic diagnosis of buried bumper syndrome. Subsequently, their medical records were searched in order to retrieve relevant clinical data.

Results: A total of 9 cases of buried bumper syndrome were identified in a total of 774 patients who performed percutaneous endoscopic gastrostomy, which corresponds to an incidence of 1.2%. Most patients were male (n=8) and median age was 75 years (range 29-96). Indications for percutaneous endoscopic gastrostomy included stroke (n=2), Alzheimer's disease (n=2), Parkinson's disease (n=1), prolonged intensive care (n=1), laryngeal cancer (n=1), traumatic cord injury (n=1) and cerebral arteriovenous malformation (n=1). Percutaneous endoscopic gastrostomy had been performed by the "pull" technique at anterior surface of distal gastric body in all patients. The caliber of the gastrostomy tube was 24 Fr (n=5) or 20 Fr (n=4). There were no immediate adverse events in any patient. The mean time interval between percutaneous endoscopic gastrostomy placement and buried bumper syndrome was 4.8 months (range 0-23).

The most common clinical manifestations were local pain (n=4), leakage around the gastrostomy tube (n=4), local tumefaction (n=4), inability to insert food along the tube (n=3), local purulent exudate (n=2) and fever (n=1). Endoscopy revealed internal gastrostomy orifice at the anterior surface of gastric body with absence of migrated internal fixation device, with endoscopic signs of infection in 2 patients. Imaging techniques were performed in 8 patients and adjacent phlegmon was detected in 2 (25%). Overall, there was evidence of local infection in 5 patients and all were successfully treated with antibiotics. Gastrostomy tube was removed in all patients after diagnosis of buried bumper syndrome and replaced with a second gastrostomy tube in 5, after mean time interval of 5 weeks. Recurrence of buried bumper syndrome was detected in 1 patient.

Conclusion: Buried bumper syndrome is a rare complication of percutaneous endoscopic gastrostomy. It may be associated with local infectious complications that may negatively impact its prognosis and therefore early detection is essential. Removal of the migrated tube and posterior replacement with a second gastrostomy tube is usually an effective management strategy. Although uncommon, recurrence is possible and prophylactic measures to avoid it should be undertaken when a second tube is placed.

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P0892

CAP ASSISTED ENDOSCOPY AS A TOOL FOR VATER PAPILLA AND DUODENAL SURVEILLANCE IN PATIENTS WITH COLONIC POLYPOSIS

C. Pinto¹, R. Ortigão¹, D. Ramos Silva², J. Chaves¹, M. Dinis-Ribeiro¹, C. Lopes Brandão¹

¹Portuguese Oncology Institute of Porto, Gastroenterology, Porto, Portugal, ²Hospital Amato Lusitano, Gastroenterology, Castelo Branco, Portugal

Contact E-Mail Address: claudia.marquespinto@gmail.com

Introduction: Colonic polyposis syndromes are not only characterized by colorectal adenomas but also as duodenal and ampullary adenomas. Duodenal endoscopic surveillance should include evaluation of the papilla of Vater by duodenoscopy.

Aims & Methods: Our aim was to evaluate the effectiveness of cap assisted endoscopy in the observation of the duodenal mucosa and particularly of the major papilla.

Patients with Familial Adenomatous Polyposis (FAP), MUTYH-associated Polyposis (MAP) or Polyposis without identified mutation with indication for surveillance were proposed to cap assisted endoscopy under sedation. The duodenal evaluation was considered completed if both the third duodenal portion and major papilla (including its orifice) were completely observed. When this evaluation was not accomplished, conventional duodenoscopy was performed.

Results: We included twenty-two (22) patients (n=16 FAP, n=4 MAP, n=2 polyposis without identified mutation) with a median age of 47 years. Thirteen (59%) were male. The major papilla was completely observed with cap assisted endoscopy in 21 (95.5%) patients. There was only one exam in which it was necessary to perform subsequent duodenoscopy. The mean time until identification of the papilla was 2 minutes and 15 seconds.

The difficulty in the evaluation of the major papilla was considered "easy" in 73% (n=16) and "medium" in 23% (n=5) of exams. Duodenal polyps were identified in 50% (n=11) and the papilla was described as adenomatous 32% (n=7). No exam required cap removal due to inadequate observation of the mucosa (esophageal, gastric or duodenal).

Conclusion: Cap assisted endoscopy seems to be a better alternative to duodenoscopy, allowing simultaneous conventional endoscopic procedure and major papilla evaluation. It may simplify surveillance protocols in these patients, with lower procedure time and friendly usability.

Disclosure: Nothing to disclose.

P0893

SUBJECTIVE ASSESSMENT OF THE PYLORIC SPHINCTER DURING ENDOSCOPY AND ITS CORRELATION IN FLIP PANOMETRY

I. Levenfus¹, J. Hente¹, M.C. Pott¹, D. Pohl¹

¹University Hospital Zurich, Gastroenterology and Hepatology, Zurich, Switzerland

Contact E-Mail Address: ian@levenfus.com

Introduction: Visual or haptic assessment of the pylorus during endoscopy sometimes results in the diagnosis of a pylorospasm. However, the visual assessment is a subjective evaluation and may be affected by inter-rater variability, the antro-duodenal motility phase as well as the distance to scope and has not been validated against technical measurements of pyloric dimensions.

We evaluated to what extent the visual impression and the endoscopic resistance of the pyloric sphincter correlates with objectively determined EndoFLIP measurements.

Aims & Methods: Patients scheduled for FLIP panometry of the upper gastrointestinal tract due to different medical conditions from January until November 2021 were considered for the study. Inclusion criteria were an EndoFLIP measurement of the pylorus using a standardized protocol for distensibility assessment (normal > 10 mm²/mmHg, borderline 8 - 10 mm²/mmHg, pathologic < 8 mm²/mmHg) as well as a documented visual impression of the pylorus size and resistance towards endoscopic intubation. The visual impression was evaluated at 10 cm distance to the pylorus by an experienced endoscopist (senior) as well as a fellow (junior) and the perceived state (tight, normal, wide) was documented for both participants separately.

Afterwards, the experienced endoscopist passed the endoscope through the pylorus to the duodenal bulb and endoscopic resistance (none, normal, strong) was documented. To quantify inter-rater variability, visual impressions by senior and junior were compared.

Results: A total number of 89 patients (65% female) with a mean age of 47.9 years ± 18 SD were included (range 15 to 87 years). In 81 patients, a visual assessment of the pylorus was performed. The endoscopic resistance was documented in 87 patients.

Group comparisons of distensibility measurements between each visually assigned group (tight, normal, wide) indicated significant differences ($p < .01$). In 76 % of cases, the visual impression of a closed pylorus was associated with a pathologic distensibility during EndoFLIP measurement. No significant differences regarding distensibility were found for endoscopic resistance. The specificity of a predicted pathologic pylorus distensibility based on visual assessment by a senior endoscopist was 85.7% with a sensitivity of 48.7% (PPV 0.76, NPV 0.64) when using the 8 mm²/mmHg cutoff for pylorospasm. The visual impression of the senior and junior investigators matched in 93.8% of the cases.

Conclusion: The visual assessment of the pyloric sphincter has a low sensitivity yet surprisingly high specificity in recognizing pylorospasm as objectified using FLIP panometry. This underlines the importance of measurements, not estimates, in the evaluation of pyloric function.

Disclosure:

Daniel Pohl is a consultant for Medtronic. All other authors disclose no conflicts of interest or financial relationships.

P0894

IMMEDIATE DISCHARGE AFTER PERCUTANEOUS ENDOSCOPIC GASTROSTOMY TUBE REMOVAL IN HEAD AND NECK CANCER PATIENTS IN ONCOLOGICAL REMISSION: A FEASIBILITY AND SAFETY STUDY

F. Francisco¹, S. Faia¹, I. Frade¹, P. Cruz¹, J. Gramacho¹, I. Claro¹

¹Instituto Português de Oncologia de Lisboa - IPOLFG, Gastroenterology, Lisboa, Portugal

Contact E-Mail Address: fatimafrancisco@sapo.pt

Introduction: In head and neck cancer patients (HNC), a significant number of percutaneous endoscopic gastrostomies (PEG) procedures are prophylactic (patients without significant dysphagia prior to starting chemoradiotherapy therapy). These patients require PEG tubes that provide exclusive or complementary enteral nutritional support to oral intake during chemoradiotherapy. Insufficient oral intake is due to anorexia and dysphagia generated by cancer and mucositis caused by cancer treatment. After treatment, patients with complete oncological response who reestablish adequate oral, a PEG tube removal procedure is scheduled.

Aims & Methods: To evaluate the feasibility and safety of PEG tube removal in patients with HNC followed by immediate discharge from the Endoscopy Unit medicated with omeprazole.

Prospective, observational, unicentric study. The current protocol assumes PEG tube removal with discharge to the outpatient clinics 30 minutes after the procedure and re-initiation of cold liquid diet after 3 hours. Additionally, patients get a prescription of omeprazole 40 mg bid orally for the next 4 weeks. All patients with PEG tube removal scheduled between October 2020 and February 2022 were included. We performed a descriptive statistical analysis.

Results: A total of 113 patients with HNC were referred for PEG removal, including 82 men and 31 women, with a mean age of 59.5±9.75 (range 39-81 years). A total of 103 patients were treated with chemoradiotherapy and 10 with radiotherapy alone.

From these 113 patients with PEG tubes, 104 (92%) had no adverse events related to the procedure, 3 had early infections, 4 late infection (all minor), 1 had immediate pain that prolonged hospitalization for 24 hours, and 1 had an hemoperitoneum that required surgery.

The average duration of PEG was 10.7±5.69 (range 3-30 months).

After PEG removal, 7 (6.19%) patients had a gastrocutaneous fistula patent for more than one month. Resolution of 5/7 fistulas occurred after 4 additional weeks of omeprazole 40 mg bid, 1/7 required endoscopic treatment with clips, and 1/7 had an associated parastomal hernia that was operated.

Conclusion: PEG removal with immediate discharge proved to be safe, with a low rate of complications. It benefited patients in terms of comfort and the Endoscopy Unit by reducing the time and resources allocated, and allowed to eliminate the waiting list for PEG tube removal procedures.

Disclosure: Nothing to disclose.

P1036

DEVELOPMENT AND VALIDATION OF A FEATURE EXTRACTION-BASED LOGICAL ANTHROPOMORPHIC DIAGNOSTIC SYSTEM FOR EARLY GASTRIC CANCER UNDER THE MAGNIFYING IMAGE ENHANCED ENDOSCOPY INCORPORATED WITH PRIOR KNOWLEDGE

J. Li¹, Y. Zhu¹, Z. Dong¹, L. Wu¹, H. Yu¹

¹Renmin Hospital of Wuhan University, Wuhan, China

Contact E-Mail Address: 2646962363@qq.com

Introduction: Early diagnosis of early gastric cancer (EGC) is crucial for improving patients' survival. However, most previous computer-aided diagnosis (CAD) systems did not concretize or explain diagnostic theories.

We aimed to develop a logical anthropomorphic artificial intelligence (AI) diagnostic system named ENDOANGEL-LA (logical anthropomorphic) for EGCs under magnifying image enhanced endoscopy (M-IEE).

Aims & Methods: We retrospectively collected 1897 images from 692 patients from Renmin Hospital of Wuhan University. The images were randomly assigned to the training set and test set by patient with a ratio of about 4:1. ENDOANGEL-LA was developed based on feature extraction combining quantitative analysis, deep learning (DL), and machine learning (ML). Seven quantitative diagnostic feature indexes including microstructures (MS) density, MS eccentricity, diameter ratio of microvessel (MV), MV tortuosity, MV cyclization, spectral principal component information of gastric mucosal background color, and image entropy of S-channel in HSI color space and four DL diagnostic feature indexes including the arrangement of M-IEE images, the demarcation line of lesions, the distribution of MV in the MV segmentation images, and the morphology of the lesions (including elevated, flat, and depressed) were integrated into seven ML models including random forest (RF), Gaussian Naive Bayes (GNB), k-Nearest Neighbor (KNN), logistic regression (LR), decision tree (DT), support vector machine (SVM), and gradient boosting decision tree (GBDT), and an optimal model was selected. The performance of ENDOANGEL-LA was evaluated and compared with endoscopists and sole DL models. The satisfaction of endoscopists on ENDOANGEL-LA and sole DL model was also compared.

Results: RF showed the best performance, and demarcation line and MS density were the most important feature indexes. The accuracy of ENDOANGEL-LA in images (88.76%) was significantly higher than that of sole DL model (82.77%, $p = 0.034$) and the novices (71.63%, $p < 0.001$), and comparable to that of the experts (88.95%). The accuracy of ENDOANGEL-LA in videos (87.00%) was significantly higher than that of sole DL model (68.00%, $p < 0.001$), and comparable to that of the endoscopists (89.00%). The accuracy (87.45%, $p < 0.001$) of novices with the assistance of ENDOANGEL-LA was significantly improved. The satisfaction of endoscopists on ENDOANGEL-LA was significantly higher than that of sole DL model.

Conclusion: We established a logical anthropomorphic system named ENDOANGEL-LA which can diagnose EGC under M-IEE with diagnostic theories concretization, high accuracy, and good explainability. It has the potential to increase interactivity between endoscopists and CADs, and improve trust and acceptability of endoscopists on CADs.

Disclosure: Nothing to disclose.

P1037

DETECTION OF GASTRIC NEOPLASMS WITH A NEW HEATMAP-BASED ARTIFICIAL INTELLIGENCE SYSTEM

H.Y. Kang¹, C. Chantaduly², P. Chang³, W. Karnes⁴

¹Seoul National University Hospital, Healthcare System Gangnam Center, Department of Internal Medicine, Seoul, Korea (Republic of), ²Center for Artificial Intelligence in Diagnostic Medicine, University of California, Irvine, United States, ³University of California, Department of Radiological Sciences and Center for Artificial Intelligence in Diagnostic Medicine, Irvine, United States, ⁴University of California, Department of Medicine and H.H. Chao Comprehensive Digestive Disease Center, Irvine, United States

Contact E-Mail Address: haeykang@gmail.com

Introduction: Endoscopic diagnosis of early gastric neoplasms is not easy even for experienced endoscopists. Recent studies showed that artificial intelligence (AI) can achieve high diagnostic accuracy in detecting upper gastrointestinal lesions. However, the endoscopic detection of gastric dysplasia and early gastric cancer (EGC) using AI still remains challenging.

Aims & Methods: We aimed to develop a novel deep learning convolutional neural network (CNN) model for detection and localization of gastric dysplasia and EGC using endoscopic images.

In this study, we included 1,010 consecutive patients (7,818 gastric cancer images and 1,067 gastric dysplasia images) who underwent EGD and were histologically diagnosed at Seoul National University Hospital. All endoscopic lesion images were obtained in 2 dimensions from standard views. Among the endoscopic images, representative images were manually selected from each patient for model development. Each lesion in any given image was manually annotated with a bounding box by one expert endoscopist.

A novel, custom CNN model was designed to predict a dense probability map output estimating likelihood of lesion at each image pixel. Application of various thresholds to the CNN output yields iso-probability lines which may be converted to a corresponding bounding-box prediction. All endoscopic images were randomly assigned to either training ($n=7,108$) or validation cohorts ($n=1,777$) using a five-fold cross-validation scheme. All model predictions were visually inspected for overall accuracy. Spatial overlap of CNN-predicted and ground-truth bounding boxes were evaluated using the Intersection-over-Union (IoU) metric. Additionally, the sensitivity of lesion detection was assessed as a function of minimum IoU overlap.

Results: Upon five-fold cross-validation, the algorithm yielded a median bounding-box IoU for 0.569 (IQR 0.393 to 0.696) across the entire 8,885 image dataset. Using a detection IoU threshold of 0.10, the algorithm was 90.9% sensitive in identifying all gastric dysplasia or EGC lesion in the dataset. In general, the intermediate probability heatmaps generated by the algorithm approximate lesion contours upon visual inspection.

In addition, false negative algorithm predictions that do not meet the minimum threshold for box prediction nonetheless exhibit mildly increased probability scores, suggesting that intermediate prediction heatmaps may be utilized as a high sensitivity diagnostic aid.

IoU Threshold	Sensitivity
0.05	0.91900
0.10	0.90900
0.15	0.89550
0.20	0.87880
0.25	0.85420
0.30	0.82270
0.35	0.78660
0.40	0.74300
0.45	0.68460

Conclusion: In this pilot study, newly developed pixel-based heatmap model was able to detect early gastric cancer and gastric dysplasia in endoscopic images with high accuracy with a speed that allows for real-time implementation. The combination of conventional bounding-boxes and probability heatmap predictions provides complementary values that facilitate the detection of subtle endoscopic findings.

Disclosure: Nothing to disclose.

P1039

A PROSPECTIVE STUDY OF DEVELOPING AND VALIDATING THE EFFECT OF ANARTIFICIAL INTELLIGENT ESOPHAGOGASTRODUODENOSCOPY REPORTING SYSTEM

L. Zhang¹, Z. Lu², L. Yao³, H. Yu¹

¹Renmin Hospital of Wuhan University, Department of Gastroenterology, Wuhan, China, ²Renmin Hospital of Wuhan University, Hubei Key laboratory of Digestive System, Wuhan, China, ³Renmin Hospital of Wuhan University, Hubei Provincial Clinical Research Center for Digestive Disease Minimally Invasive Incision, Wuhan, China

Contact E-Mail Address: 273320630@qq.com

Introduction: Gastrointestinal (GI) disorder is one of the most common diseases in humans, resulting of considerable health care utilization and spending¹. Gastrointestinal endoscopy plays an important role in GI disorder screening with direct mucosal exposure². Gastrointestinal endoscopy reports are the documentations to deliver findings in procedure, and they were essential materials for communication between different endoscopists during medical consultation, transferring treatment, surveillance and et al³.

With the increasing need for precise storage, standard recording of instant finding in both images and literature was especially vital for endoscopy⁴. European Society of Gastrointestinal Endoscopy of societies (ESGE) and the American Society for Gastrointestinal Endoscopy (ASGE) have incorporated standard reporting contents into the criteria for endoscopic quality measurement⁵. Minimal Standard Terminology (MST), accurate photo-documentation of anatomical landmarks and abnormal findings were required for reporting generation⁶. However, reports were sub-optimal in practice, with insufficiency of report contents and low consistency between endoscopists and institutions at present.

In this study, we aim to develop and validate an artificial intelligent system to generate standard structured endoscopic reports during endoscopy. We hypothesize that AI-assistant was effective to ensure the standardization and completeness of endoscopic records, improving the quality of upper gastrointestinal endoscopic reporting.

Aims & Methods: A total of 99174 esophagogastroduodenoscopy (EGD) images were retrospectively collected to conduct this system, 75742 images for anatomical landmarks identifying model, 15256 images for esophageal lesions classifying model, including dysplasia, heterotopic gastric mucosa, submucosal tumor, esophagitis, gastroesophageal reflux and Barrett's esophagus, 21460 images for gastric lesions classifying model, including including dysplasia, submucosal tumor, gastric ulcer, erosion, benign polyp, and xanthelasma. Other models were conducted to capture eligible images during endoscopy, selected by clarity, mucosal exposure, and confidence coefficient of lesion detection. Five-hundred esophagogastroduodenoscopy video clips containing lesions above were collected to validate the performance of the system. Forty-four esophagogastroduodenoscopy were prospectively collected for crossover study which aims to validate effect of the system on improving competence of endoscopic reports among 12 endoscopists.

Results: Our models achieved an accuracy of 90.45% and 89.1%, respectively, to classify gastric and esophagus lesions in image validation. In video validation, the system detected lesions with a sensitivity of 95%, reported lesions with standard structured description with an accuracy of 75.6% and missed only 2% lesions in automatic report. In crossover study, the system improved the completeness (with AI vs without AI: 73.84% vs 52.21%) and accuracy (with AI vs without AI: 65.87% vs 46.32%) of gastric lesions records. The reporting time with AI assistance was a little longer than that of traditional reporting system (191.76 seconds vs 175.87 seconds).

Conclusion: In this study, an artificial intelligent based system was developed and validated to generate structured literal recording and image capture. Its effect on improving the standardness, completeness and precise of endoscopic reports has been validated. This system holds the potential to facilitate and standardize endoscopic reporting procedure in clinical practice.

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Disclosure: Nothing to disclose.

P1040

EFFECT OF AN AUTOMATED FLEXIBLE ENDOSCOPE CHANNELS BRUSHING SYSTEM ON IMPROVING THE REPROCESSING QUALITY: A PROSPECTIVE, RANDOMIZED CONTROLLED STUDY

R. Shang¹, J. Liu¹, H. Yu¹

¹Renmin Hospital of Wuhan University, Department of Gastroenterology, Wuhan, China

Contact E-Mail Address: riddle@whu.edu.cn

Introduction: Qualified reprocessing, of which meticulous channels brushing is the most crucial step, is essential for the prevention and control of endoscopy-associated infections. However, channels brushing is often omitted in practice, due to the pressure of endoscope turnover, the lack of reprocessing technicians and weak supervision.

Aims & Methods: This single-center, prospective, randomized controlled study aimed to evaluate the effect of an automated flexible endoscope channels brushing system (AECBS) on reducing bioburden and improving the quality of endoscope reprocessing. This study was conducted, between Nov 24, 2021 and Jan 22, 2022, at Renmin Hospital of Wuhan University, China. Eligible endoscopes were randomly allocated to the auto group (channels brushed by AECBS) or the manual group (channels brushed manually), with sampling and culturing after high-level disinfection and drying. The primary endpoint was the positive rate of cultures for endoscopes.

Results: 204 endoscopes in the auto group and 205 in the manual group were eventually analyzed. The positive rate of cultures was significantly lower in the auto group than in the manual group (15.2% vs 23.4%, relative risk 0.649 [95% CI 0.432-0.976]; p=0.035).

Conclusion: AECBS could reduce the endoscope bioburden and improve the reprocessing quality. It has great potential to replace manual channels brushing and lower the risk of endoscopy-associated infections, providing a new idea for the optimization of reprocessing protocols.

Disclosure: Nothing to disclose.

P0895

EVALUATION OF STANDARD BOWEL PREPARATION REGIMES VERSUS PLENVU (NOVEL LOW VOLUME REGIME): CLEANSE STUDY

A. Ahmad¹, S. Marshall¹, K. Thiruvilangam¹, A. Dhillon¹, B.P. Saunders¹

¹Wolfson Unit for Endoscopy, Imperial College London, London, United Kingdom

Contact E-Mail Address: ahmir.ahmad@nhs.net

Introduction: Poor bowel preparation is the leading cause of failed colonoscopies and increases procedure costs significantly. Poor preparation affects procedure quality and efficiency. Several 2 day regimes are currently available and recently, Plenvu, a low-volume regime that can be administered on the same day for afternoon/evening appointments has emerged.

Aims & Methods: The aim of this study is to assess efficacy and tolerability of bowel preparation regimes.

In this service evaluation, patients undergoing bowel cancer screening colonoscopy at St Mark's Hospital, London (Feb 2020-Dec 2021) were provided Plenvu (1 or 2 day regime), Moviprep (2 day regime), or Senna & Citramag (2 day regime).

During the colonoscopy, the Boston Bowel Preparation Scale (BBPS) score, fluid volumes, and procedure times were recorded. In addition, patients completed a bowel preparation experience questionnaire including assessment of taste, volume acceptability, completion and side effects.

Results: There were 545 patients invited to participate with 10 exclusions (flexible sigmoidoscopies). Of 535 included patients there were: 214 Moviprep 2 day, 108 Senna & Citramag 2 day, 150 Plenvu 2 days, and 63 Plenvu 1 day.

	Moviprep 2 day	Senna & Citramag 2 day	Plenvu 2 days	Plenvu 1 day	P value
n	214	108	150	63	
Boston Bowel Preparation Scale score (mean)	7.0	6.7	7.6	7.6	<0.001
Net fluid volume (mL; total introduced – total suctioned)	-82	-121	-125	-167	0.10
Total procedure times (minutes)	25.0	23.6	25.4	28.8	0.03
Inadequate preparation requiring repeat colonoscopy or CTVC (%)	6.1% (13/214)	6.5% (7/108)	7.3% (11/150)	3.2% (2/63)	0.72

Table 1. Summary of bowel preparation regime outcomes

BBPS scores were significantly higher in the Plenvu 1 day and 2 day regimes (p=0.01 and 0.001 respectively) compared with Senna & Citramag. BBPS score was also significantly higher in the Plenvu 2 day group compared with Moviprep (p=0.007). There were no other significant differences in BBPS score between regimes. There was no significant difference in inadequate bowel preparation rates between the groups (p=0.72).

In the patient questionnaire, taste was rated to be most pleasant with Senna & Citramag which achieved statistical significance when compared with Plenvu 1 day and 2 day groups (p<0.001) and compared with Moviprep (p=0.01).

Conclusion: In this service evaluation, there was a significantly improved BBPS score for both 1 day and 2 day Plenvu regimes compared with Senna & Citramag, and an improved BBPS score for 2 day Plenvu compared with Moviprep. Plenvu may offer the potential for improved bowel preparation outcomes with the potential advantage for patients of a lower volume and same-day administration for afternoon/evening appointments.

Disclosure: Nothing to disclose.

P0896

AUTOMATED MEASUREMENT OF COLONOSCOPY WITHDRAWAL TIME USING CONVOLUTIONAL NEURAL NETWORKS

R. Kader^{1,2,3}, T.d. Carvalho^{2,4}, P. Brandao⁴, D. Toth⁴, O. Ga Young^{1,2}, S.-P. Leung^{1,2}, R. Vega^{3,2}, E. Seward^{3,2}, P. Mountney⁴, D. Stoyanov^{1,2}, L. Lovat^{1,2,3}

¹University College London (UCL), Wellcome/EPSCRC Centre for Interventional and Surgical Sciences (WEISS), London, United Kingdom, ²University College London, Division of Surgery and Interventional Sciences, London, United Kingdom, ³University College London Hospital, Gastroenterology, London, United Kingdom, ⁴Odin Vision, London, United Kingdom

Contact E-Mail Address: rawen.kader.17@ucl.ac.uk

Introduction: Withdrawal time (WT) is a key performance indicator of colonoscopy. It is defined as the time taken from the endoscope reaching the caecum to exiting the anal canal minus time spent cleaning the colon and performing interventions such as polypectomy. Deducting these phases from the WT is not feasible in clinical practice as it requires manual measurement in real-time. The result is inaccuracies in the measurement of endoscopists WT. Recent years has demonstrated the ability of artificial intelligence (AI) models to measure WT by detecting caecal landmarks and the anal verge. However, its potential to detect phases of cleaning and intervention during withdrawal is yet to be explored.

Aims & Methods: Our aim was to develop convolutional neural networks (CNN) to detect phases of cleaning and intervention during colonoscopy withdrawal.

Lower gastrointestinal endoscopy videos were prospectively collected at a single centre. Individual video frames after the appendicular orifice or ileocaecal valve were first detected was reviewed. Frames during 'cleaning' and 'intervention' were annotated with image-level labels, with the remaining frames contributing to the procedural WT ('withdrawal' frames). The annotations were referenced as the gold standard.

The interventional phase was defined as:

1. Frames where the forceps were visualised
2. The first frame an instrument was visualised during polypectomy (e.g. injection needle, snare) up until the end of inspecting the resection margins post-polypectomy ('intervention'). The cleaning phase was defined as frames during suctioning of colonic content or washing colonic mucosa ('cleaning').

Two ResNet-101 CNNs pre-trained on ImageNet were developed to detect the phases of cleaning and intervention. For both CNNs, a prediction score of 0.66 – 1.0 was defined as a 'cleaning' or 'interventional' frame, and 0.0 – 0.65 as a 'withdrawal' frame.

Results: The dataset consisted of 87 procedures and 1,288,319 annotated video frames from the withdrawal of the colonoscope (Table 1). The videos were split into training (70%), validation (10%) and testing (~20%) with no overlap of patients.

	Withdrawal frames	Cleaning frames	Intervention frames	Total frames (withdrawal only)
Frame count	437,359	232,384	618,576	1,288,319

Table 1: Breakdown of the frame count of the three phases of withdrawal ('cleaning', 'intervention', 'withdrawal') in the dataset which consisted of a total of 87 videos.

Evaluated against a test set of 17 videos, on a per-frame analysis, the CNNs identified the interventional frames with 92.4% sensitivity, 95.8% specificity, 95.0% accuracy and area under the curve (AUC) of 94.1%. For cleaning, the sensitivity was 83.0%, specificity 89.5%, accuracy 88.2% and AUC of 86.3%.

Across the 17 videos, there was a total of 306 minutes of withdrawal (including cleaning and intervention phases) with a mean WT of 8 minutes and 51 seconds. The absolute mean error of the AI predicted WT was 39 seconds per procedure. The AI system correctly categorised a procedure as less than or more than 6 minutes in 16 of the 17 procedures (94%). One procedure of more than 6 minutes was incorrectly categorised as under 6 minutes.

Conclusion: This pilot study demonstrated the feasibility of CNNs to differentiate the phase of withdrawal and its potential to fully automate measurement of colonoscopy withdrawal time.

Disclosure: Professor Laurence Lovat and Professor Danail Stoyanov are shareholders in Odin Vision.

P0897

EFFECTIVENESS AND SAFETY OF 1L PEG-ASC VERSUS STANDARD BOWEL PREPARATIONS FOR COLONOSCOPY: A SYSTEMATIC REVIEW AND META-ANALYSIS

M.F. Maida¹, M. Ventimiglia², A. Vitello¹, E. Sinagra³, G. Marasco^{4,5}

¹S. Elia-Raimondi Hospital, Gastroenterology and Endoscopy Unit, Caltanissetta, Italy, ²Italian Ministry of Health, Directorate General of Medical Device and Pharmaceutical Service, Rome, Italy, ³Fondazione Istituto San Raffaele Giglio, Gastroenterology and Endoscopy Unit, Cefalù, Italy, ⁴IRCCS Azienda Ospedaliero-Universitaria di Bologna, Bologna, Italy, ⁵University of Bologna, Department of Medical and Surgical Sciences, Bologna, Italy

Contact E-Mail Address: marcello.maida@hotmail.it

Introduction: A 1L polyethylene glycol plus ascorbate (PEG-ASC) bowel preparation has been recently developed to improve patients' experience in colonoscopy.

Aims & Methods: This meta-analysis aims to estimate the effectiveness and safety of 1L PEG-ASC vs other bowel preparations for colonoscopy. MEDLINE via PubMed, Ovid Embase, Scopus and Cochrane Library were systematically searched through March 2022 for studies comparing 1L PEG-ASC vs other bowel preparations.

Cleansing success (CS) was defined by a total BBPS $\geq$ 6 with a partial BBPS $\geq$ 2 in each segment, and high-quality cleansing (HQC) of the right-colon by a partial BBPS=3. The adenoma detection rate (ADR) was defined by the percentage of patients with at least one adenoma in the analyzed population. Safety was evaluated through number of patients with AEs and the overall number of AEs. A random-effect model was applied for pooling results; heterogeneity was expressed as I^2 .

Results: Eleven studies met the inclusion criteria and were included in the meta-analysis (nine RCTs, two prospective observational studies, 5474 participants).

The analysis showed a significant higher CS for 1L PEG-ASC compared to other preparation both overall (OR 1.66; 95% CI 1.35-2.05; $p<0.01$, $I^2=34\%$) and in the split regimen subgroup (OR 1.44; 95% CI 1.17-1.77; $p<0.01$, $I^2=0\%$), as well as a significant greater HQC of the right colon overall (OR 2.00; 95% CI 1.41-2.85; $p<0.01$, $I^2=74\%$) and in the split regimen subgroup (OR 1.77; 95% CI 1.30-2.43; $p<0.01$, $I^2=57\%$).

The pooled estimate of ADR showed no significant difference among the two groups either overall (OR 1.02; 95% CI 0.87-1.20; $p=0.79$, $I^2=0\%$), or in the split regimen subgroup (OR 0.99; 95% CI 0.84-1.18; $p=0.94$, $I^2=0\%$).

A significant higher pooled estimate of patients with adverse events (AEs) (OR 1.35; 95% CI 1.05-1.73; $p=0.02$, $I^2=45\%$) and of AEs incidence (IRR 1.28; 95% CI 1.09-1.52; $p<0.01$, $I^2=71\%$) was observed for 1L PEG-ASC compared to other preparations. No serious AEs or deaths occurred.

Subgroup analysis including only studies comparing 1L PEG-ASC vs 2L PEG-ASC confirmed a significant higher CS (OR 1.52; 95% CI 1.16-1.99; $p<0.01$, $I^2=0\%$), as well as a greater HQC of the right colon (OR 1.86; 95% CI 1.43-2.42; $p<0.01$, $I^2=0\%$) for 1L PEG-ASC compared to 2L PEG-ASC. Also in this case, the analysis showed no difference in the pooled estimate of ADR among the two groups (OR 1.07; 95% CI 0.84-1.36; $p=0.60$, $I^2=0\%$) and a significant higher pooled estimate of patients with AEs (OR 1.56; 95% CI 1.17-2.09; $p<0.01$, $I^2=0\%$) for 1L PEG-ASC compared to 2L PEG-ASC.

Conclusion: Compared to traditional preparations, 1L PEG-ASC showed higher overall CS and HQC of the right-colon, and similar ADR. A significant higher number of patients with AEs and total AEs was observed for 1L PEG-ASC in the absence of serious AEs.

Disclosure: Marcello Maida served as advisory board member and received lecture grants from Norgine. Giovanni Marasco received consultation fees from AlfaSigma.

P0898

COMAPRISONS UNDERWATER ENDOSCOPIC SUBMUCOSAL DISSECTION AND CONVENTIONAL ENDOSCOPIC SUBMUCOSAL DISSECTION FOR SUPERFICIAL COLORECTAL NEOPLASIAS

C.K. Oh¹

¹The Hallym University of Korea, Hallym University Kangnam Sacred Heart Hospital, Division of Gastroenterology, Department of Medicine, Seoul, Korea (Republic of)

Contact E-Mail Address: ckdryekd@gmail.com

Introduction: Colorectal endoscopic submucosal dissection (ESD) remains challenging because of technical difficulties, long procedure time, and high risk of adverse events. The underwater ESD provides a clearer view and better traction of the submucosal layer compared with the conventional ESD. This pilot study aimed to compare the efficacy and safety between underwater ESD and conventional ESD in patients with superficial colorectal neoplasias (20-50 mm).

Aims & Methods: In this pilot study, we conducted underwater ESD and conventional ESD at each groups. This pilot study was conducted from May 2021 to March 2022. Exclusion criteria were as follows:

1. Lesions located at appendiceal orifice, ileocecal valve, anal involve,
2. Lesions exceed 50 mm on colonoscopy,
3. Patients with inflammatory bowel disease, uninterrupted antithrombotic therapy, and coagulopathy. Primary outcome was procedure time. Secondary outcomes were en bloc rates, complete resection rates, and adverse events.

Results: Twenty patients were included in this study. 10 patients were assigned to each group. Procedure time (median [range]) for the underwater ESD group was significantly shorter than that for the conventional ESD group (46.5 [20 - 74] min vs 68 [22 - 98] min, respectively; $P=0.035$). There were no significant difference in complete resection rates (100% vs 100%, $p=1.000$), en bloc resection rates (100% vs 100%, $p=1.000$), and mean size of lesions (33.8 ± 6.8 mm vs 33.1 ± 7.9 mm, $P=0.833$) between underwater ESD and conventional ESD. The adverse events rate was not significantly different between both groups.

Conclusion: In this pilot study, underwater ESD reduced the procedure time. Underwater ESD can be an alternative method for resection of superficial colorectal neoplasias. However, further prospective randomized controlled trials are needed to ensure our pilot study results of underwater ESD in superficial colorectal neoplasias.

Disclosure: Nothing to disclose.

P0899

THE SNARE DEVICE WITH THINNER LOOP WIRE COULD PROVIDE HIGHER PERFORMANCE FOR COLD SNARE POLYPECTOMY IN AN EXPERIMENTAL MODEL

K. Maejima¹, S. Ono^{2,1,3}, S. Ito¹, S. Hosaka^{2,1}, K. Umeki¹, S. Sato¹, K. Akamine⁴, D. Asai⁴, M. Fujishiro³

¹Chiba-Nishi General Hospital, Gastroenterology, Chiba, Japan,

²Tokyo Metropolitan Geriatric Medical Center, Tokyo, Japan,

³University of Tokyo, Endoscopy & Endoscopic Surgery, Tokyo, Japan,

⁴Chiba-Nishi General Hospital, Surgery, Chiba, Japan

Contact E-Mail Address: ykuhioe.sky-xxx-ju.a@ezweb.ne.jp

Introduction: Snare devices play an important role for the treatment of intestinal polyps. However, there are no objective measurements for the characteristics of the various types of snare devices.

Aims & Methods: This study was aimed to characterize snares related to the quality of cold snare polypectomy. Seven snare devices from four manufactures were evaluated by the original measurements. The evaluated factors were stiffness, cutting quality, and the change in force required for cutting depending on the shape of the sheath. The latter two factors were evaluated by measuring the force required to cut 20% gelatin-cylinders, which simulated intestinal polyps. The cutting sharpness was evaluated by observation of the sectional surface of cut gelatin-cylinders using a stereoscope. The correlation between these measurements and the characteristics of the snare devices were investigated.

Results: A strong positive correlation, with an R^2 value of 0.863, was shown between the force required to cut gelatin-cylinders and the loop wire diameter. The loop wire diameter also had a strong correlation, with an R^2 value of 0.799, with the change in force required for cutting gelatin-cylinders depending on the shape of the sheath. No correlations were detected between the loop stiffness and the characteristics of the snare devices. Further, the edge-enhanced image revealed that the rougher surfaces of the gelatin-cylinders were cut by snares with a thicker diameter.

Conclusion: The thinner loop wire could provide a higher performance in cold snare polypectomy in an experimental model.

Disclosure: Nothing to disclose.

P0900

FACTORS AFFECTING POLYP DETECTION ON SCREENING COLONOSCOPY: A PROSPECTIVE OBSERVATIONAL STUDY

A. Ioannou¹, G. Sachtouris², I. Marakis², E. Manthopoulou², E. Michalopoulou², I. Patakos², X. Tsamakidis², A. Kontos², N. Saribegioglou², S. Stavriniadis², D. Kypraios², D. Dimitroulopoulos², K. Tsamakidis²

¹Aretaieio University Hospital, Kapodistrian University of Athens, Gastroenterology Unit, Athens, Greece, ²St. Savvas Oncology Hospital, Gastroenterology, Athens, Greece

Contact E-Mail Address: gsaxtoug@gmail.com

Introduction: Colonoscopy is currently the best modality for the detection of colorectal polyps and colorectal cancer (CRC), which is the third most common malignancy worldwide. The development of CRC can be prevented when the detection of colon adenoma is followed by polypectomy. Therefore revealing factors affecting polyp detection is very important for CRC prevention.

Aims & Methods: This study aimed to investigate factors affecting polyp detection in patient undergoing colonoscopy. Epidemiological, clinical and preparation data of patients undergoing colonoscopy in our department were prospectively collected. Age, sex, body mass index, history of digestive surgery, constipation, diabetes, thyroid disease, medica-

tion intake, type of preparation, method of administration, liquid intake and Boston bowel preparation scale (BBPS) were statistically analyzed, through multivariate analysis and correlated with polyp detection.

Results: Data of 775 consecutive patients (415 F, Av.Age 68.9) were analyzed. Average BMI was 27.5 (<18.5: 8.7%, 18.5-24.9: 34.7%, 25-29.9: 34.1%, >30: 24.9%). Clinical data analysis reveals 191 (24.6%) patients affected by constipation according to Rome IV criteria, 152 (19.61%) by hypothyroidism, 100 (12.9%) by type 2 diabetes. 308 (39.7%) patients had an abdominal surgery history and 75 (9.7%) were using anxiolytic therapy. BBPS data analysis demonstrate 142 (18.3%) non adequate and 663 (81.7) adequate bowel preparations (BBPS 0-6 and BBPS 7-9 respectively). 128 (16.5%) underwent split-dose while 647 (83.5%) non-split-dose bowel preparation. Multifactorial statistical analysis reveals that higher BMI ($p=0.016$), male sex ($p=0.014$), adequate BBPS ($p=0.016$), constipation ($p=0.015$), diabetes ($p=0.021$), higher liquid intake ($p=0.032$) positively correlates with polyp detection on screening colonoscopy.

Conclusion: Patients with high BMI, male sex, adequate BBPS, high liquid intake in bowel preparation, constipation and diabetes positively correlates with polyp detection. These factors are directly affecting the diagnostic outcome of their colonoscopy.

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Disclosure: Nothing to disclose.

P0901

QUALITY OF COLONOSCOPY IN A LARGE ENDOSCOPY CENTER IN ESTONIA

T. Zimmerer¹, M. Tammaru², A.-L. Velsberg¹

¹East-Tallinn Central Hospital, Centre for Gastroenterology, Tallinn, Estonia, ²East-Tallinn Central Hospital, Research office, Tallinn, Estonia

Contact E-Mail Address: Thomas.Zimmerer@itk.ee

Introduction: Regular control of colonoscopy quality parameters is essential to ensure save and state of the art treatment for patients undergoing colonoscopy (1). We report the results of a colonoscopy quality study from our endoscopy unit in the East Tallinn Central Hospital in Tallinn, Estonia.

Aims & Methods: We evaluated cecal intubation rate, bowel preparation quality, adenoma detection rate (ADR) and draw back time for all colonoscopies performed in the year 2000. Since 01.01.2020, cecal intubation, bowel preparation quality (using a 4 grade scale: excellent, good, fair, inadequate) and draw back time are documented prospectively for each colonoscopy. To assess ADR we correlated polypectomy codes and histology diagnosis codes in patients ≥ 50 years and without chronic inflammatory bowel disease.

Results: 2691 colonoscopies were performed in our unit. The mean age of the patients was 60,4 years, 2074 (77%) of patients were ≥ 50 years old. 1772 (65,8%) colonoscopies were diagnostic ambulatory procedures, 418 (15,5%) day surgery procedures in sedation, 501 (18,6%) colonoscopies were performed in hospitalized patients, 432 (16,15) colonoscopies were performed within the national large bowel cancer screening program. Referring physicians were gastroenterologists in 71,1%, surgeons in 9,2%, family practitioners in 7,1% and other specialties (e.g. internal medicine, oncology) in 12,6%. The colonoscopies were performed by 6 gastroenterologists, doing each 402 procedures in average (n: 212 – 556).

Colonoscopy quality parameters were documented in 94,7% (2550) of the procedures. Cecal intubation rate was 95,3%, the bowel preparation was adequate (excellent, good or fair) in 85,8% of the patients, the draw back time in procedures without intervention was at least 6 min in 99,1%.

The average ADR in patients ≥ 50 years and without chronic inflammatory bowel disease was 29%, ranging from 16,8% - 37,9% between individual endoscopists.

Comparing different patient groups we found significant differences in the bowel preparation quality between ambulatory and hospitalized patients (adequate 87,9% vs. 74,9%; $p < 0,001$). In ambulatory patients the bowel preparation quality differed significantly between the referring specialty, being inadequate in 11% of patients referred by a gastroenterologist, 17% of patients referred by a family practitioner, 19% in patients referred by a surgeon and 28,7% in patients referred by another specialty ($p < 0,001$). The bowel preparation was the best in bowel cancer screening patients (adequate 90,6%).

Also the cecal intubation rate differed significantly between ambulatory and hospitalized patients (96,4% vs. 91,4%, $p < 0,001$). The ADR in screening colonoscopy patients was 58,1%, 40,2% in hospitalized patients and 23,3% in patients with diagnostic colonoscopy.

Conclusion: This is the first study reporting colonoscopy quality parameters from a large endoscopy unit in the Baltic states. Regarding cecal intubation rate, average ADR and draw back time our unit fulfills the minimum quality thresholds of ESGE. However, there is a need for improvement of ADR in individual endoscopists.

The main problem of colonoscopy quality in our unit is the high rate of inadequate bowel preparation in hospitalized patients and ambulatory patients referred by other specialties. Upon these results we plan to optimize the bowel preparation process in hospitalized patients and launch a study to clarify the reasons for inadequate bowel preparation in ambulatory patients. Colonoscopy quality will be part of an annual clinic quality audit in future.

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Disclosure: Nothing to disclose.

P0902

CLINICAL OUTCOMES AND RISK FACTORS RELATED WITH POOR PROGNOSIS AFTER ENDOSCOPIC RESECTION IN ≥ 10 MM SIZED RECTAL NEUROENDOCRINE TUMOR: A MULTICENTER, RETROSPECTIVE STUDY

H.W. Kim¹, D.-H. Baek², H.-S. Lee³, J.-Y. Lee⁴, S.B. Park¹, D.-H. Kang¹, C.W. Choi¹, S.-J. Kim¹, H.S. Nam¹, D.G. Ryu¹

¹Pusan National University Yangsan Hospital, Internal Medicine, Yangsan, Korea (Republic of), ²Pusan National University Hospital, Internal Medicine, Pusan, Korea (Republic of), ³Inje University Busan Paik Hospital, Internal Medicine, Pusan, Korea (Republic of), ⁴Dong-A University Hospital, Internal Medicine, Pusan, Korea (Republic of)

Contact E-Mail Address: mdkhwook@gmail.com

Introduction: The curative treatment of rectal neuroendocrine tumor (NET) is an endoscopic or surgical resection, but the efficacy of endoscopic resection for ≥ 10 mm sized rectal NET remains controversial.

Aims & Methods: We evaluated the clinical outcomes and risk factors related with poor prognosis after endoscopic resection for the confirmation the efficacy and proper indication of endoscopic resection in these cases. From January 2009 to November 2020, ≥ 10 mm sized rectal NETs resected by endoscopic methods in four tertiary hospitals were enrolled and the data related with clinical outcomes and prognosis were retrospectively analyzed.

Results: A total of 105 rectal NETs resected by endoscopic methods (ESD (n=65, 61.9%), modified EMR (n=31, 29.5%), conventional EMR (n=9, 8.6%)) were enrolled. The mean follow-up period was 33.8 ± 28.1 months. In gross/endoscopic findings, the mean size was 11.6 ± 2.2 mm, the shape was mostly polypoid (96.2%), and depression in surface was showed in 41.9%. In histologic findings, G1 and G2 in WHO classification was showed in 87.6% and 12.4% respectively. In clinical characteristics and outcomes according to endoscopic methods, large size ($P = 0.01$) and long procedure time ($P < 0.01$) were significantly related to ESD group, respectively. In margin involvement in histology, depression in the surface ($P = 0.02$) was only significant related. Regional or distant recurrences developed in 3 patients (2.9%) and were significantly related to female gender ($P = 0.045$), redness in surface ($P = 0.046$), G2 in WHO classification ($P = 0.04$) and non-ESD methods ($P = 0.041$).

Conclusion: Endoscopic resection of large rectal NET had good prognosis, but, the risk factors with female gender, redness in surface, G2 WHO classification and non-ESD methods were associated with regional or distant recurrences. Therefore, the patients with above risk factors may require careful monitoring.

Disclosure: Nothing to disclose.

P0903

AUTOMATED DETECTION OF ANATOMICAL LANDMARKS DURING COLONOSCOPY USING A DEEP LEARNING MODEL

M. Taghiakbari¹, S. Hamidi Ghalehjegh², E. Jehanno², T. Berthier², L. di Jorio², A.N. Barkun³, M. Takla¹, M. Bouin⁴, E. Deslandres⁴, S. Bouchard⁴, S. Sidani⁴, Y. Bengio⁵, D. von Renteln⁴

¹University of Montreal, University of Montreal Hospital Research Center (CRCHUM), Montreal, Canada, ²Imagia Canexia Health Inc., Montreal, Canada, ³McGill University, Division of Gastroenterology, McGill University Health Center, McGill University, Montreal, Canada, ⁴University of Montreal, Division of Gastroenterology, University of Montreal Hospital Center (CHUM), Montreal, Canada, ⁵University of Montreal, Montreal, Canada

Contact E-Mail Address: mahtakbar@gmail.com

Introduction: Identification and photo-documentation of the ileocecal valve (ICV) and appendiceal orifice (AO) confirm completeness of colonoscopy examinations. We hypothesized that an artificial intelligence (AI)-empowered solution could help us automatically differentiate anatomical landmarks such as AO and ICV from polyps and normal colon mucosa.

Aims & Methods: We aimed to develop and test a deep convolutional neural network (DCNN) model that can automatically identify ICV and AO, and differentiate these landmarks from normal mucosa and colorectal polyps. We prospectively collected annotated full-length colonoscopy videos of 318 patients undergoing outpatient colonoscopies.

We created three non-overlapping training, validation, and test datasets with 25,444 unaltered frames extracted from the colonoscopy videos showing four landmarks/image classes (AO, ICV, normal mucosa, and polyps). For each landmark, we extracted an average of 30 frames for each time of its appearance. As consecutive frames within a video are correlated, we introduced a stride of 4 frames (i.e., the amount of movement over the frames of a video) for the AO, ICV, and polyp landmarks, and a random stride of between 4 and 15 frames for the normal mucosa landmark during the frame extraction.

All the extracted frames were reviewed and annotated by a team of three clinicians. Using a quality assessment tool, the clinicians examined a total of 86,754 frames (7982 AO, 8374 ICV, 32,971 polyps, and 37,427 normal mucosa) and verified whether or not the frame contained one unique landmark. For this research, all frames were extracted from the white-light

colonoscopies, and all narrow-band imaging frames were excluded. A DCNN classification model was developed, validated, and tested in separate datasets of images containing the four different landmarks.

The primary outcome was the proportion of patients in whom the AI model could identify both ICV and AO, and differentiate them from polyps and normal mucosa, with an accuracy of detecting both AO and ICV above a threshold of 40% (representing a value in which reliable identification of the landmarks can be assumed without increasing false-positive alerts).

Results: We trained a DCNN AI model on 21,503 unaltered frames extracted from the recorded colonoscopy videos of 272 patients, and validated and tested the model on 1,924 (25 patients) and 2,017 (21 patients) unaltered frames, respectively.

The DCNN model used in the current study is an off-the-shelf network based on the Inception V3 architecture¹ and pre-trained on the ImageNet dataset.²

We applied a transfer learning technique to fine-tune the model parameters to the endoscopic images using a cross-entropy loss function and back-propagation algorithm.³

After training and validation, the DCNN model could identify both AO and ICV in 18 out of 21 patients (85.71%), if accuracies were above the threshold of 40%. The accuracy of the model for differentiating AO from normal mucosa, and ICV from normal mucosa were 86.37% (95% CI 84.06% to 88.45%), and 86.44% (95% CI 84.06% to 88.59%), respectively. Furthermore, the accuracy of the model for differentiating polyps from normal mucosa was 88.57% (95% CI 86.60% to 90.33%).

Conclusion: This model offers a novel tool to assist endoscopists with automated identification of AO and ICV during colonoscopy. The model can reliably distinguish these anatomical landmarks from normal mucosa and colorectal polyps. It can be implemented into automated colonoscopy report generation, photo-documentation, and quality auditing solutions to improve colonoscopy reporting quality.

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P0904

MEASURING THE OBSERVER (HAWTHORNE) EFFECT ON ADENOMA DETECTION RATES

M. Taghiakbari¹, D.E. Coman², M. Takla¹, A.N. Barkun³, M. Frija-Gruman¹, M. Bouin⁴, S. Bouchard⁴, E. Deslandres⁴, S. Sidani⁴, D. von Renteln⁴

¹University of Montreal, University of Montreal Hospital Research Center (CRCHUM), Montreal, Canada, ²University of Montreal, Division of Internal Medicine, University of Montreal Hospital Center (CHUM), Montreal, Canada, ³McGill University, Division of Gastroenterology, McGill University Health Center, McGill University, Montreal, Canada, ⁴University of Montreal, Division of Gastroenterology, University of Montreal Hospital Center (CHUM), Montreal, Canada

Contact E-Mail Address: mahtakbar@gmail.com

Introduction: The effectiveness of colonoscopy screening to prevent colorectal cancer (CRC) is directly linked to its procedural quality. An independent observer (Hawthorne effect) can improve colonoscopy procedural quality metrics, including adenoma detection rate (ADR). However, the results of studies are limited or controversial.

Aims & Methods: In a single-center, case-control study, consecutive patients aged 45–80 years who underwent a routine screening or diagnostic colonoscopy at the Centre Hospitalier de l'Université de Montréal (CHUM) were prospectively enrolled.

We aimed to evaluate the colonoscopy quality metrics in a group of patients undergoing screening or diagnostic colonoscopies under stringent observer conditions, meaning all procedural steps and quality metrics were observed and documented during the procedure by an independent research assistant, and each colonoscopy was video recorded in full length (*case group*).

Findings were compared with those of a *control group* of patients in whom standard and routine colonoscopies were performed without any form of procedural observation or documentation. Colonoscopy quality metrics such as polyp, adenoma, serrated lesions, and advanced adenoma detection rates (PDR, ADR, SLDR, AADR), the mean number of adenomas detected per patient (MAP), and the mean number of adenomas and serrated lesions detected per patient (MASP) were compared. A propensity score was estimated to balance baseline patient and procedural characteristics between case and control groups using logistic regression, with the presence of a research assistant as the dependent variable and the following variables as the independent variables: sex (male vs. female), age, colonoscopy indications (screening, adenoma or CRC surveillance, fecal immunologic test [FIT], diarrhea, anemia or bleeding, other [such as a change in bowel habit]), endoscopists (considering the ADRs among endoscopists with various level of experience), period of colonoscopy (performed in the same month), procedure time (morning vs. afternoon procedure, considering lower afternoon ADR due to endoscopist fatigue), and physician-assessed bowel preparation quality (adequate vs. inadequate). Then, the probabilities of increased quality metrics were evaluated through regression analyses weighted by the inversed probability of observation during the procedure (IPTW).

Results: We included a total of 687 patients (327 cases and 360 controls) in the final analyses. The case group had significantly higher PDRs (62.4% vs. 53.1%) and ADRs (39.4% vs. 28.3%) compared with the control group. The SLDR was also higher in the case group than in the control group, but the difference was not significant (7.3% vs. 4.4%; $P = 0.14$). The AADR was not significantly increased.

After adjusting for potential confounders, the ADR and SLDR were 50% (odds ratio [OR] 1.51; 95%CI 1.05–2.17) and more than twofold (OR 2.17; 95%CI 1.05–4.47) more likely to be higher in the case group than in the

control group. The MAP and MASP were significantly increased in the case group compared with the control group ($P < 0.001$). The regression analyses for both metrics demonstrated the direct and significant association between the Hawthorne effect and elevated MAP/MASP.

Conclusion: The presence of an independent observer documenting colonoscopy quality metrics and video recording the colonoscopy resulted in a significant increase in ADR and other quality metrics. The Hawthorne effect should be considered an alternative strategy to advanced devices to improve colonoscopy quality in routine practice.

Disclosure: DvR is supported by a "Fonds de Recherche du Québec Santé" career development award. He has also received research funding from ERBE, Ventage, Pendopharm, and Pentax, and is a consultant for Boston Scientific and Pendopharm. The remaining authors declare that they have no conflict of interest.

P0905

DEEP LEARNING FOR INSTRUMENT RECOGNITION FOR POLYPECTOMIES IN COLONOSCOPY

T.J. Lux¹, Z. Saßmannshausen¹, J. Troya¹, B. Sudarevic^{1,2}, W.G. Zoller², A. Meining¹, A. Hann¹

¹University Hospital Würzburg, Interventional and Experimental Endoscopy (InExEn), Internal Medicine II, Würzburg, Germany,

²Katharinenhospital, Klinikum Stuttgart, Department of Gastroenterology, Hepatology, Pneumology and Infectious Diseases, Stuttgart, Germany

Contact E-Mail Address: TroyaSebas_J@ukw.de

Introduction: Polyp detection and characterization using artificial intelligence already reached the clinic. Artificial intelligence to distinguish and document endoscopic interventions after polyp identification is not established yet.

Aims & Methods: The aim of this work is to recognize endoscopic interventions and differentiate between polypectomy with snare and grasper. A total of 1,083 different examinations from 8 different centers using 4 different processor types were screened for instruments and represented the training dataset (10,449 images in total). 476 of these images contained a grasper, 927 contained a snare. The validation dataset included 50 full-colonoscopy videos that were analysed for the recognition of visible instruments. The highest confidence image in each sequence of at least 2 seconds with continuous and simultaneous detection of polyp and an instrument were presented to a physician for evaluation. The physician rated if the predicted instrument was correct and assigned each image a polyp number to identify duplicates or images without polyp.

Results: Overall, 103 polyp resections, 91 with a snare and 12 with a grasper, were documented in the report of the 50 full-colonoscopy validation data set. The artificial intelligence predicted 133 sequences with polyp and instrument with one representative image per sequence. From these 133 corresponding images, 1 did not contain a polyp and 20 did not predict the correct instrument. For 2 images both were the case. Overall, 111 (83.46 %) predictions were correct. Further analysis revealed that these 111 sequences represented 78 (75.73 %) of the 103 reported polyp resections.

Conclusion: Detection and recognition of endoscopic instruments in colonoscopy using artificial intelligence technology is reliable and achieves high sensitivity. Consequently, the new convolutional neuronal network could be used to automatically generate standardized colonoscopy reports in real-time during the procedure. Thereby, helping the examiner to save time in writing the endoscopic report.

Disclosure: Nothing to disclose.

P0906 WITHDRAWN

P0907

PLENVU (1L PEG PLUS ASCORBATE) VERSUS MOVIPREP (2L PEG PLUS ASCORBATE) IN A COLORECTAL CANCER SCREENING SETTING, A RANDOMIZED CONTROLLED TRIAL (PLEMO)

S. Roepstorff¹, T. Bryrup², M. Rasmussen¹

¹Copenhagen University Hospital Bispebjerg, Digestive Disease Center, Copenhagen NV, Denmark, ²University of Copenhagen, Novo Nordisk Foundation Center for Basic Metabolic Research, Section for Metabolic Genetics, Copenhagen N, Denmark

Contact E-Mail Address: soeren@roepstorff.info

Introduction: Colorectal cancer (CRC) remains the fourth most common cancer worldwide and is responsible for the second highest cancer mortality in developed countries. Screening for CRC with use of faecal occult blood test and subsequent colonoscopy has proven to reduce mortality. Increasing adenoma detection (ADR) rate correlate inversely with the risk of interval cancers, making ADR one of the most important quality indicators in colonoscopy. Polyp detection rate and cecal intubation rate have been shown to correlate inversely with cleansing quality. Recently, studies evaluating the efficacy of a novel 1 litre polyethylene glycol with ascorbate (1L PEG + Asc) versus standard 2 litre polyethylene glycol with ascorbate (2L PEG + Asc) have shown promising results regarding bowel cleansing. Nonetheless superiority of the novel 1L PEG + Asc has not been shown.

Aims & Methods: The aim of this study was to evaluate the bowel cleansing efficacy of either 1L PEG + Asc in a single-center randomized controlled superiority trial. The hypothesize of the study was that participants randomized to 1L PEG + Asc will show superior efficacy of the bowel cleansing compared to participants randomized to 2L PEG + Asc. A power calculation based on an expected cleansing success of 90% in the 2L PEG + Asc and 95% in the 1L PEG + Asc group, a significance level of 5%, a power of 90% and an expected dropout rate of 10% resulted in 637 participants in each group.

Primary endpoint was colonoscopy incompleteness rate due to insufficient bowel cleansing.

Efficacy of the bowel preparation was assessed according to the Boston Bowel Preparation Scale (BBPS). Adequate bowel preparation was defined as a score of ≥ 2 for either right, transverse or left colon. Eligible study participants were participants in the Danish national colorectal screening program. Participants were randomized 1:1 to receive 1L PEG + Asc or 2L PEG + Asc, both administered as evening/morning split-dose. All participants underwent colonoscopy by an experienced endoscopist. Endoscopists and investigators were blinded to the randomization.

EudraCT number: 2018-003304-39

	1L PEG + Asc	2L PEG + Asc	p-value
Overall colonoscopy data, n (%)	617 (98.3)	629 (97.4)	
Complete colonoscopy, n (%)	582 (94.3)	569 (90.5)	0.010*
Incomplete colonoscopy, n (%)	35 (5.7)	60 (9.5)	
Insufficient cleansing	20 (3.2)	46 (7.3)	0.001*
BBPS ≥ 2			
Left colon, mean (sd)	2.72 (0.45)	2.60 (0.49)	<0.001***
Transverse colon, mean (sd)	2.73 (0.44)	2.62 (0.48)	<0.001***
Right colon, mean (sd)	2.71 (0.45)	2.59 (0.49)	<0.001***
Total, mean (sd)	8.16 (1.23)	7.81 (1.33)	<0.001***

* Chi²

** Fisher's Exact test

*** Wilcoxon rank sum test

Table.

Results: From September 2019 until April 2022, 1274 participants were randomized to 1 L PEG + Asc (n=628) or 2 L PEG + Asc (n=646). In the 1L PEG + Asc respective 2L PEG + Asc group 322 (51%) and 310 (48%) were male, mean age was 63.0 (sd 7.6) and 62.9 (sd 7.8) years, ASA classification was 1.76 (sd 0.57) and 1.78 (sd 0.58), 54 (8.6%) and 60 (9.3%) had diabetes and the usual mean Bristol stool score was 3.85 (sd 1.30) and 3.97 (sd 1.24).

Conclusion: In conclusion this single-center randomized controlled superiority trial showed superior bowel cleansing efficacy of 1L PEG + Asc in all colonic parts and resulted in a significantly higher colonoscopic completion rate compared to 2L PEG + Asc.

Disclosure: Norgine provided financial support for study medicine and study nurse salary.

P0908

DEVELOPMENT AND VALIDATION OF THE GLOBAL POLYPECTOMY ASSESSMENT TOOL (GPAT) - A NOVEL ONLINE ASSESSMENT TOOL FOR ANY COLORECTAL POLYPECTOMY

A. De Crem¹, L. Debelis¹, C. Schoonjans², L. Desomer³, J. Anderson⁴, R. Valori⁵, D.J. Tate¹

¹University Hospital of Ghent, Ghent, Belgium, ²AZ Sint-Jan

Brugge-Oostende AV, Brugge, Belgium, ³AZ Delta,

Gastroenterology and Hepatology, Roeselare, Belgium,

⁴Cheltenham General Hospital, Cheltenham, United Kingdom,

⁵Gloucestershire NHS Foundation Trust - Medicine, Gloucestershire NHS Foundation Trust; Cheltenham/GB, Medicine, Cheltenham, United Kingdom

Contact E-Mail Address: djtate@gmail.com

Introduction:

Colorectal polypectomy is commonly incompletely performed with high variability between endoscopists resulting in the potential for interval cancer or repeated procedures. Existing scores to assess polypectomy technique are cumbersome and difficult to use.

Aims & Methods:

We developed a simple, user-friendly online assessment tool for any colorectal polypectomy (small or large polyps (≥ 20 mm), Hot or Cold snare): the Global Polypectomy Assessment Tool (GPAT). [1] We aimed to validate this tool with endoscopists of varied experience through demonstrating the inter-rater agreement.

GPAT was developed using statements derived from a Delphi-consensus between 11 internationally recognized polypectomy-experts. The score has 20 items (Table 1) and calculates an overall quality score and a complexity score. Evidence-based statements and videos demonstrating the technique enhance the reliability of the score.

We included nine endoscopic-view videos of polypectomies and recruited twelve international assessors (4 gastro-enterologists, 2 surgeons, 3 trainees and 3 medical students) via email. The videos were assessed in random order after watching a 2 minute 37 second explanatory video of GPAT. The assessors scored the SMSA-score [2] and GPAT-criteria for each video. The inter-rater agreement was calculated with the Fleiss Kappa-value (κ).

Results: We analyzed 108 GPAT-assessments of 12 assessors.

Moderate agreement on the overall GPAT score was demonstrated for the target population (gastroenterologists κ : 0.413 95%CI [0.348-0.478] and trainee gastroenterologists κ : 0.460 95%CI [0.360- 0.560]). The surgeons and medical students demonstrated fair agreement (respectively κ : 0.381 95%CI [0.226- 0.537] and κ : 0.248 95%CI [0.134-0.362]). Moderate agreement was found when analyzing the SMSA-scores separately for the gastroenterologists (κ : 0.415 95%CI [0.095-0.735] and trainee-gastroenterologists (κ : 0.518 95%CI [0.043-0.993]). Positive feedback was received regarding content and ease of use of GPAT.

Global competencies	- Tip control - Fully appreciates/demonstrates extent of the polyp to be resected - Positioning with respect to the polyp - Technique selected is appropriate for the polyp resected?
Injection Technique	- Correct Plane - Dynamic Injection - Lesion Access improved
Snare Placement Technique	- Stable 6 'o clock position - Stable position with lesion at 6 'o clock OR transformed to 6 'o clock - Snare visualised during placement and closure - Residual islands avoided if piecemeal resection OR macroscopically complete if en-bloc resection attempted
Safety Checks (Hot Snare only)	- Checks mobility in relation to deeper structures prior to resection - Lifts the snare away from the muscularis propria prior to application of diathermy
Defect Assessment	- Looks for, detects and removes residual at margin and within defect - Thermal ablation of the POST EMR margin - Looks for, detects and treats any bleeding vessels within the defect - Looks for, detects and treats Deep Mural Injury ($\geq$ Type 2 on the Sydney Classification)
Accessory Techniques	- Appropriate placement of clips - Appropriate use of Polyp Retrieval device - Appropriate use of the coagulation grasper

Table 1. Components of Global Polypectomy Assessment Tool (GPAT)

Conclusion: This validation demonstrates standardized scoring of colorectal polypectomy quality and difficulty with moderate inter-observer agreement amongst a varied panel of gastroenterologists and trainee-gastroenterologists with similar agreement found for the broadly used SMSA-score.

With further study, GPAT may allow standardized assessment of trainees' polypectomy competency with feedback on performance, demonstration of improvement over time and a method to accredit endoscopists in different levels of polypectomy.

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Disclosure: Nothing to disclose.

P0909

WATER EXCHANGE TECHNIQUE IMPROVES COLONOSCOPY IN PATIENTS WITH SPINAL CORD INJURY - RESULTS OF A MATCHED RETROSPECTIVE COHORT STUDY

T. Brechmann^{1,2}, M. Ach³, T.A. Schildhauer⁴, D. Grasmücke³

¹Berufsgenossenschaftliches University Hospital Bergmannsheil GmbH, Department of Gastroenterology and Hepatology,

Bochum, Germany, ²St. Elisabeth Hospital, Internal

Medicine and Gastroenterology, Gütersloh, Germany,

³Berufsgenossenschaftliches University Hospital Bergmannsheil GmbH, Department of General and Trauma Surgery, Spinal Cord

Injury Unit, Bochum, Germany, ⁴Berufsgenossenschaftliches University Hospital Bergmannsheil GmbH, Department of General and Trauma Surgery, Bochum, Germany

Contact E-Mail Address: thorsten.brechmann@rub.de

Introduction: Due to neurogenic bowel alterations patients with spinal cord injury (SCI) present with poorer bowel preparation and the colonoscopies itself remain incomplete frequently [1]. The water exchange technique shows certain advantages in the routine setting [2-5], but the feasibility and impact in SCI patients is unknown.

Aims & Methods: The aim was to evaluate common quality parameters of water exchange colonoscopy (WEC) such as completeness and cleansing level in SCI patients in a retrospective cohort study. Two age-, gender- and time-of-performance-matched control groups (SCI patients with carbon dioxide-based colonoscopy and non-injured patients with WEC) were evaluated in a 1:1:1 ratio.

Patients were compared regarding completeness of the endoscopy, cleansing level based on a five step scale during forward feed and drawback, complications and polyp and adenoma detection rate. The study protocol was approved by the institutional review board (registry number 22-7450-BR).

Results: A total of 93 patients were included (61.2 ± 12.5 years, 75 male, 80.6 %). Only a minority of colonoscopies were performed for screening purposes (9.7 %), with slight, but significant differences between the groups. The other indications included anaemia and overt or occult bleeding (29.3 %), constipation (25.3 %), abdominal pain (20.2 %), follow-up (13.1 %), weight loss (7.1 %), diarrhoea (6.1 %) and others (9.1 %). A total of 24 colonoscopies (24.2 %) resulted in a normal finding. In decreasing order the pathologies included polyps (51.5 %), any kind of inflammation (17.2 %), diverticula (21.2 %), anal prolaps (15.2 %), angiodysplasia (1.0 %), carcinoma (1.0 %) and others (3.0 %).

Water exchange colonoscopy achieved similar results both in SCI patients and the general population. The caecum and the terminal ileum was intubated in every case of WEC; in the SCI standard colonoscopy group the respective intubation rates were 93.5 % (*ns*) and 64.5 % ($p < .001$).

The cleansing level during forward feed did not differ between both SCI groups while the control group presented a significantly better bowel preparation.

On the contrary, during drawback both WEC groups showed better cleansing results than the SCI standard carbon dioxide colonoscopy group. Among the SCI patients the improvement of the cleansing was highest in the WEC group (improvement based on the five step scale 1.4 ± 0.8 vs. 0.8 ± 0.8 , $p = .001$).

Though not significantly the polyp detection rate was highest in the SCI WEC group and lowest in the WEC control group (61 % vs. 55 % vs. 42 %, *ns*). Similarly, the mean number of polyps detected in the SCI WEC group exceeded both other groups (1.7 ± 1.9 vs. 1.2 ± 1.5 vs. 1.3 ± 2.0 , *ns*). The adenoma detection rate (46 % vs. 33 % vs. 33 %, *ns*) as well as the average number of adenomas resected (1.2 ± 1.8 vs. 0.9 ± 1.7 vs. 0.9 ± 1.7) were numerically highest in the SCI WEC group. Except of one bleeding after extensive piecemeal mucosectomy in the rectum no relevant complication occurred.

Conclusion: Water exchange colonoscopy in SCI patients is feasible and safe and has the potential to improve the quality of colonoscopies in SCI patients substantially. A controlled randomised trial is warranted to confirm the encouraging results.

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Disclosure: Nothing to disclose.

P0910

ARE DIMINUTIVE AND SMALL POLYPS DANGEROUS?

A. Ben Mohamed¹, M. Yakoubi¹, A. Khsiba¹, M. Medhioub¹, M. Mahmoudi¹, M.L. Hamzaoui¹, M.M. Azzouz¹

¹Department of Gastroenterology, Mohame Taher Maamouri Hospital, Gastroenterology, Nabeul, Tunisia

Contact E-Mail Address: asmabenmed2014@gmail.com

Introduction: Small colonic (6-9 mm) and diminutive (1-5 mm) polyps are frequently found at colonoscopy. Histology remains to this day the gold-standard for the evaluation of polyps despite important histo-pathological inter-observer differences in the distinction between adenomas and hyperplastic polyps.

Due to the relatively high prevalence and clinical insignificance of small hyperplastic polyps on the left side of the colon, the cost associated with their removal and pathological study remains unjustified.

Aims & Methods: The aim of this study was to identify the histological features of diminutive and small polyps in order to verify the safety of strategies proposing to resect only polyps of 10 mm or more. Patients who underwent polypectomy during 12 months were identified through our endoscopy database and those with polyps <1 cm were enrolled.

Results: Two hundred and four patients (117 men and 87 women, sex ratio M / W = 1.34) were identified. The mean age was 63.57 ± 12.14 years (31 to 90 years). There were 431 polyps of which 239 (55.45%) were diminutive. Sixty-three percent of all polyps were on the left colon and 30.3% (n = 131) were hyperplastic. Eighteen percent of the polyps on the right side were hyperplastic versus 37.26% on the left side. This histological difference was statistically significant ($p < 0.0001$). High grade dysplasia (HGD) was present in 14% of adenomatous polyps and serrated polyps were observed in 11.5% of cases. Adenocarcinoma was found in 3 small polyps on the left side (9 mm) causing a rate of degeneration at 0.69%.

Conclusion: These data demonstrate that only a third of the polyps on the left side were hyperplastic, mainly represented by diminutive polyps (<5 mm). However the pathological findings of small polyps (6-9 mm) are not reassuring proving that polypectomy remains well justified.

Disclosure: Nothing to disclose.

P0911

CHARACTERISTICS AND RENTABILITY OF URGENT COLONOSCOPY IN LOWER GASTROINTESTINAL BLEEDING. EXPERIENCE IN A THIRD LEVEL CENTER

M.M. Rodriguez Gonzalez¹, N. Garcia Morales¹, N. Fernández Fernández¹, L.A. Cid Gomez¹, M. Ayude Galego¹, S. Alonso Lorenzo¹, D. Nogueira Senties¹, A. Iglesias Doallo¹, V. Pena¹, A. Alonso¹, V. Marquez¹, M. Casares¹, J.I. Rodriguez Prada¹

¹University Hospital Álvaro Cunqueiro, Gastroenterology, Vigo, Spain

Contact E-Mail Address: mrodriguez95@hotmail.com

Introduction: Colonoscopy is an useful tool on the management of patients with lower gastrointestinal bleeding (LGIB). Its diagnostic and therapeutic yield varies and the optimal timing for its performance is a reason of controversy.

Aims & Methods: Aims: We aim to describe the characteristics of patients with LGIB having an urgent colonoscopy done, as well as the diagnostic and therapeutic yield of this procedure.

Methods: Descriptive and observational study of the urgent colonoscopies due to LGIB done at the Vigo University Hospital between June 2019 and April 2021.

Results: A total of 110 urgent colonoscopies were done, from which 92 were due to LGIB, meaning a 10.4% of all the urgent endoscopies done at the said period of time. The average age of patients presenting LGIB was 68.84 years old (SD 14) and 58 (63%) of them were male. At the moment of bleeding, 16 (17.4%) were receiving anticoagulant treatment and 17 (18.5%) antiagregant treatment. We registered 56 colonoscopies (60.9%) being done in the morning and 36 (39.1%) during the afternoon and evening.

At the endoscopy unit 64 colonoscopies were done (69.6%), while 28 (30.4%) were done at the Intensive Care Unit. In 79 patients (85.9%) the procedure was done under sedation. The etiology of the bleeding was post-polypectomy in 24 patients (26.1%), colon ischemia in 8 patients (8.7%), inflammatory bowel disease in 5 patients (5.4%), diverticular disease in 12 patients (13%), vascular disease in 1 patient (1.1%) and other causes in 26 patients (28.3%). In 16 patients (17.4%) the etiology was not filiated. Only 29 patients (31.5%) received endoscopic treatment, which was successful in 28 (96.6%).

No complications were documented. The need for surgical/radiologic intervention was registered in 4 patients (4.3%). A total of 56 (61.5%) colonoscopies were made within the first 24 hours of presentation (urgent colonoscopy), while 35 (39.4%) were made after this period of time.

We found that timing to colonoscopy is associated with the possibilities to apply endoscopic treatment ($p < 0.05$), but not with the diagnostic capability ($p 0.154$). Previous bowel preparation was given to 28 patients (30.4%) and not given to 64 (69.6%), mostly of whom underwent recto-sigmoidoscopy and not a complete colonoscopy. Giving previous bowel preparation was related to the diagnostic capacity of the colonoscopy ($p 0.05$). The 40.2% were complete colonoscopies, the 18.5% uncomplete colonoscopies and the 41.3% rectosigmoidoscopies, which was related to giving previous bowel preparation ($p < 0.01$) and with the diagnostic findings ($p < 0.05$). Dead from bleeding occurred in a 2.2 % and it was not related to colonoscopy timing ($p 0.691$).

Conclusion: Urgent colonoscopy is an infrequent indication for diagnostic and treatment in LGIB. Performing an urgent colonoscopy does not increase the diagnostic yield of the procedure, but it does increase the possibilities of applying endoscopic treatment.

Giving adequate previous bowel preparation improves the chance of endoscopic diagnose, so it seems that performing colonoscopy without it is not profitable.

Disclosure: Nothing to disclose.

P0912

INTEREST OF ENDOSCOPICTREATMENT OFSIGMOID VOLVULUS

R. Laroussi¹, I. Elkoti², A. Benhamdane², S. Mrabti², T. Addajou², F. Rouibaa², A. Benkirane², H. Seddik²

¹Faculty of Medicine and Pharmacy, Gastroenterology Department of the Mohamed V Military Hospital, Rabat, Morocco,

²Faculty of Medicine and Pharmacy, Rabat, Morocco

Contact E-Mail Address: laroussirachid89@gmail.com

Introduction: Sigmoid volvulus is the twisting of the sigmoid loop on its mesocolic axis, achieving a low occlusion, by strangulation. The etiology remains unknown, however there are factors that are incriminated in the occurrence of this pathology.

The therapeutic management of sigmoid volvulus in emergency is controversial between endoscopic and surgical treatment. The objective of this work is to evaluate the results of the treatment of sigmoid volvulus by endoscopic detortion and exsufflation.

Aims & Methods: This is a retrospective study including patients who underwent endoscopic exsufflation between December 2017 and March 2022. All emergency exsufflation colonoscopies performed for sigmoid volvulus were collected. The results of the endoscopic management, the percentage of recurrence as well as the need for recourse to surgery were evaluated.

Results: During the study period, 16 patients with acute intestinal obstruction due to sigmoid volvulus underwent emergency exsufflation colonoscopy. There were 12 men and 4 women with an average age of 59.8 years [26-81 years]. Endoscopic exsufflation was performed successfully and without incident in 13 patients, i.e. a primary success rate of 81.25%.

No complications were noted. Failure of exsufflation was observed in 3 patients, two patients had signs of endoscopic colic pain and only one patient had stenosis of the neck of the volvulus which was impassable requiring emergency performance. of a colectomy with a colostomy. Early recurrence within an average of 11 days [7.20] was observed in four patients, representing a secondary success of endoscopic treatment of 69.2%.

Sigmoidectomy was performed in 69.2% of patients who underwent endoscopic exsufflation ($n=9$) within an average of 29 days [5.50].

Conclusion: In the absence of signs of severity, devolvulization and primary endoscopic exsufflation is the treatment of choice for sigmoid volvulus occlusions. Its primary and secondary success rates are satisfactory. It thus makes it possible to get out of the acute phase, and to program the sigmoidectomy in better conditions.

Disclosure: None.

P0913

COMPARISON OF SYNERGISTIC SEDATION WITH MIDAZOLAM AND PROPOFOL VERSUS MIDAZOLAM AND PETHIDINE IN COLONOSCOPES: A PROSPECTIVE, RANDOMIZED STUDY

Y. Lee¹, D.H. Kim¹, H. Kim¹, S.-Y. Park¹, E. Cho¹, H.A. Cho¹, Y. Jung¹

¹Chonnam National University Hospital, Department of Internal Medicine, Division of Gastroenterology and Hepatology, Gwangju, Korea (Republic of)

Contact E-Mail Address: tgb-follower@daum.net

Introduction: Benzodiazepines, combined or not with opioids, has been used as standard regimen for gastrointestinal endoscopy for decades, also referred to as "traditional sedation"(1). However, there has been a strong interest in propofol-based sedation recently and tends to replace traditional sedation in several countries(2). Propofol sedation showed better patient satisfaction, efficacy and similar safety versus traditional sedation for colonoscopy(3, 4). However, data directly comparing midazolam with propofol and midazolam with pethidine in colonoscopy are limited.

Aims & Methods: The aim of our study was to compare the safety and efficacy of the synergistic sedation with midazolam combined with propofol versus midazolam and pethidine for conscious sedation in colonoscopy. We performed prospective randomized single blind study. Forty-two patients were randomly assigned to one of two medication regimens in colonoscopy. Patients in group A received midazolam and propofol. Patients in group B received midazolam and pethidine.

Results: A total of 42 patients were enrolled and 20 were assigned to group A and 22 to group B. Median dose of propofol was 40mg (range 10-80) in group A, and median dose of pethidine was 25 mg (range 25-75) in group B.

Pain score index was 1.1 versus 1.8 ($p = 0.083$). Cecal intubation rate was 100% in both groups and cecal intubation time was 7.8 minutes versus 9.3 minutes ($p = 0.468$). Patient's position change frequency was 1.0 versus 1.5 ($p = 0.019$). Manual compression was applied on 50% versus 77.3% ($p = 0.065$). Difficulty of the procedure was 2.3 vs 3.3 ($p = 0.170$). Elapsed time until discharge criteria are satisfied was 22.5 minutes versus 22.1 minutes ($p = 0.837$). Patient's satisfaction score was 96.5 points versus 94.1 points ($p = 0.497$). Adverse events rate was 25.0% versus 13.6% respectively ($p = 0.445$).

	Group A (n = 20)	Group B (n = 22)	P value
Drop in O2 saturation	0 (0%)	1 (4.5%)	ns
Drop in blood pressure	2 (10%)	0 (0%)	ns
Alteration in heart rate	3 (15%)	2 (9.1%)	ns
Pain (VAS)	1.7 ± 1.2	2.0 ± 1.4	ns
Cecal intubation time	7.8 ± 5.3	9.3 ± 7.0	ns
Position change frequency	1.0 ± 0.5	1.5 ± 0.7	0.01
Manual compression	10 (50%)	17 (77.3%)	ns
Aldrete score (20 min)	9.9 ± 0.3	9.8 ± 0.5	ns
Satisfaction score	96.5 ± 11.4	94.1 ± 11.4	ns

Table 1 The efficacy and safety of two groups.

Conclusion: Safety and recovery profile was similar in both groups. In terms of efficacy, the combination of midazolam and propofol resulted in fewer position changes. In addition, the cecal intubation time, the number of manual compressions, and the difficulty of the procedure showed a better trend. Patients also tended to feel less pain and be more satisfied.

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Disclosure: Nothing to disclose.

P0914

SHORT AND LONG-TERM OUTCOMES OF ENDOSCOPIC REMOVAL OF LARGE (>20 MM) COLORECTAL POLYPS

A. Rawa-Golebiewska¹, M. Bugajski^{1,2,3}, P. Wieszczy^{1,2,3}, J. Pachlewski^{1,2}, N. Pilonis¹, A. Mroz^{4,1,2}, J. Regula^{1,2}, M.F. Kaminski^{1,3,2}
¹The Maria Skłodowska-Curie National Research Institute of Oncology, Department of Cancer Prevention and Department of Oncological Gastroenterology, Warsaw, Poland, ²Medical Center for Postgraduate Education, Department of Gastroenterology, Hepatology and Clinical Oncology, Warsaw, Poland, ³University of Oslo, Oslo, Norway, Clinical Effectiveness Research Group, Oslo, Norway, ⁴The Maria Skłodowska-Curie National Research Institute of Oncology, Department of Pathology and Laboratory Medicine, Warsaw, Poland

Contact E-Mail Address: agolebiewska111@gmail.com

Introduction: Outcomes of endoscopic treatment of large colorectal polyps depends on many variables, of which size and morphology (flat, sessile or pedunculated) are assumed to be important predictors of technical success. Up to date, there was no assessment of both short- and long-term (including colorectal cancer [CRC] risk) outcomes of endoscopic treatment of large lesions with regards to polyp morphology.

Aims & Methods: To assess technical success rate and risk of CRC after endoscopic removal of large colorectal polyps.

We performed an observational, retrospective study of all patients referred for colonoscopy at our Department between 2000 and 2015, with the intention to remove the large (>20mm) colorectal lesion. We collected data on patient and lesion characteristics, technical factors, histology findings and follow-up date, including local recurrence and CRC occurrence. Polyps' morphology was divided into three groups, based on Paris and LST classification: I. Sessile polyps (SP, 0-Is), II. Pedunculated polyps (PP, 0-Ip), III. Flat polyps (FP, 0-IIa-c, LST, LST-Is). We used forward stepwise regression at 0.1 significance level for variable selection. Adjusted risk (AR) was calculated using margins at the means of the models' covariates. All hypothesis were tested at 5% significance level.

Results:

	Technical success OR* (95% CI)	Carcinomatous polyp OR** (95% CI)	Bleeding OR*** (95% CI)	Disease recurrence OR†(95% CI)
Polyp's morphology (ref. FP)				
PP	9.33 (1.18-73.54)	3.84 (2.19-6.72)	1.00 (0.63-1.60)	0.09 (0.03-0.24)
SP	0.50 (0.25-0.99)	4.76 (2.88-7.88)	0.69 (0.42-1.12)	0.45 (0.29-0.71)
Polyp's histology (ref. LGD)				
HGD	1.34 (0.59-3.05)	N/A	1.46 (0.97-2.21)	0.86 (0.58-1.28)
Carcinomatous polyp		N/A	2.98 (1.68-5.27)	1.48 (0.78-2.81)
Polyp's size (ref. <30 mm)	0.15 (0.07-0.33)			
30-39 mm	0.25 (0.10-0.63)	1.35 (0.88-2.09)	1.75 (1.14-2.68)	1.45 (0.94-2.25)
≥40 mm	0.08 (0.03-0.20)	2.50 (1.43-4.37)	2.03 (1.21-3.39)	2.10 (1.33-3.31)

Table 1. Multivariable logistic regression models.

Abbreviations: LGD= low-grade dysplasia, HGD= high-grade dysplasia. OR were adjusted for variables found significant in stepwise selection, i.e. *missing histology and year of colonoscopy, **use of APC, ***missing histology, year of colonoscopy and use of forceps, †use of APC and forceps, patient's age.

We identified 1,814 procedures of endoscopic treatment of 1,983 large lesions in 1,723 patients. We excluded 332 (16.7%) lesions (4 due to administrative error, 64 due to inflammatory bowel disease, 3 due to lack of information on morphology and 261 were disqualified by the endoscopist). In total, 1,651 polyps (24.9% SP, 31.5% PP, 43.6% FP) among 1,441 patients (mean age, 64.6 years; 54.6% males) were analyzed.

The adjusted technical success rate was 98.6% for FP, 99.8% for PP ($p=0.034$ compared to FP) and 97.2% for SP ($p=0.048$ compared to FP). The AR of carcinomatous polyp for FP was 3.0% which was significantly less than for PP (10.3%, $p<0.001$) and SP (13.1%, $p<0.001$).

There was no significant difference in AR of bleeding: FP (7.8%) and PP (7.9%, $p=0.983$) or SP (5.5%, $p=0.130$). AR of disease recurrence was higher in FP (15.9%) than in PP (1.6%, $p<0.001$) and SP (7.9%, $p=0.001$).

Results of logistic regression can be found in Table 1. During the median follow up of 4 years, a total of 8 CRCs were found, which turned out to be too small group to perform analyzes of risk for CRC incidence and mortality.

Conclusion: Endoscopic removal of large colorectal lesions is effective and the incidence of CRC is very low in long-term follow-up. These findings could be helpful for community centers as a first-step qualification for removal of large lesions and to inform decisions on which lesion should undergo endoscopic treatment in referral centers.

Disclosure: Kaminski, M.F.

P0915

PRE-COLONOSCOPY PREPARATION GUIDED BY A PERSONALIZED DIGITAL PLATFORM IS ASSOCIATED WITH LOWER RATES OF INADEQUATE PREPARATION COMPARED TO DIGITAL WRITTEN INSTRUCTIONS

L. Deutsch (Mlynarsky)^{1,2}, O. Shibolet^{1,2}

¹Tel Aviv University, Sackler School of Medicine, Tel Aviv, Israel, ²Tel Aviv Sourasky Medical Center, Gastroenterology and Hepatology, Tel Aviv, Israel

Contact E-Mail Address: Liatml@tlvmc.gov.il

Introduction: Inadequate Bowel preparation is a cause of failed cecal intubation, leading to missed colonic lesions.

Aims & Methods: Study aim was to evaluate whether implementation of a new personalized digital platform leads to better bowel preparation and patient related outcomes through better patient engagement.

We retrospectively analyzed prospectively collected data regarding ambulatory colonoscopies. The GistMD digital platform includes a patient-tailored animated video of bowel preparation instructions, individualized according to age, gender, comorbidities and language, links to instruction forms and consent forms, and a set of reminders. A link to the GistMD system was randomly sent to patients before a scheduled colonoscopy during platform implementation period (04/2021-10/2021). The control group received standard written instructions.

The selection of prep regime was according to the referring physician discretion prior to prep instructions assignment. Patients with any history of colorectal surgery were excluded.

Results: Out of 2447 colonoscopies, the GistMD link was randomly sent to 913 (37.3%) patients and standard written prep instructions to 1534 (62.7%) controls. Inadequate bowel preparation (Boston bowel preparation scale (BBPS)<6) was documented in 27.6% of controls and only in 21.2% of the "GistMD link" group ($P<0.001$). Among the "GistMD link" receivers, 470/913 (51.5%) watched >75% of the video ("GistMD full-users") while 443/913 (48.5%) did not. BBPS<6 rate was the lowest among "GistMD full-users" compared to less-users and the control group (19.1%, 23.5% and 27.6%, respectively, $P<0.001$).

Cecal intubation rates were higher among "GistMD" link group compared to the control group (881(96.5%) vs.1450 (94.5%), $P=0.026$) and propofol dose was lower (233.7 ± 97.5 mg vs. 244.3 ± 105.9 mg, $P=0.020$). Logistic regressions adjusted for age, gender and morning/afternoon colonoscopy, showed that "GistMD link" and "GistMD full-users" were each independently associated with BBPS $\geq$ 6 [(OR 1.459, $P<0.001$) and (OR 1.639, $P<0.001$), respectively].

In sub-group analysis "GistMD link" showed the same benefit in achieving BBPS $\geq$ 6 among native Russian speakers (OR 1.769, $P=0.018$), female patients (OR 1.589, $P=0.004$), male patients (OR 1.366 $P=0.015$), and 50-70years old patients (OR 1.636, $P=0.001$). Polyp detection rate and adenoma detection rate were comparable between the "GistMD link" and the control group (36.8% vs. 40.3%, $P=0.095$, and 27.1% vs. 28.2%, $P=0.531$, respectively).

Conclusion: A personalized digital platform for pre-colonoscopy preparation guidance leads to lower rates of inadequate preparation and higher procedure completion rates.

Disclosure: Nothing to disclose.

P0916

ACUITY OF ARTIFICIAL INTELLIGENCE ASSISTED COLONOSCOPY IN LYNCH SYNDROME PATIENTS

C. Pinto¹, R. Ortigão¹, J. Chaves¹, D. Ramos Silva², M. Dinis-Ribeiro¹, C. Lopes Brandão¹

¹Portuguese Oncology Institute of Porto, Gastroenterology, Porto, Portugal, ²Hospital Amato Lusitano, Gastroenterology, Castelo Branco, Portugal

Contact E-Mail Address: claudia.marquespinto@gmail.com

Introduction: Lynch Syndrome (LS) is the most common cause of hereditary colorectal cancer. In these patients, the adenoma-carcinoma progression is faster – hence, precursor lesion detection should be optimized to reduce false-negatives and subsequent potential interval cancer. Artificial intelligence (AI) based systems have been used during colonoscopy to raise both adenoma detection rate and the number of adenomas detected by patient.

Aims & Methods: Our aim was to determine the sensitivity of AI assisted colonoscopy in LS patients.

We included patients with LS submitted to screening colonoscopies. Patients were submitted to two passages in both the ascending colon and cecum. The first passage was performed with the AI-assisted system (GI Genius®) – all identified polyps (true-positives) were removed. The second passage was aided by high-definition white light – all identified polyps were removed (false-negatives). We also described polyps identified by the AI-assisted system but not by an endoscopy expert (false-positives).

Results: We included 36 patients with a median age of 50 years. Twenty-six (26, 72.2%) were male. Polyps were detected in 11 patients (30.5%). In the first passage, 13 polyps were identified – 11 (84.6%) with dimensions <10mm and 9 (69.2%) adenomas. In the second passage, 6 additional polyps were identified – 5 (83.3%) with dimensions <10mm and 4 (66.7%). AI-assisted colonoscopy has an estimated sensitivity of 68.4% (95% Confidence Interval – 63.8-72.0). False-positives were identified in 31 (86.0%) colonoscopies.

Conclusion: AI based systems may be useful in minimizing detection errors during colonoscopy in LS patients. Our preliminary results show the need for optimization of these systems, especially due to high percentage of false-positives.

Disclosure: Nothing to disclose.

P0917

IMPACT OF REINFORCED EDUCATION BY TELEPHONE AND SHORT MESSAGE SERVICE ON THE QUALITY OF BOWEL PREPARATION: A RANDOMIZED CONTROLLED STUDY

A. Ait errami¹, I. Haraki¹, K. Krati¹

¹UHC Mohammed VI, Hepatogastroenterology, Marrakech, Morocco

Contact E-Mail Address: harakiimane@gmail.com

Introduction: Inadequate preparation of the bowel for colonoscopy can result in both missed pathological lesions and cancelled procedures.

Aims & Methods: This study aimed to assess the impact of reinforced education by telephone or short message service (SMS) on the quality of bowel preparation.

A prospective, endoscopist-blinded, randomized, controlled study was conducted. Reinforced education groups received additional education via reminders by telephone or SMS 2 days before colonoscopy. The primary outcome was the quality of the bowel preparation according to the Boston Bowel Preparation Scale (BBPS). The secondary outcomes included polyp detection rate (PDR), adenoma detection rate (ADR), tolerance, and subjective feelings of patients.

Results: A total of 220 patients were included. Total BBPS score was significantly higher in the reinforced education groups than in the control group (mean [SD] telephone vs. control: 7.1 [1.2] vs. 6.3 [1.4], $P < 0.001$; SMS vs. control: 6.8 [1.3] vs. 6.3 [1.4], $P = 0.027$).

Between the two interventions, there was no significant difference in total BBPS score. PDR and ADR were not different among groups. Reinforced education groups showed lower anxiety and better tolerance compared with controls.

A preparation-to-colonoscopy time of >6 hours and $<80\%$ of the purgative ingested were independent factors associated with inadequate bowel preparation (BBPS < 5), whereas re-education by telephone was inversely related to inadequate bowel preparation.

Conclusion: SMS was the optimal education modality, and was as effective as telephone reminders for the quality of bowel preparation. A reinforced educational approach via telephone or SMS should be individualized, depending on the resource availability of each clinical practice

Disclosure: Nothing to disclose.

P0918

SEDATION FOR COLONOSCOPY IN PATIENTS WITH SPINAL CORD INJURY DEPENDS ON THE INJURY'S CHARACTERISTICS, BUT IS FEASIBLY AND SAFELY ADMINISTERED AS NURSE ASSISTED SEDATION

M. Beckmann¹, M. Aach², T.A. Schildhauer³, W. Schmiegell⁴, T. Brechmann^{5,1}

¹Berufsgenossenschaftliches University Hospital Bergmannsheil GmbH, Department of Gastroenterology and Hepatology, Bochum, Germany, ²Berufsgenossenschaftliches University Hospital Bergmannsheil GmbH, Department of General and Trauma Surgery, Spinal Cord Injury Unit, Bochum, Germany, ³Berufsgenossenschaftliches University Hospital Bergmannsheil GmbH, Department of General and Trauma Surgery, Bochum, Germany, ⁴Ruhr University Bochum, Bochum, Germany, ⁵St. Elisabeth Hospital, Internal Medicine and Gastroenterology, Gütersloh, Germany

Contact E-Mail Address: thorsten.brechmann@rub.de

Introduction: Colonoscopy is a routine method both for screening and work-up of suspected diseases of the lower gastrointestinal tract. Though it has been shown that colonoscopy is feasible and safe even in patients

with spinal cord injury (SCI), there is no data available that describes the utilisation and safety of the sedation applied during SCI patients' colonoscopy.

Aims & Methods: Consecutive patients with SCI who underwent colonoscopy between 2008 and 2018 were included in a retrospective matched case control study. On that account a gender-, age-, and year-of-performance-matched control group (CG) without SCI was assigned.

The demographic characteristics including parameters of the spinal cord injury, the indication and results of the endoscopy, the medication and the staff involved in the procedure as well as adverse events were collected from the electronic data base. Hypotension was defined as a fall below 75% of the baseline.

The primary objectives were the rate of adverse events and severe adverse events related to the sedation.

Secondary objectives included the frequency of demanding a sedation, dose of medication administered, the occurrence of adverse events such as desaturation, need of mechanical ventilation, hypotension, bradycardia, premature discontinuation, need for intensive medical care, nausea/vomiting, intolerance reaction, need for resuscitation and death related to the sedation. Characteristics of SCI, such as the aetiology, AIS classification, and duration were investigated as risk factors for sedation.

For the statistical analyses descriptive statistics, Chi squared test, Fisher's Exact test, paired t-test, variance analysis (ANOVA), Mann-Whitney-U-test, and Kruskal Wallis test were used. Potentially influencing factors on hypotension were evaluated by a regression analysis.

Results: Of 282 patients with SCI, 169 (59.9%) demanded a sedation during colonoscopy (CG: 259 (91.8 %), $p < .01$). Although the sedation lasted 5.5 min longer in the SCI group ($p < .05$), fewer sedative drugs were administered (Propofol: 0.08 ± 0.07 mg/kg/min vs. 0.11 ± 0.07 mg/kg/min, $p < .01$; Midazolam: 3.2 ± 1.2 mg vs. 3.7 ± 1.3 mg, $p < .01$). Hypotension occurred significantly more often in patients with SCI (60.0 % vs. 42.3 %, $p < .01$); other adverse events were equally distributed in both groups.

The SCI's characteristics had a relevant influence on the sedation and its adverse events. The average propofol dose was higher in subjects with chronic than acute injuries (0.09 ± 0.07 mg/kg/min vs. 0.05 ± 0.04 mg/kg/min, $p < .01$) and lumbar (0.14 ± 0.12 mg/kg/min) than thoracic (0.08 ± 0.05 mg/kg/min) than cervical (0.06 ± 0.05 mg/kg/min $p < .05$) lesions; the midazolam dose presented similarly (3.7 ± 1.2 mg vs. 3.2 ± 1.2 mg vs. 2.8 ± 1.0 mg, $p < .05$).

Both drugs differed according to the AIS classification (propofol: AIS-A: 0.08 ± 0.05 vs. AIS-B: 0.10 ± 0.06 vs. AIS-C: 0.12 ± 0.16 vs. AIS-D: 0.07 ± 0.05 mg/kg/min, $p < .05$; midazolam: AIS-A: 3.1 ± 1.1 vs. AIS-B: 3.1 ± 1.2 vs. AIS-C: 3.3 ± 1.2 vs. AIS-D: 3.4 ± 1.4 mg, $p < .05$).

Hypotension was more likely in persons with chronic lesions (65.4 % vs. 34.6 %, $p < .01$) and associated to the level of the injury (thoracic 70.3 % vs. cervical 51.2 % vs. lumbar 33.3%, $p < .01$).

Conclusion: Compared to the able-bodied population SCI patients demand a sedation during colonoscopy significantly less often. The sedation differs depending on the SCI's characteristics. Though mild hypotension occurs frequently, nurse assisted sedation is feasible and safe even in the particular setting of colonoscopy in SCI patients.

Disclosure: Nothing to disclose.

P0919

CLINICAL OUTCOMES: A PILOT FIT PROGRAM TO TRIAGE NON-URGENT COLONOSCOPY REFERRALS

L. Kumar¹, E. Shannon¹, S. Sihag², H. Kerr², C. Steele², E. Slattery¹
¹University Hospital Galway, Gastroenterology, Galway, Ireland,
²Letterkenny University Hospital, Gastroenterology, Donegal, Ireland

Contact E-Mail Address: kumarl@tcd.ie

Introduction: In the post-COVID era, colonoscopy waiting lists poses a significant challenge. Faecal Immunochemical Test (FIT) is mainly used in colorectal cancer screening to predict pre-malignant/malignant lesions on colonoscopy but their utility beyond cancer screening has yet to be determined.

Aims & Methods: To assess the utility of FIT as a safety net in addition to conventional triaging methods to determine the outcomes of patients undergoing non-urgent colonoscopies.

Patients awaiting for a routine colonoscopy (waiting >3 months), in 2 tertiary referral centres, were sent a FIT kit. Positive-FITs (i.e. >50ng/mL) were re-triaged for urgent colonoscopy. Basic demographics, colonoscopy and histology findings were collected, and median FIT levels calculated to correlate with findings on colonoscopy.

Results: In total, 1226 patients were invited to perform a FIT to which 715 (58%) participants responded. Of these 115 (16.1%) samples were positive and results in re-triaging for an urgent colonoscopy. 102 underwent a colonoscopy. The median age was 58 years (IQR:47-72) and 47.1% were male. The median time to endoscopy from a positive-FIT result was 56 days (IQR:49-62).

Most common indications for colonoscopy included altered bowel habit (29.4%) and rectal bleeding (22.5%). Positive findings were seen in 77.5% of procedures (0% malignancies, 43.1% polyps, 33.3% diverticulosis, 11.8% colitis, 9.8% haemorrhoids). High risk adenomas were found in 16 (15.7%) patients. Patients with a FIT ≥1000ng/mL were more likely to have a positive finding compared to those with a FIT of <1000ng/mL (96% vs 72%, p=0.02).

Conclusion: Reassuringly there were no findings of malignancy, although diagnostic yield was high. This highlights the importance of good clinical triage. Further comparison with the negative-FIT group after colonoscopy along with patient reported outcomes are being followed-up in this study.

Disclosure: Nothing to disclose.

P0920

REAL-TIME COMPUTER-AIDED POLYP/ADENOMA DETECTION DURING SCREENING COLONOSCOPY: A SINGLE-CENTER DIAGNOSTIC TRIAL

C. Robles-Medrandá¹, C. Cifuentes-Gordillo¹, M. Arevalo-Mora¹, M. Puga-Tejada¹, M. Egas-Izquierdo², J. Baquerizo-Burgos², R. Del Valle Zavala¹, J. Alcivar-Vasquez¹, H. Alvarado-Escobar¹, J. Rodriguez¹, D. Calle-Loffredo¹, H. Pitanga-Lukashok¹
¹Instituto Ecuatoriano de Enfermedades Digestivas, Endoscopy and Gastroenterology, Guayaquil, Ecuador, ²Instituto Ecuatoriano de Enfermedades Digestivas (IECED), Endoscopy and Gastroenterology, Guayaquil, Ecuador

Contact E-Mail Address: carlosokm@yahoo.es

Introduction: Screening colonoscopy has decreased the incidence of colorectal carcinoma in the previous decades. However, several factors affect polyp/adenoma detection rate: bowel preparation, percentage of mucosal surface evaluation, and the training levels of operators. The Discovery Artificial Intelligence assisted polyp detector (Pentax Medical, Hoya Group) was recently launched for clinical practice.

This AI software was trained with 120,000 files from approximately 300 clinical cases. The visual aided detection (bounding box locating a polyp on the monitor) alerts the endoscopist if a polyp/adenoma was missed during the standard, screening procedure.

Aims & Methods: We aim to evaluate the real-world effectiveness of AI-assisted colonoscopy in clinical practice. Consecutive patients who underwent HD colonoscopy (Nov/2020-Mar/2021). Patients >45 years old were invited to participate during outpatient clinic visits. Patients with BBPS≤6, history of inflammatory bowel disease, familial polyposis syndrome, colorectal carcinoma, colorectal surgery or uncontrolled coagulopathy were not considered. A first operator was assessed only with HD colonoscopy, and a second operator (blinded to previous findings) with an AI-assisted HD colonoscopy. The study protocol and written consent form were approved by the local Institutional Review Board (IRB).

The study protocol was conducted according to the declaration of Helsinki. All patients provided informed written consent. Data were analyzed in R v4.0.

Results: A total of 115 colonoscopies were performed on 115 patients. Mean age 57.0 (51.0 - 67.5) years old, 82 (71.3%) females, with a BMI index <25, 25-30 and >30 kg/m² in 6/115 (5.2%), 89/115 (77.4%) and 20/115 (17.4%) patients, respectively. At the morning, 93/115 (80.9%) procedures were performed. An expert endoscopist performed 67.8% of procedures, while a GI fellow in training 32.2%. The median time until withdrawal was 09:05 minutes. The polyp and adenoma detection rate were 132 (64.3%) and 73 (35.6%), respectively detected in 58/115 (50.4%) patients: 19/205 (9.3%) NICE II, 7/205 (3.4%) >10 mm (Table 1).

	Total (n=205)	Rectum (n=46)	Sigmoid (n=34)	Descending (n=20)	Trans- verse (n=24)	Ascending (n=54)	Cecum (n=27)
Nice (I/II/III)	186/19/-	44/2/-	32/2/-	16/4/-	22/2/-	49/5/-	23/4/-
Size (mm), 0-5/5-10/>10	132/66/7	44/2/-	28/6/-	13/7/-	22/2/-	1/48/5	24/1/2
Removal (forceps/cool loop/hot loop)	181/16/8	44/1/1	29/3/2	14/6/-	21/3/-	48/3/3	25/-/2

Table 1. Polyp/adenoma characterization.

From them, 44 polyps and 4 adenomas were detected by the second operator assisted by AI. The frequency of patients with polyps/adenomas appropriately detected by AI (sensitivity) among different colon segments ranged from 56.25% (rectum) to 78.26% (ascending colon). Meanwhile, the capability of AI for appropriate polyp/adenoma presence discharging (negative predictive value, NPV) ranged from 61.54% (sigmoid) to 89.09% (cecum). However, there were observed lower rates for specificity (8.42-49.49%) and positive predictive value (PPV, 9.89-19.78%) due to high false positives.

Conclusion: The Discovery Artificial Intelligence assisted polyp detector is a feasible tool to aid endoscopists during screening colonoscopy. However, a high rate of false-positive limits its overall accuracy. Development of this technology with more normal colonoscopies videos could decrease the false-positive rate, increasing overall accuracy.

Disclosure: Nothing to disclose.

P1038

LOCAL RECURRENCE AFTER ENDOSCOPIC RESECTION OF SESSILE SERRATED LESIONS: A MULTICENTER PROSPECTIVE STUDY BY THE OSAKA GUT FORUM

S. Shichijo¹, S. Yamaguchi², D. Nakamatsu³, T. Inoue⁴, M. Nakahara⁵, H. Ogiyama⁶, T. Yamada⁷, K. Kinoshita⁸, R. Ishihara⁹, T. Nishida¹⁰, Y. Tsujii¹¹, Y. Hayashi¹², S. Shinzaki¹¹, K. Fukui^{13,14}, Y. Ito^{13,15}, M. Kitamura¹⁶, K. Honma^{16,17}, E. Morii¹⁷, T. Takehara¹²

¹Osaka International Cancer Institute, Department of Gastrointestinal Oncology, Osaka, Japan, ²Kansai Rosai Hospital, Hyogo, Japan, ³Toyonaka Municipal Hospital, Hyogo, Japan, ⁴Osaka University Graduate School of Medicine, Department of Gastroenterology, Osaka, Japan, ⁵Ikeda Municipal Hospital, Osaka, Japan, ⁶Itami City Hospital, Hyogo, Japan, ⁷Osaka Rosai Hospital, Gastroenterology & Hepatology, Sakai, Japan, ⁸Otemae Hospital, Osaka, Japan, ⁹Osaka International Cancer Institute, Osaka, Japan, ¹⁰Toyonaka Municipal Hospital, Gastroenterology, Toyonaka, Japan, ¹¹Osaka University Graduate School of Medicine, Department of Gastroenterology and Hepatology, Suita, Japan, ¹²Osaka University Graduate School of Medicine, Department of Gastroenterology and Hepatology, Osaka, Japan, ¹³Osaka International Cancer Institute, Center for Cancer Control and Statistics, Osaka, Japan, ¹⁴Hiroshima University, Department of Mathematics Program, Graduate School of Advanced Science and Engineering, Hiroshima, Japan, ¹⁵Osaka Medical and Pharmaceutical University, Osaka, Japan, ¹⁶Osaka International Cancer Institute, Diagnostic Pathology and Cytology, Osaka, Japan, ¹⁷Osaka University Graduate School of Medicine, Department of Pathology, Osaka, Japan

Contact E-Mail Address: shichijyou-ky@umin.ac.jp

Introduction: Sessile serrated lesions (SSLs) act as precursors to colorectal cancer and sometimes harbor carcinomas. With indistinct margins, SSLs are sometimes incompletely resected.

Aims & Methods: This prospective, single-arm, observational study was performed at eight Japanese tertiary institutions to evaluate the local recurrence after endoscopic resection of SSLs ≥ 10 mm. Colorectal lesions ≥ 10 mm were resected endoscopically and the pathological diagnosis of the lesion was either SSL or hyperplastic polyp (HP). Central pathological review was performed for all the registered lesions. Follow-up colonoscopy was performed 1 year later, and the local recurrence was evaluated by biopsy.

Results: From October 2018 to October 2019, a total of 104 cases with 123 lesions were registered. Size was 15.6 ± 6.6 mm. The macroscopic type was IIa in 107 cases (87%) and Is in 13 cases (11%). Endoscopic mucosal resection (EMR) was performed for 59 (48%) lesions, underwater EMR (UEMR) in 39 (32%), endoscopic submucosal dissection in 12 (10%), and cold snare polypectomy in 8 (6.6%). En bloc resection was achieved in 98 (80%). Two delayed bleeding events occurred after EMR and were managed by endoscopy. Regarding pathological margins, two (1.6%, both treated by UEMR) were positive, 80 (66%) were negative, and 40 (33%) were indeterminate. Among the pathologically diagnosed 105 SSLs and 18 HPs, 95 and 7 were diagnosed as SSL and HP, respectively, by central pathological review (Table).

Among the 104 endoscopically diagnosed SSLs, 86 were diagnosed with SSLs, while among the 11 endoscopically diagnosed HPs, 2 were diagnosed as HPs by central pathological review (the rest were SSLs). Follow-up endoscopy was performed for the 95 patients with 113 lesions after 0.99 ± 0.38 years (4–24 months) until September 2021. Among them, resection scars were identified in 95 (84%) lesions. Three (3.1%; 95% confidence interval 0.6–8.7%) local recurrences were diagnosed pathologically

among ninety-eight pathologically diagnosed SSLs. Three cases with local recurrences were 1) Is lesion sized 25 mm in the cecum, and performed UEMR with indeterminate pathological margins, 2) IIa lesion of 10 mm in the ascending colon resected en bloc by EMR, resulting in negative margins, and 3) 30 mm, Is lesion in the sigmoid colon, resected en bloc by underwater EMR with negative margins. Cases 1) and 2) were diagnosed as local recurrences by follow-up endoscopy, and confirmed pathologically. Case 3 was not suspected recurrence endoscopically, but biopsy revealed recurrence. When classified by size, 2 out of 15 (13%) SSLs ≥ 25 mm and 1 out of 83 (1.0%) SSLs < 25 mm were diagnosed with local recurrence ($p = 0.06$).

Central pathological review	SSL with CD	SSL without CD	Hyperplastic polyp	Tub1	TSA	Total
Endoscopic diagnosis						
SSP with dysplasia		2				2
SSP without dysplasia	4	85	13	1		103
Hyperplastic polyp	1	8	2			11
adenoma	2	4		1		7
Pathological diagnosis at each institute						
SSL with dysplasia	1	3				4
SSL without dysplasia	5	86	8	1	1	101
Hyperplastic polyp	1	10	7			18
Total	7	99	15	1	1	123

Table.

Conclusion: The local recurrence rate after endoscopic resection of SSL ≥ 10 mm was 3.1%. Careful follow-up is recommended after endoscopic resection of large SSLs. Endoscopically diagnosed HPs ≥ 10 mm were sometimes pathologically diagnosed as SSL and should be considered for resection.

Disclosure: Nothing to disclose.

P1040

ARTIFICIAL INTELLIGENCE ASSISTANCE IMPROVES AS ENDOSCOPIST FATIGUE INCREASES: SECONDARY ANALYSIS OF TWO RANDOMIZED TRIALS

Z. Lu¹, L. Yao¹, L. Zhang¹, H. Yu¹

¹Renmin Hospital of Wuhan University, Gastroenterology, Wuhan, China

Contact E-Mail Address: 704941677@qq.com

Introduction: Ensuring high adenoma detection rate (ADR) is paramount in the prevention and prognosis of colorectal cancer (CRC). Endoscopist-related characteristics especially endoscopist fatigue had been proved to be an indispensable factor that related to decline ADR. Unfortunately, objective approaches to minimize the degradation of colonoscopy quality caused by endoscopists fatigue are still lacking. We further hypothesized that AI system may be an effective tool to address this challenge.

Aims & Methods: The aim of this study was to evaluate whether estimate of endoscopist fatigue at the time of the day was associated with ADR, and further evaluate whether the assistance of AI system overcome the inversely effect of endoscopist fatigue, based on secondary analysis of two randomized trials^{1,2}.

The AI group was defined as the combination of all intervention groups, including a computer-aided polyp detection (CADE) system and a computer-aided quality improvement (CAQ) system based on deep learning.

There's no intervention in the control group. We use time of the day as a surrogate of endoscopist fatigue. Colonoscopy procedure start time was therefore divided into two groups. The first group consisted of procedures commenced in the early session per half-day (08:00-11:00 or 13:00-15:00), which was defined as non-fatigue group, and the second group consisted of procedures commenced in the later session per half-day (11:00-13:00 or 15:00-17:00), which was defined as fatigue group. Adjusted odds ratio (OR) with 95 %CIs and corresponding P values were calculated.

Results: A total of 1780 patients were enrolled in this study, among which, 34.83% (620/1780) procedures were randomized into the control group, with 61.61% (382/620) performed at non-fatigue time and 38.39% (238/620) at fatigued time, and 65.17% (1160/1780) procedures were randomized into the AI group, with 61.38% (712/1160) performed at non-fatigue time and 38.62% (448/1160) at fatigued time. In the control group, the ADR at non-fatigue time was significantly higher compared with that of fatigued time (12.83% vs 6.30%, $P<0.05$).

With the assistance of AI systems, as expected, no statistically significant difference was found in the ADR between the non-fatigue and fatigue time (23.74% vs 20.76%, $P=0.238$), which demonstrated that AI systems could overcome the limitation of endoscopist fatigue during colonoscopy.

Furthermore, the assistance capabilities of AI systems were compared through OR values. The AI systems had higher assistance capabilities in fatigue group (OR=4.68, 95%CI: 2.66, 8.23) compared with non-fatigue group (OR=1.87, 95%CI: 1.32, 2.66), which demonstrated the potential benefit of using AI to improve the lower ADR during fatigue period.

Conclusion: In conclusion, our results suggest that later session per half-day, as a surrogate of endoscopist fatigue, was associated with decline ADR. Also, we found no such relationship between time of the day and adenoma detection after the assistance of AI systems, which indicating that the AI system has the potential to be an effective tool minimizing the inversely effect of endoscopist fatigue in colonoscopy.

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Disclosure: Nothing to disclose.

P1041

LONG-TERM EFFECTIVENESS OF ARTIFICIAL INTELLIGENCE SYSTEM IN IMPROVING ADENOMA DETECTION RATE: A MULTICENTER SELF-CONTROLLED STUDY

Z. Lu¹, L. Huang¹, L. Wu¹, H. Yu¹

¹Renmin Hospital of Wuhan University, Gastroenterology, Wuhan, China

Contact E-Mail Address: 704941677@qq.com

Introduction: Colorectal cancer (CRC) is the third most common cancer worldwide. Adenoma detection rate (ADR) is a quality measure of screening colonoscopy and associated inversely with the risks of interval CRC. Artificial intelligence (AI) has been successfully applied to medicine and demonstrated its positive impact in colonoscopy. To date, the short-term effectiveness of AI system in increasing ADR had been demonstrated through randomized control trials. However, little is known about the long-term effectiveness of AI system in real clinical practice.

Aims & Methods: The aim of this study was to estimate the long-term efficacy of AI system for colonoscopy through multicenter self-control study. We constructed a real-time computer-aid system based on deep learning

for polyp detecting and withdrawal speed monitoring during colonoscopy. Colonoscopy procedures for screening, diagnostic, and surveillance were retrospectively collected from 6 hospitals between 2017 and 2021, including Renmin Hospital of Wuhan University (RHWU), Central Hospital of Wuhan (CHW), the First Hospital of Wuhan (FIRHW), the Fourth Hospital of Wuhan (FOURHW), the First People's Hospital of Yichang (FPHYC), Yichang Central People's Hospital (YCPH).

Pathological results were also collected except for CHW and FIRHW. The ADR and polyp detection rate (PDR) in these hospitals were compared before and after the use of the AI system.

Specially, the ADR and PDR in YCPH were compared between colonoscopy procedures with or without the assistance of AI system during the same time. A total of 7164 and 39160 colonoscopy procedures were collected without and with the use of the AI system in RHWU, respectively, and 12866 and 7508 in CHW, 10759 and 1911 in FIRHW, 4935 and 478 in FOURHW, 6390 and 10843 in FPHYC, 13660 and 7344 in YCPH, respectively.

Results: For adenoma detection, the ADR was significantly increased with the use of the AI system compared with that of without the use of it in RHWU (16.4% vs 9.5%, $P<0.001$), and FOURHW (3.8% vs 2.2%, $P<0.05$), FPHYC (2.7% vs 4.7%, $P<0.001$), respectively. In YCPH, the ADR was found increase from 7.80% without the use of the AI system to 7.98% with the use of it, but this didn't reach statistical significance ($P=0.667$).

For polyp detection, the PDR was significantly increase with the use of the AI system compared with that of without the use of it in RHWU (40.3% vs 29.1%, $P<0.001$), CHW (25.2% vs 30.4%, $P<0.001$), FOURHW (26.5% vs 42.5%, $P<0.001$), FPHYC (29.8% vs 34.9%, $P<0.001$), YCPH (30.6% vs 28.7%, $P<0.05$), respectively. However, no such relational was found in FOURHW (27.6% vs 27.4%, $P=0.890$).

Conclusion: The AI system significantly improved adenoma and polyp detection through long-term application and has the potential to improve the quality of colonoscopy in clinical practice.

Disclosure: Nothing to disclose.

P0921

CHOLANGIOSCOPY-GUIDED BIOPSY IN THE DIAGNOSIS OF INDETERMINATE BILIARY STRICTURES- DISAPPOINTING RESULTS AFTER 6 YEARS HARD WORK

P. Karagyozov¹, I. Zhecheva², I. Tishkov¹, K. Draganov²

¹Acibadem City Clinic Tokuda University Hospital, Department of Interventional Gastroenterology, Sofia, Bulgaria, ²Acibadem City Clinic Tokuda University Hospital, Sofia, Bulgaria

Contact E-Mail Address: petko.karagyozov@gmail.com

Introduction: Indeterminate biliary strictures remain a significant clinical problem despite the advancements of imaging modalities, endoscopy and biopsy techniques. By definition no tumor mass can be detected on imaging. Despite the high suspicion of malignancy the results of biliary forceps biopsy and/or brush cytology are negative or inconclusive. Most of the strictures are malignant but could be benign in up to 15% of cases. Precise diagnosis is crucial for the proper therapy.

Aims & Methods: To access the role of cholangioscopy-guided forceps biopsy in the diagnostic work-up of indeterminate biliary strictures.

Data were collected retrospectively from March 2016 to August 2021. All the patients with indeterminate biliary strictures underwent cholangioscopy with the SpyGlass DS System. After visual assessment of the stricture at least 4 biopsies were taken under direct visual control using the specially dedicated mini forceps.

Results: One hundred and eighty patients (n=180, 111 men, 69 women) underwent cholangioscopy for evaluation of indeterminate biliary strictures for the study period. The biliary stenosis were classified according

to the histology results as follows :72 malignant, 71 benign, 37 inconclusive for malignancy. Final diagnosis was made on the basis of definitive malignant histology, surgical findings, diagnostic laparoscopy or clinical follow-up of at least 6 months. Among the 71 patients with benign histology, the final diagnosis was changed to "malignant" in 50. Among the 37 patients with histology "inconclusive for malignancy", the final diagnosis was malignant in 35.

Conclusion: Despite the significant technological advancements in the cholangioscopy in recent years, making the procedure easier, more accessible and with very good image quality, further improvement of biopsy technique is needed. The biliary strictures still remain a diagnostic challenge for the pancreato-biliary endoscopist due to the low sensitivity of the visually guided sampling.

Disclosure: Nothing to disclose.

P0922

RISK FACTORS FOR POST-ENDOSCOPIC RETROGRADE CHOLANGIO-PANCREATOGRAPHY PANCREATITIS (PEP) IN CHILDREN WITH CHRONIC PANCREATITIS AND ITS PREDICTION USING 4-HOUR POST-PROCEDURE SERUM AMYLASE AND LIPASE LEVELS

A. Samanta¹, S. Vadlapudi¹, A. Srivastava¹, S. Mohindra², U. Poddar¹, M. Sen Sarma¹, V. A. Saraswat²

¹Sanjay Gandhi Post Graduate Institute of Medical Sciences, Department of Pediatric Gastroenterology, Lucknow, India,

²Sanjay Gandhi Post Graduate Institute of Medical Sciences, Department of Gastroenterology, Lucknow, India

Contact E-Mail Address: arghyasamanta2905@gmail.com

Introduction: Post-endoscopic retrograde cholangiopancreatography (ERCP) pancreatitis (PEP) has a reported incidence of 10-20% in children undergoing ERCP for any indication.^{1,2}

Literature on PEP in children with chronic pancreatitis (CP) is scarce. As PEP carries potential risk of morbidity and mortality, early PEP prediction would allow earlier detection and timely management. Serum amylase and lipase levels, measured at 4 hours post-ERCP, predict PEP with good sensitivity and specificity in adults.³ Literature regarding the same in children is not available.

Aims & Methods: This cross-sectional study was done to identify risk factors for PEP in children with CP and to assess the usefulness of 4-hour post-ERCP serum amylase and lipase levels for early PEP prediction.

Children with CP who were admitted and underwent ERCP between January 2021 and March 2022 were enrolled. The diagnosis of CP was according to INSPPIRE criteria.⁴ Definition and severity of PEP was classified according to the consensus criteria.⁵

Detailed history of previous and current ERCP procedures (prior ERCP and PEP, difficult cannulation [>5 attempts], endoscopic sphincterotomy, contrast injection, balloon dilatation, presence of pancreatic duct stone, pancreatic duct stent placement, etc) and complications were noted in a pre-designed proforma. Patients with PEP were given standard treatment as per protocol. Serum amylase and lipase levels before the procedure, at 4 hours and 24 hours after the procedure were measured.

Univariate and multivariate analysis was done to compare patients with and without PEP. The receiver operating characteristic (ROC) analysis was done to determine the predictive efficacy of 4-hour post-ERCP amylase and lipase levels for diagnosis of PEP.

Results: Total 62 ERCP procedures were done in 30 children (27 boys). Eight children had PEP. One child who underwent ERCP 3 times, had PEP twice. Thus, PEP occurred in 9(14.5%) out of 62 ERCP procedures (5 mild, 2 moderate, 2 severe). There was no mortality. In the univariate analysis, endoscopic sphincterotomy (p 0.04), difficult cannulation (p 0.004) and

prior PEP (p 0.036) were identified as risk factors while prior ERCP (p 0.04) was protective. In the multivariate analysis, difficult cannulation [Odds ratio 5.83, 95% confidence interval (CI) 1.329-25.592; p 0.008] was the sole independent risk factor for PEP (Table 1).

On ROC analysis, 4-hour post-ERCP serum amylase [area under the curve (AUC) 0.930, 95% CI 0.858-0.999, p < 0.001] and lipase level [AUC 0.948, 95% CI 0.890-0.998, p < 0.001] showed good test performance as predictor of PEP. A 4-hour serum amylase of 298 U/L [upper normal limit (UNL) 90 U/L] showed sensitivity of 90%, specificity of 84.2%, positive predictive value (PPV) of 50%, negative predictive value (NPV) of 98%, comparable to 4-hour serum lipase of 186 U/L (UNL 40 U/L; sensitivity 90%, specificity 89.5%, PPV 60%, NPV 98%).

Variables	ERCP sessions with PEP, n=9	ERCP sessions without PEP, n=53	Univariate p value	Multivariate p value	Adjusted Odds ratio (95% Confidence interval)
Prior ERCP	3/9(33.3%)	39/53(73.6%)	0.041	0.728	
Prior post-ERCP pancreatitis	2/9(22.2%)	2/53(3.7%)	0.036	0.698	
Endoscopic sphincterotomy	7/9(77.8%)	16/53(30%)	0.041	0.076	
Difficult cannulation (>5 attempts)	8/9(88.9%)	13/53(24.5%)	0.004	0.008	5.832 (1.329-25.592)
Minor papilla cannulation	2/9(22.2%)	7/53(13%)	0.907		
Pancreatogram	9/9 (100%)	53/53(100%)	1		
Stricture dilatation	7/9(77.8%)	37/53(70%)	0.638		
Pancreatic duct stent placement	7/9(77.8%)	37/53(70%)	0.386		
Pancreatic duct stone	6/9 (60%)	23/53(38.3%)	0.22		

Table 1: Logistic regression analysis of procedure-related risk factor for post-ERCP pancreatitis (PEP) in children with chronic pancreatitis.

Conclusion: PEP complicated 14.5% of ERCP procedures in children with CP. On multivariate analysis, difficult cannulation significantly increased risk of PEP. Post-ERCP 4-hour serum amylase and lipase have good sensitivity and specificity for predicting PEP early.

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Disclosure: Nothing to disclose.

P0923

REAL LIFE PATENCY OF PLASTIC BILIARY STENTS IN THE PANDEMIC ERA - IS STENT REMOVAL AFTER 6 MONTHS SAFE?

M. Freitas^{1,2,3}, T. Lima Capela^{1,2,3}, V. Macedo Silva^{1,2,3},
T. Cúrdia Gonçalves^{1,2,3}, P.B. Carvalho^{1,2,3}, B. Rosa^{1,2,3},
C. Marinho^{1,2,3}, J. Cotter^{1,2,3}

¹Hospital da Senhora da Oliveira, Gastroenterology Department, Guimarães, Portugal, ²Life and Health Sciences Research Institute (ICVS), School of Medicine, University of Minho, Braga, Portugal, ³ICVS/3B's, PT Government Associate Laboratory, Braga/Guimarães, Portugal

Contact E-Mail Address: martasfreitas@gmail.com

Introduction: The SARS-CoV-2 pandemic emerged in 2019 and conditioned the optimal timing of some endoscopic procedures. ESGE guidelines recommend replacement or removal of the plastic biliary stents within 3-6 months to reduce the rate of complications, mainly cholangitis.

Aims & Methods: Our aim was to analyse the outcomes of patients who had delayed plastic biliary stent removal following endoscopic retrograde cholangiopancreatography (ERCP).

We performed a retrospective study including consecutive patients submitted to ERCP with plastic biliary stent placement between January 2019 and December 2021. Delayed removal was defined as presence of biliary stent >6 months after ERCP. The evaluated outcomes were stent migration, stent dysfunction, hospitalization, obstructive jaundice, acute cholangitis, acute pancreatitis, and biliary pathology-related mortality.

Results: One-hundred and twenty patients were submitted to ERCP with plastic biliary stents placement, 56.7% were male, with mean age of 69.4±15.7 years. Indications for plastic biliary stent insertion were bile duct stones (72.5%), benign biliary stricture (20.0%) and post-cholecystectomy biliary fistula (7.5%), and did not differ between patients with or without delayed stent removal. Delayed stent removal occurred in 32.5% of the patients. The median time to stent removal was 3.5±1.3 (min 2, max 6) months for early removal and 8.6±3.1 (min 7, max 19) months for delayed removal.

Patients who had delayed stent removal did not have a significant higher frequency of stent migration (20.5 vs 11.1%, $p=0.17$), stent dysfunction (17.9 vs 13.6%, $p=0.53$), hospitalization (17.9 vs 14.8%, $p=0.66$), obstructive jaundice (2.6 vs 0.0%, $p=0.33$), acute cholangitis (10.3 vs 13.6%, $p=0.77$), acute pancreatitis (0.0 vs 1.2%, $p=1.0$), or biliary pathology-related mortality (2.6 vs 1.2%, $p=0.55$).

Conclusion: Delayed plastic biliary stent removal does not seem to have a negative impact on patients' outcomes. In the current pandemic situation, while scheduled endoscopic procedures may be delayed, replacement or removal of plastic biliary stents can be safely deferred.

Disclosure: No conflicts of interest.

P0924

THE ROLE OF PROPHYLACTIC OCTREOTIDE IN PREVENTING ERCP INDUCED PANCREATITIS

A. Garg¹

¹Vydehi Institute of Medical Sciences, Medical Gastroenterology, Bengaluru, India

Contact E-Mail Address: achal1210@gmail.com

Introduction: Post ERCP Pancreatitis (PEP) has been defined into 3 categories as mild, moderate and severe according to Revised ATLANTA Classification.

Octreotide is a synthetic somatostatin analogue with a longer half-life.

Similar to somatostatin, octreotide is a potent inhibitor of pancreatic enzyme secretion and effect on the contractility of sphincter of Oddi.

Aims & Methods: ESGE 2020 guidelines recommends that future studies to evaluate the efficacy of Octreotide in a dose ≥ 0.5 mg.

The present study is a Double Blinded Randomised Control Study which was carried out in the Department of Gastroenterology and a total of 150 patients were taken which were divided into 2 groups as Control group (N=74) receiving Normal Saline and Study group (N=76) receiving Octreotide.

2 ml of normal saline and octreotide were given according to respective groups subcutaneously 1 hour before procedure followed by 6 hour and 12 hours after ERCP and Serum Amylase and Lipase were measured along with clinical features. The following protocol was followed based on previous studies.

Results: The overall mean age of the study population including study and control group was 52 years.

Most common Indications for ERCP was Choledocholithiasis (50%) followed by malignant cause (30%), Benign Biliary Stricture (10-15%).

Clinical and Procedure related risk factors according to ESGE Guidelines were present in nearly 50-60%.

Hyperamylasemia was present in Study group in 36 patients (47.5%) and amongst Control group in 33 patients (45.7%).

Incidence of Post ERCP Pancreatitis was present in only 5% in study group and 11.4% in control group though statistically it was not significant ($p=0.47$).

Conclusion: Though, Hyperamylasemia was more in Study group but there is decrease in the incidence of Post ERCP pancreatitis in the group receiving octreotide, but the same was not statistically significant as compared with the control (5% vs 11.4%).

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Disclosure: Nothing to disclose.

P0925

RADIATION DOSE OPTIMIZATION IN ERCP: PROSPECTIVE INTERVENTIONAL STUDY

C. Frias Gomes¹, B. Morão¹, C. Nascimento¹, J. Revés¹, E. Barjas¹, C. Gouveia¹, J. Cortez-Pinto¹, R. Loureiro¹, M.L. Gloria¹, A.O. Ferreira¹

¹Hospital Beatriz Ângelo, Gastroenterology, Loures, Portugal

Contact E-Mail Address: catarinagomes27@gmail.com

Introduction: Radiation exposure during endoscopic retrograde colangiopancreatography (ERCP) has led to major concerns in medical societies because of its potential harmful health effects, including increased cancer risk.

Aims & Methods: Our goal was to compare the radiation dose (RD) before and after introducing RD optimization procedures during ERCP (reducing the frameset and magnification; collimation use). An educational session on how to minimize radiation exposure was performed to doctors, nurses and radiologic technicians who are involved in ERCP.

Results: Overall, 162 patients were included (45 control group, 117 post-intervention group). In 52% (84/162) of the cases, the exam was performed by an experienced endoscopist, with the participation of a fellow or training nurse in 78% (127/162). The exams were difficult in 52% (84/162). The mean RD was not different between the two groups (2064 vs 1630 cGycm², p=0.34).

The post-intervention group had higher participation rates of a fellow or training nurse (89% vs 51%, p < 0.001). The RD was lower in the presence of an experienced endoscopist (1126 vs 1580 cGycm², p=0.01) and higher in difficult exams (1653 vs 987 cGycm², p<0.001).

In multiple linear regression, no difference was found between the two groups (B=-171, p=0.67). A more difficult exam (B=1184, p=0.001) and lower endoscopist experience (B=845, p=0.01) were associated with higher RD. The participation of a fellow or training nurse did not influence RD (B=-203, p=0.63).

Conclusion: No difference was found in RD between the two groups, but difficult exams and lower endoscopist experience were associated with higher RD.

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Disclosure: Nothing to disclose.

P0926

WIRE-GUIDED CYSTOTOME DILATATION OF DIFFICULT BENIGN BILIO-PANCREATIC STRICTURES: SINGLE CENTER EXPERIENCE

O. Ksissa¹, L. Dioscoridi¹, E. Forti¹, F. Pugliese¹, M. Cintolo¹, G. Bonato¹, M. Bravo¹, A. Palermo¹, M. Mutignani¹

¹Niguarda-Ca' Granda Hospital, Endoscopy Unit, Milan, Italy

Contact E-Mail Address: kramo89@hotmail.it

Introduction: Usually, benign biliary and pancreatic strictures are dilated endoscopically by using standard devices over a guidewire (such as Soehendra dilator or dilatation balloons) preliminary to place a stent (plastic or metal stent).

Sometimes these techniques fail to overpass the stricture. In these cases, difficult strictures can be managed using other devices (Soehendra screw/cystotome). We report our experience in the use of cystotome for the treatment of difficult strictures.

Aims & Methods: Data were collected from October 2018 to December 2021 and 12 consecutive patients were included (5 males, 7 female; mean age 53 years old).

Total Nr Cases	12
• Males	5 (42%)
• Females	7 (58%)
Age	53 years (mean); range 24-83
Biliary strictures	7 (58%)
• Post surgery	5
• Chronic flogosis	2
Pancreatic strictures	5 (42%)
• Chronic pancreatitis	4
• Post surgery	1

Table 1. Patients characteristics.

Results: Of the 12 patients, 7 had difficult biliary and 5 difficult pancreatic strictures. The treatment using cystotome was successful in 11 patients and allowed to place a stent. Nobody developed major post-procedure adverse events.

Conclusion: The use of a cystotome can be considered an alternative method for dilation of difficult pancreatic and biliary strictures, after the failure of conventional modalities.

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P0927

CLINICAL OUTCOMES OF ENDOSCOPIC PAPILLECTOMY; A LARGE MULTICENTER RETROSPECTIVE STUDY

E. Iwasaki¹, H. Kawashima², A. Katanuma³, S. Ryozaawa⁴, K. Yamamoto⁵, S. Hashimoto⁶, T. Yamao⁷, K. Kubota⁸, T. Iwai⁹, K. Hara¹⁰, A. Sakai¹¹, K. Ikezawa¹², J. Ushio¹³, H. Kato¹⁴, N. Fujimori¹⁵, K. Nakahara¹⁶, E. Ozawa¹⁷, Y. Nakai¹⁸, H. Isayama¹⁹, A. Irisawa²⁰, Y. Igarashi²¹, N. Fujita²², T. Ueki²³, K. Inui²⁴, A. Kayashima¹, A. Nakagawa²⁵, T. Itoi⁵

¹Keio University School of Medicine, Division of Gastroenterology and Hepatology, Department of Internal Medicine, Tokyo, Japan, ²Nagoya University, Department of Gastroenterology and Hepatology, Nagoya, Japan, ³Teine-Keijinkai Hospital, Center for Gastroenterology, Sapporo, Japan, ⁴Saitama Medical University International Medical Center, Gastroenterology, Hidaka, Saitama, Japan, ⁵Tokyo Medical University, Gastroenterology and Hepatology, Tokyo, Japan, ⁶Kagoshima University, Department of Digestive And Lifestyle Diseases, Kagoshima, Japan, ⁷Sasebo City General Hospital, Gastroenterology, Nagasaki, Japan, ⁸Yokohama City University, Department of Gastroenterology and Hepatology, Kanagawa, Japan, ⁹Kitasato University Hospital, Department of Gastroenterology, Sagami-hara-City, Japan, ¹⁰Aichi Cancer Center, Department of Gastroenterology, Nagoya, Japan, ¹¹Kobe University Graduate School of Medicine, Gastroenterology, Kobe, Japan, ¹²Osaka International Cancer Institute, Department of Hepatobiliary and Pancreatic Oncology, Osaka, Japan, ¹³Jichi Medical University, Department of Internal Medicine, Division of Gastroenterology, Tochigi, Japan, ¹⁴Okayama University Graduate School of Medicine, Gastroenterology & Hepatology, Okayama, Japan, ¹⁵Kyushu University, Department of Medicine and Bioregulatory Science, Fukuoka, Japan, ¹⁶St. Marianna University, School of Medicine, Department of Gastroenterology and Hepatology, Kawasaki, Japan, ¹⁷Nagasaki University School of Medicine, Gastroenterology and Hepatology, Nagasaki, Japan, ¹⁸The University of Tokyo, Endoscopy and Endoscopic Surgery, Tokyo, Japan, ¹⁹Juntendo University, Gastroenterology, Tokyo, Japan, ²⁰Dokkyo Medical University School of Medicine, Tochigi, Japan, ²¹Toho University Omori Medical Center, Gastroenterology And Hepatology, Tokyo, Japan, ²²Miyagi Health Check-up Plaza, Sendai, Japan, ²³Fukuoka University Chikushi Hospital, Department of Gastroenterology, Fukuoka, Japan, ²⁴Yamashita Hospital, Department of Gastroenterology, Aichi, Japan, ²⁵Keio University Hospital Clinical and Translational Research Center, Division of Clinical Research Education and Training, Tokyo, Japan

Contact E-Mail Address: iwaiwa2007@gmail.com

Introduction: Endoscopic papillectomy (EP) for duodenal ampullary tumors is rare. Thus, there is insufficient information. Gradually, procedural details regarding EP have been established. However, most clinical reports have been small case series, complicating success rate and complication frequency analyses. Therefore, we conducted a large-scale retrospective multicenter study to clarify the outcomes of EP.

Aims & Methods: We retrospectively collected data on the backgrounds, procedure details, and outcomes of patients with an ampullary tumor who underwent EP at 22 institutions between January 2009 and December 2019. Then, we analyzed the endoscopic complete resection, en bloc resection, adverse events (AEs), clinical success, and overall recurrence rates. Clinical success was defined as endoscopic complete resection without remnant recurrence after one year.

Results: We included 890 patients with a median age of 66 (range, 58–73) years; 534 patients were men (60 %), and 48 had familial adenomatous

polyposis (9.3 %). The median lesion size was 14 (range, 10–20) mm. There were 812 pathological adenoma and adenocarcinoma cases, and the endoscopic complete resection rate was 94.6 %, the en bloc resection rate was 84.7 %, and the R0 resection rate was 44.0%. Furthermore, the pathological negative vertical margin, negative horizontal margin, and negative ductal margin rates were 65.6 %, 68.5 %, and 82.5 %, respectively. Overall, 23.8 % of the patients experienced AEs, 19.4 % experienced delayed bleeding, 13.6 % had pancreatitis, 2.1 % had cholangitis, 2.0 % had perforation, and 2.3 % had bile duct stricture, and 2.4 % had pancreatic stricture; one patient died from procedure-related complications. The clinical success rate was 85.2 %, and the overall recurrence rate was 17.2 % (n = 140). In total, 102 and 35 patients required additional endoscopic treatment or surgical resection, respectively. Multivariate analysis determined that bile duct invasion (odds ratio [OR]: 0.40, p = 0.046), adenocarcinoma component (OR: 0.367, p < 0.0001), pathological R0 resection (OR: 6.2, p < 0.0001), and en-block complete resection (OR: 2.8, p < 0.0001) were independent factors for clinical success without remnant recurrence.

Conclusion: EP is feasible and suitable owing to its high clinical success rate. However, the incidence of complications and remnant recurrence is high, which is cause for concern.

Disclosure: Nothing to disclose.

P0928

ERCP IN PATIENTS WITH ROUX-EN-Y RECONSTRUCTION AFTER GASTRECTOMY: A SINGLE-CENTER OBSERVATIONAL STUDY

A. Palermo^{1,2}, L. Dioscoridi¹, E. Forti¹, F. Pugliese¹, M. Cintolo¹, G. Bonato¹, M. Bravo¹, O. Ksisa¹, M. Mutignani¹

¹ASST Grande Ospedale Metropolitano Niguarda, Digestive and Interventional Endoscopy Unit, Milan, Italy, ²Università degli Studi di Milano Bicocca, Medicine & Surgery, Milan, Italy

Contact E-Mail Address: a.palermo21@campus.unimib.it

Introduction: Roux-en-Y reconstruction after gastrectomy is generally challenging for performing therapeutic ERCP. Principal issues are the difficulty in reaching the papilla and the cannulation in not-standard orientation.

Aims & Methods: This is a retrospective cohort study of consecutive patients with total and subtotal gastrectomy and Roux-en-Y reconstruction (without biliary anastomosis) who underwent ERCP from February 2019 to March 2022 at a tertiary endoscopy center. Use of pediatric colonoscope with or without see-through cap on the tip was the standard method. Alternative approach was EUS-guided approach. Technical success meant as reaching and cannulation of the papilla and clinical success intended as resolution of the indication for ERCP were evaluated as primary outcomes.

Results: Thirty patients with Roux-en-Y reconstruction after gastrectomy underwent ECRP (15 M, 15 F, age 74.5 ± 8.9 yr). Twenty patients underwent subtotal gastrectomy (67%), while the remaining 10 underwent total gastrectomy (33%). ERCP was performed previously to surgery in 10% of patients (3/30).

ERCP indications included common bile duct stones/intrahepatic stones in 67% (20/30), undetermined biliary strictures in 10% (3/30), biliary leak after cholecystectomy in 10% (3/30), chronic pancreatitis in 6.5% (2/30), acute cholangitis in 6.5% (2/30).

In all cases, a forward-viewing pediatric colonoscope was used, with a cap mounted on the tip in 40% of the cases (12/30).

Overall technical success was 84% (25/30). The papilla was reached retrogradely in 60% (18/30) of the cases, and the access to common bile duct/main pancreatic duct was performed using a ball-tip and straight hydrophilic guidewire. Needle knife sphincterotomy in 72% (13/18) and

endoscopic papillary balloon dilation in 28% (5/18) of the cases were subsequently performed. In 23% (7/30) of cases, EUS-guided ERCP was performed: in 57% of cases (4/7), ERCP was conducted anterogradely through hepatico-gastric access; in the remaining 43% (3/7), the papilla was reached across endoscopic entero-enteral bypass [Mutignani et al., 2019]. Technical insuccess was due to impracticability of a EUS-guided trans-gastric access in 3 cases or cannulation failure in the remaining two cases.

Clinical success was achieved in 100% of treated cases (25/25). Bile duct stones extraction was performed in 13 patients; biliary stenting was made using fully covered self-expandible metal stents in 4 cases or plastic stent in one case; plastic pancreatic stents were placed in 3 cases; double pig-tail cholecystic plastic stents were positioned in 3 cases; a naso-gallbladder drainage in one patient.

Adverse events were observed in 7% (2/30) of the patients: one case of post-ERCP pancreatitis, and another case of acute cholangitis.

Conclusion: ERCP in patients with Roux-en-Y reconstruction after gastrectomy remains a challenge and endoscopic multimodal approach may be the key to achieve the best clinical outcome.

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P0929

ENDOSCOPIC TREATMENT OF COMPLICATIONS OF HYDATID CYSTS OF LIVER RUPTURED IN THE BILE DUCTS

T. Addajou¹, A. Benhamdane¹, S. Mrabti², M.O. Guelleh¹, R. Laroussi¹, A. Sair¹, B. Aourarh¹, B. Khadija¹, M. Moussa Ahmed¹, I. elkoti¹, F. Rouibaa¹, A. Benkirane¹, H. Seddik¹

¹Military Hospital Mohammed V, Rabat, Morocco, ²Military Hospital Mohammed V, Gastroenterology II, Rabat, Morocco

Contact E-Mail Address: addajoutarik@gmail.com

Introduction: Hepatic hydatid cyst usually runs asymptotically, while clinical symptoms, are usually due to complications that supervene. The most commonly encountered complication is rupture into the biliary tree with secondary biliary obstruction by intracystic material or cholangitis

Aims & Methods: The objective of our study is to evaluate the contribution of endoscopic retrograde cholangio-pancreatography (ERCP) in the diagnostic and particularly therapeutic management of ruptured liver hydatid cysts in the bile ducts.

Retrospective descriptive and analytical study, from January 2002 to August 2021, which included 50 patients with a hydatid cyst fistulized in the bile ducts. ERCP and endoscopic sphincterotomy were performed in all patients. Overall success was defined by definitive vacuity of the main bile duct.

Results: Among the ERCPs performed in our department during the study period, 4.6% (n = 50) were for a hepatic hydatid cyst communicating with the bile ducts.

The mean age was 46.1 ± 14.8 years with a male predominance of 66%.

For our 50 patients included in the study, ERCP was performed in 52.2% of cases preoperatively, and in 47.8% postoperatively.

ERCP was indicated for acute angiocholitis in 44.9% and persistent external biliary fistula in 34%.

The median bile duct diameter was 10[7-14]mm and the median cyst diameter was 35[27-47].

Sphincterotomy was performed in 96% of patients allowing extraction of hydatid material by balloon or Dormia in 87.8%. Nevertheless 24% required naso-biliary drainage and 8% benefited from biliary prosthesis placement.

The overall success rate was 96% (n=46). The immediate complication rate was 8%(n=4), 1 patient had hemobilia and 3 patients had edge bleeding.

The evolution was marked by the disappearance of jaundice after 5 to 10 days and by the drying up of the external biliary fistula after 10 days.

Conclusion: Our study confirms that endoscopic treatment of ruptured hydatid cyst in the bile ducts is an effective therapeutic alternative, with a low rate of immediate complications and a good long-term evolution.

Disclosure: Nothing to disclose

P0930

SECONDARY SCLEROSING CHOLANGITIS IN PATIENTS WITH COVID-19 ARDS - A CLINICAL-ENDOSCOPIC ANALYSIS

P. Göggelmann¹, V. Pavel¹, S. Schmid¹, P. Dobsch¹, I. Zuber-Jerger¹, M. Müller-Schilling¹, A. Kandulski¹

¹University Hospital Regensburg, Internal Medicine I, Gastroenterology, Endocrinology, Rheumatology, Infectiology, Emergency Medicine, Regensburg, Germany

Contact E-Mail Address: pavel_vlad2008@yahoo.com

Introduction: The SSC-CIP (sclerosing cholangitis in critically ill patients) is a separate entity of SSC in patients with long intensive care stay. Hypotension and prolonged vasopressor therapy are discussed as risk factors. In the context of the COVID-19 pandemic, an increased prevalence of SSC-CIP was seen at our center, especially in the second and third pandemic "waves", which made an intervention using endoscopic retrograde cholangiography (ERC) necessary.

Aims & Methods: The aim of the study was to analyse the clinical, laboratory, microbiological and endoscopic findings and therapies of patients with SSC-CIP and COVID-19 ARDS in association with the clinical course. Retrospectively, the data of 15 patients who were treated by ERC in the Clinic and Polyclinic for Internal Medicine I at the University Hospital Regensburg between February 1st, 2020 and February 1st, 2022 due to SSC-CIP on the basis of a COVID-19 ARDS were analyzed. The focus was on the endoscopic findings, the laboratory values at the time of the initial diagnosis and the microbiological results.

Results: 12 male and 3 female patients were included in the analysis. The mean age was 61 years (range 40-76). All patients had COVID-19 ARDS and were mechanically ventilated. All required catecholamines.

On average 2.4 ERCs were performed. Biliary casts were found in all patients and rarefaction of the intrahepatic bile ducts in 60%. Bile duct stenosis could only be detected in 3 patients. The casts were therapeutically extracted and the stenoses dilated.

9 patients died within the study period. 6 patients are in follow-up with repeated endoscopic intervention and close re-evaluation with regard to a future liver transplantation.

Conclusion: The mortality rate in patients who develop SSC-CIP as part of a COVID-19 infection is high. Endoscopic treatment may improve temporarily liver function, however these patients must be evaluated for liver transplantation.

Disclosure: Nothing to disclose.

P0931

OUTCOMES OF ENDOSCOPIC DRAINAGE IN CHILDREN WITH PANCREATIC FLUID COLLECTIONS: A SYSTEMATIC REVIEW AND META-ANALYSIS

Z. Nabi¹, R. Talukdar¹, S. Lakhtakia¹, D.N. Reddy¹

¹Asian Institute of Gastroenterology, Gastroenterology, Hyderabad, India

Contact E-Mail Address: zaheernabi1978@gmail.com

Introduction: Endoscopic drainage is an established treatment modality in adult patients with pancreatic fluid collections (PFCs). There is limited data regarding the efficacy and safety of endoscopic drainage in pediatric cases.

Aims & Methods: In this systematic review and meta-analysis, we aim to analyze the outcomes of endoscopic drainage in children with PFCs. Literature search was performed in Embase, PubMed, Google scholar for studies evaluating the outcome of endoscopic drainage with or without endoscopic ultrasonography (EUS) guidance in pediatric PFCs from inception to May 2021. Primary objective of the study was clinical success defined as resolution of PFCs. Secondary outcomes included technical success, adverse events and recurrence rates.

Results: 14 studies (187 children, 70.3% boys) with pooled mean age of 11.7 years (95%CI 10.2-13.2 years) were included in the review. The subtypes of fluid collection included pseudocysts in 60.3% and WON in 39.7%. Endoscopic drainage of PFCs were performed with and without EUS guidance in ten and three studies, respectively. The most common route for drainage was trans-gastric (n=139) followed by trans-esophageal (n=4) and trans-duodenal (n=2). The type of stent used for endoscopic transmural drainage were reported in ten studies including one or more plastic stents in six, either plastic or metal stent in three, and exclusively metal stents in one study.

The pooled technical success rates in studies performing drainage of PFCs with and without EUS guidance were 95.3% (95% CI 89.6 - 98%; $I^2=0$) and 93.9% (95% CI 82.6 - 98%; $I^2=0$), respectively. The pooled clinical success after one and two endoscopic interventions was 88.7% (95% CI 82.7 - 92.9%; $I^2=0$) and 92.3% (95% CI 87.4% - 95.4%; $I^2=0$), respectively.

The pooled mean follow-up after endoscopic drainage reported in ten studies was 26.6 months (95% CI 20.9 - 32.3 months; $I^2=78\%$). The pooled rate of recurrent PFCs after endoscopic drainage was 10.4% (95% CI 6.1 - 17.1%; $I^2=0$). The pooled rates of overall and major adverse events were 16.8% (95% CI 9.8% - 27.2%; $I^2=28.6\%$) and 6.3% (95% CI 3.3%-11.4%; $I^2=0$), respectively.

Conclusion: Endoscopic drainage is a safe and effective procedure in selected children with PFCs. Future studies are required to compare endoscopic versus EUS guided drainage of PFCs in children.

Disclosure: Nothing to disclose.

P0932

TRANSESOPHAGEAL EUS IN THE DIAGNOSIS OF THE LUNG MASSES: A MULTICENTER EXPERIENCE WITH FINE-NEEDLE ASPIRATION (FNA) AND FINE-NEEDLE BIOPSY (FNB) NEEDLES

B.P. Mangiavillano¹, F. Spatola², A. Facciorusso³, G. De Nucci⁴, D. Ligresti⁵, L.H. Eusebi⁶, A. Lisotti⁷, F. Auriemma⁸, L. Lamonaca⁹, D. Paduano², S.F. Crinó¹⁰, S. Scarlata¹¹, E. Troncone¹², G. Del Vecchio Blanco¹³, G. Manes¹⁴, M. Traina¹⁵, A. Bertani¹⁶, A. Ofosu¹⁷, C. Binda¹⁸, C. Fabbri¹⁹, N. Muscatiello²⁰, P. Fusaroli²¹, A. Repici²², S. Carrara²³

¹Humanitas - Mater Domini, Gastrointestinal Endoscopy, Castellanza (VA), Italy, ²Humanitas - Mater Domini, Castellanza (VA), Italy, ³University of Foggia, Gastroenterology, Foggia, Italy, ⁴ASST Rhodense, Gastroenterology and Endoscopy Unit, Milano, Italy, ⁵IRCCS - ISMETT, Endoscopy Service, Department of Diagnostic and Therapeutic Services, Palermo, Italy, ⁶Policlinico Sant'Orsola - University of Bologna, Gastroenterology and Endoscopy Unit, Bologna, Italy, ⁷Hospital of Imola, University of Bologna, Gastroenterology Unit, Bologna, Italy, ⁸Humanitas Mater Domini, Gastroenterology and Digestive Endoscopy, Castellanza, Italy, ⁹Humanitas Mater Domini, Gastroenterology and Endoscopy Unit, Chieti, Italy, ¹⁰Ospedale di Verona, Digestive Endoscopy Unit, Verona, Italy, ¹¹CBM, Rome, Italy, ¹²Humanitas Research Hospital, Digestive Endoscopy Unit, Division of Gastroenterology, Rozzano (MI), Italy, ¹³Giovanna Del Vecchio Blanco University of Rome Tor Vergata, University of Rome Tor Vergata, Roma, Italy, ¹⁴ASST Rhodense, Gastroenterology, Garbagnate, Italy, ¹⁵Ismett / UPMC ITALY, Endoscopic Service, Palermo, Italy, ¹⁶ISMETT, Palermo, Italy, ¹⁷University of Cincinnati, Cincinnati, United States, ¹⁸AUSL Romagna, Gastroenterology and Digestive Endoscopy Unit, Forlì-Cesena Hospitals, Forlì, Italy, ¹⁹AUSL Romagna, Forlì-Cesena Gastroenterology, Gastroenterology, Bologna, Italy, ²⁰Sofar Riuniti di Foggia, Gastroenterologia, Foggia, Italy, ²¹University of Bologna, Gastroenterology, Imola, Italy, ²²Ist. Clinico Humanitas Rozzano, Gastroenterology, Milano, Italy, ²³Istituto Clinico Humanitas, Gastrointestinal Endoscopy, Milano, Italy

Contact E-Mail Address: danilo.paduano@libero.it

Introduction: Intraparenchymal lung masses inaccessible through bronchoscopy or endobronchial ultrasound guidance pose a diagnostic challenge.

Furthermore, some fragile or hypoxic patients may be poor candidates for transbronchial approaches. Endoscopic ultrasound-guided fine-needle aspiration/biopsy (EUS-FNA/FNB) offers a potential diagnostic approach to lung cancers adjacent to the esophagus.

Aims & Methods: We aimed to evaluate the feasibility, accuracy, and safety of trans-esophageal EUS-FNA/FNB for tissue sampling of pulmonary nodules. We retrospectively analyzed data from patients with pulmonary lesions who underwent EUS-FNA/FNB between March 2015 and August 2021 at eight Italian endoscopic referral centers.

Results: A total of 47 patients (36 males; mean age 64.47 ± 9.05 years) were included (22 EUS-FNAs and 25 EUS-FNBs). Overall diagnostic accuracy rate was 88.9% (76.3%-96.2%). The sensitivity and diagnostic accuracy were superior for EUS FNB sampling versus EUS-FNA (100% vs 78.73%); $p = 0.05$, and (100% vs 78.57%); $p = 0.05$ respectively. Additionally, sample adequacy was superior for EUS FNB sampling versus EUS-FNA (100% vs 78.5%); $p = 0.05$.

Multivariate logistic regression analysis for diagnostic accuracy showed nodule size at the cut-off of 15 mm (OR 2.29, 1.04-5.5, $p = 0.05$) and use of FNB needle (OR 4.33, 1.05-6.31, $p = 0.05$) as significant predictors of higher diagnostic accuracy. There were no procedure-related adverse events.

Conclusion: This study highlights the efficacy and safety of EUS-FNA/FNB as a minimally invasive procedure for diagnosing and staging of periesophageal parenchymal lung lesions. The diagnostic yield of EUS-FNB was superior to EUS-FNA.

Disclosure: Nothing to disclose.

P0933

ENDOSCOPIC ULTRASOUND-GUIDED FINE NEEDLE BIOPSY- PROMISING RESULTS WITH NEWLY DESIGNED NEEDLE WITH MULTI-BLADE THREE-PRONG TIP

P. Karagoyozov¹, I. Zhecheva¹

¹Acibadem City Clinic Tokuda University Hospital, Department of Interventional Gastroenterology, Sofia, Bulgaria

Contact E-Mail Address: petko.karagoyozov@gmail.com

Introduction: Endoscopic ultrasound-guided fine needle core biopsy (EUS-FNB) is currently the procedure of choice to obtain samples to reach the definitive diagnosis of lesions of the gastrointestinal tract and of surrounding organs. It has the advantage of providing well preserved tissue for histologic grading and subsequent molecular biological analysis.

Aims & Methods: The aim of this study was to assess the performance of EUS-FNB using a new needle with multi-blade three-prong tip for histologic diagnosis of lesions, accessible for endoscopic ultrasound-guided biopsy. Data was collected retrospectively from April 2021 to October 2021. All the patients underwent endoscopic ultrasound with a linear scope (Fujifilm EG-580UT) and fine needle biopsy using a new needle with multi-blade three-prong tip-22G Trident™ (Micro-Tech Endoscopy).

Results: Forty nine patients (24 men, 25 women) underwent EUS-guided biopsy during the study period. Pancreatic ductal adenocarcinoma was proven in 25. Only 2 patients with solid pancreatic lesions had false negative histology. Gastric adenocarcinoma(after negative forceps biopsy) was proven in 2. Metastatic paraesophageal lymph nodes were proven in 6. Liver metastasis from pancreatic cancer were proven in 2. Gastric, esophageal and colonic GIST were proven in 7 patients. Gastric lipoma was proven in 1. Benign pancreatic lesions (pseudocysts) were proven in 2. Mediastinal lymphoma was proven in 2. Median number of needle passes was 3,45 (2-5).

No complications were observed during the first 48 hours and after 30 days follow-up. The procedure yielded tissue for histologic diagnosis in 95,92% of cases. Imunochemical analysis was possible in all where needed.

Conclusion: Endoscopic ultrasound-guided fine needle biopsy using the new needle with multi-blade three-prong tip is safe and highly effective. Histologic diagnosis is possible in nearly 100% in all accessible areas.

Disclosure: Nothing to disclose.

P0934

ENDOSCOPIC ULTRASONOGRAPHIC FINDINGS OF SUBEPITHELIAL LESION IN THE UPPER GASTROINTESTINAL TRACT WITH AN INCREASE IN SIZE

S.Y. Cho¹, D.H. Kim¹, H.-S. You¹, C.H. Park¹, H.-S. Kim¹, S.K. Choi¹, S.-Y. Park¹

¹Chonnam National University Hospital, Division of Gastroenterology, Department of Internal Medicine, Gwangju, Korea (Republic of)

Contact E-Mail Address: chouseyeon@hanmail.net

Introduction: Endoscopic ultrasonography (EUS) is beneficial modality for evaluating subepithelial lesion (SEL) in the upper gastrointestinal (GI) tract¹. It can provide useful information such as size, layer of origin, echo-

genicity and specific foci of SEL². One of the most worrisome characteristics of SEL is its large size³. Therefore, it is helpful to predict an increase in size of SEL in deciding proper follow-up and management strategy.

Aims & Methods: We aimed to figure out EUS findings of SEL with an increase in size at the first examination. Medical records of 2539 patients with SEL in the upper GI tract (esophagus, stomach, duodenum) detected in our hospital between 2004 and 2016 were reviewed retrospectively. We analyzed 672 of SELs which were evaluated by EUS at the first detection and were followed-up over at least 36 months.

We evaluated size, echogenicity, border, anechoic foci, calcification, deep attenuation, septation and involving layer of SEL on EUS. The size of SEL was measured by visual estimation compared to size of biopsy forceps. We defined 'an increase in size' as 25% increase in the longest diameter of SEL. We performed Cox proportional hazards regression and controlled relevant variables in a regression analysis.

Results: SEL in the esophagus accounted for 22.6% (152/672), 64.0% (430/672) of SEL was in the stomach and 13.4% (90/672) of SEL was in the duodenum. Mean initial diameter of SEL was 10.7±4.1mm (range, 3–20 mm). During the mean follow-up period of 68 months (range, 36–190months), 14.4% (97/672) of SEL showed an increase in size.

There was a difference in age (age 56.8±10.6 VS 54.2±10.6, P=0.03) and initial size (11.7±4.2mm VS 10.5±4.1mm, P=0.01) at the time of diagnosis of SEL in the upper GI tract between a group with an increase in size and a group without an increase in size. An increase in size of SEL was more frequently observed in the stomach than in the esophagus and duodenum (P<0.01).

Cox regression analysis showed that homogeneity of echo, border, septation and deep attenuation of SEL are not related to an increase in size. Anechoic foci and calcification of SEL are negatively correlated with an increase in size and deep involving layer (4th layer) is positively correlated with an increase in size.

Variables	Crude odds ratio	95% CI	P-value	Adjusted odds ratio	95% CI	P-value
Age	1.039	1.018-1.061	<0.001	1.039	1.018-1.061	<0.001
Initial diameter in EUS	1.126	1.074-1.181	<0.001	1.112	1.063-1.164	<0.001
Homogeneity (Homogenous/Heterogenous)	Reference/1.146	0.475-2.764	0.762			
Border (Indistinct / Distinct)	Reference/0.793	0.289-2.173	0.652			
Anechoic foci	0.381	0.122-1.189	0.096	0.326	0.129-0.827	0.018
Calcification	0.306	0.092-1.012	0.052	0.297	0.093-0.949	0.040
Deep attenuation	0.514	0.121-2.189	0.368			
Septation	0.444	0.153-1.287	0.135			
Involving layer (Superficial: 1~3rd layer/ Deep:4th layer)	Reference/1.644	1.038-2.604	0.034	1.870	1.212-2.884	0.005

Table.

Conclusion: SEL in older age, with larger initial size and in the stomach tends to show an increase in size. Also, SEL involving deep layer, absence of anechoic foci and absence of calcification on EUS is more likely to increase in size. Therefore, short-term follow-up and endoscopic or surgical management have to be considered in upper GI SEL presenting such characteristics on EUS.

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Disclosure: Nothing to disclose.

P0935

SAFETY AND EFFICACY OF ENDOSCOPIC CONVENTIONAL CYANOACRYLATE GLUE VS EUS-GUIDED COIL PLUS CYANOACRYLATE TECHNIQUE IN THE TREATMENT OF GASTRIC VARICES: A RANDOMIZED CONTROLLED TRIAL (NCT05038319)

T.S.A. Satya Maharshi¹, J. Basha¹, R. Gupta¹, S. Lakhtakia¹, R. Yarlagadda¹, M. Ramchandani¹, Z. Nabi¹, N. Jagtap¹, P. Pal¹, M. Vamsi Turpati¹, S. Asif¹, D. Nageshwar Reddy¹

¹Asian Institute of Gastroenterology, Hyderabad, India

Contact E-Mail Address: maharshi2059@gmail.com

Introduction: Gastric varices are typically treated by Endoscopic injection of cyanoacrylate glue. Various complications have been described related to this treatment, with systemic embolism being the most severe. Endoscopic Ultrasound (EUS) offer a unique opportunity to directly visualize and access gastric varices for the treatment.

Aims & Methods: Aim: This was a randomized controlled trial (RCT) to compare the safety and efficacy of Endoscopic conventional Cyanoacrylate injection technique to the EUS guided coil with cyanoacrylate injection for the treatment of gastric varices.

Methods: This RCT was done at a large tertiary care center from 1st February 2020 to 31st August 2021. Patients with gastric varices requiring endoscopic treatment constituted the study population and were randomized into 2 groups (Group A & B).

Group A patients received standard endoscopic treatment with injection of a cyanoacrylate and Group B patients received EUS-guided coils deployment and cyanoacrylate injection.

Patients were assessed for immediate complications including bleeding, embolism, pain. A Contrast CT scan of the Chest was performed in all the patients post procedure to detect any evidence pulmonary embolism. Patients were followed at 1, 3 and 6 months.

The Primary outcome was to compare the occurrence of pulmonary embolism between the 2 groups. Secondary outcome was to evaluate the efficacy of the 2 techniques in the complete obliteration of the varices, rebleed rates and reinterventions required in both the groups.

Results: In this RCT, a total of 34 patients were enrolled and 17 patients were included in each group. Pulmonary embolism was documented on CECT Chest, in 3 (17.6%) patients in group A and in only 1 (5.8%) patient in group B ($p=0.591$). All cases of embolism were asymptomatic. Though there was no significant difference between the 2 groups, a greater tendency towards embolism was observed in the group A.

Of the 16 patients in group A, 10 (62.5%) had complete obliteration at 1 month, whereas 15 (93.75%) had complete obliteration of the gastric varices in group B ($p=0.03$).

In group A, 7 (43.75%) required reintervention on follow up due to incomplete obliteration, whereas in group B, only 1 out of 16 (6.25%) required reintervention ($p=0.03$). In group A, 2 (12.5%) had rebleed at 3 months follow up whereas in group B, none of the patient had rebleed ($p=0.144$). The

mean quantity of cyanoacrylate required for varix obliteration was found to be significantly lower in group B when compared to group A (1.18 ± 0.39 ml vs. 2.47 ± 0.71 ml; $p=0.001$).

Outcome measures	Group A (n=17) (Endoscopic Glue)	Group B (n=17) (EUS Coil + Glue)	P value
Primary outcome			
Pulmonary embolism	3/17 (17.6%)	1/17 (5.8%)	P=0.59
Secondary Outcomes			
Complete obliteration of varix at 1 month	10/16 (62.5%)	15/16 (93.75 %)	P=0.03
Overall Rebleeding	2/16 (12.5 %)	0/15 (0%)	P=0.14
Overall Reintervention	7/16 (43.75%)	1/16 (6.25%)	P=0.01

Conclusion: EUS-guided coil and cyanoacrylate injection was highly effective in obliteration of gastric varices and reducing the need for reinterventions when compared to conventional endoscopic cyanoacrylate injection. Also, the risk of embolism with EUS guided treatment was low when compared to Endoscopic treatment, though the difference was not statistically significant.

Disclosure: Nothing to disclose.

P0936

ENDOSCOPIC ULTRASOUND-GUIDED ELASTOGRAPHY FOR DETERMINING MALIGNANCY OF SOLID PANCREATIC LESIONS. PROSPECTIVE REGISTRY FROM A REFERRAL CENTER

J. Iglesias-Garcia^{1,2}, M. Galego-Fernandez^{1,2}, M. Otero-Iglesias^{1,2}, A. Rama-Fernandez^{1,2}, M. Loureiro-Veira^{1,2}, J. Lariño-Noia^{1,2}, D. de la Iglesia-Garcia^{1,2}, J.E. Domínguez Muñoz^{1,2}

¹University Hospital of Santiago de Compostela, Gastroenterology, Santiago de Compostela, Spain, ²Health Research Institute of Santiago de Compostela (IDIS), Santiago de Compostela, Spain

Contact E-Mail Address: julio.iglesias.garcia@sergas.es

Introduction: Endoscopic ultrasound (EUS) guided elastography allows the evaluation of tissue stiffness. It is considered a very useful tool in the differential diagnosis of solid pancreatic tumors.

Aims & Methods: The aim of our study was to evaluate the accuracy of EUS-guided elastography to confirm malignancy of solid pancreatic tumors in clinical routine.

Material and Methods: Analysis of a prospective EUS registry at the University Hospital of Santiago de Compostela, Spain, of patients who underwent EUS-guided elastography for the evaluation of a solid pancreatic tumors between 2008 and 2020. Patients with a definitive histological diagnosis (based on cyto-histological findings of biopsy and/or surgical specimens) were identified and included in the study. EUS-guided elastography was performed with linear Pentax echoendoscopes and Hitachi systems. Elastographic patterns were evaluated, defining hard lesions (blue predominant pattern) as malignant. Sensitivity, specificity, positive and negative predictive value, and overall diagnostic accuracy for malignancy were calculated.

Results: 864 patients were finally included, mean age 67.7 ± 12.3 years, 486 males (56.3%). Mean size of pancreatic tumors was 34.2 ± 13.8 mm (range 6-112). 511 tumors (59.1%) were located in the head of the pancreas, 263 (30.4%) in the body, 64 (7.4%) in the tail and the remaining 26 (3.01%) in the uncinate process. Final diagnosis was a malignant tumor in 746 patients (86.5%) and a benign lesion in 116 (13.5%).

Sensitivity, specificity, positive and negative predictive value, and overall diagnostic accuracy for determining malignancy was 98.5%, 86.8%, 98%, 90% y 97%, respectively.

Conclusion: EUS-guided elastography is a very useful tool for the evaluation of solid pancreatic tumor, allowing the confirmation or exclusion of malignancy with a very high accuracy.

Disclosure: Julio Iglesias-Garcia: International advisor Pentax Medical, Itachi, Boston Scientific, Mediglobe

José Lariño Noia: International advisor Pentax Medical, Boston Scientific

J. Enrique Domínguez Muñoz: International advisor Boston Scientific.

P0937

ACCURACY OF EUS-GUIDED TISSUE SAMPLING FOR THE PATHOLOGICAL DIAGNOSIS OF SOLID LIVER LESIONS

J. Iglesias-Garcia^{1,2}, A. Jardi-Cuadrado^{1,2}, A. Rama-Fernandez^{1,2}, M. Galego-Fernandez^{1,2}, J. Lariño-Noia^{1,2}, D. de la Iglesia-Garcia^{1,2}, H. Lazare-Iglesias³, I. Abdulkader-Nallib³, J.E. Domínguez Muñoz^{1,2}

¹University Hospital of Santiago de Compostela, Gastroenterology, Santiago de Compostela, Spain, ²Health Research Institute of Santiago de Compostela (IDIS), Santiago de Compostela, Spain,

³University Hospital of Santiago de Compostela, Pathology, Santiago de Compostela, Spain

Contact E-Mail Address: julio.iglesias.garcia@sergas.es

Introduction: Endoscopic ultrasound (EUS)-guided tissue acquisition is an accurate technique for the diagnosis of solid focal lesions from different locations. Current clinical guidelines have included solid liver lesions (SLL) as an accepted indication for this method.

Aims & Methods: Aim of our study was to analyze the diagnostic yield of EUS-guided tissue acquisition for the pathological evaluation of SLL.

Material and Methods: Patients who underwent EUS-guided tissue acquisition (fine needle aspiration –FNA– or biopsy –FNB–) for the evaluation of SLL between January 2013 and March 2021 were identified from a prospective EUS registry. EUS and EUS-guided tissue acquisition were performed with linear Pentax echoendoscopes and Hitachi systems.

Sampling was performed with cytological (FNA) and/or histological (FNB) needles. Samples were analyzed on-site by an expert pathologist (FNA) or collected in a cytological solution (Cytolit®) and processed for histological evaluation (FNB). Data are shown as mean and/or percentage as appropriate. Indications, number of needle passes, complications and diagnostic accuracy were evaluated using the histopathological analysis of the surgical specimen or the clinical-radiological evaluation and a minimum follow-up of 6 months in non-operated patients, as gold standard.

Final Diagnosis	Number of cases (correct diagnosis base on EUS-guided tissue acquisition)
Metastasis:	
adenocarcinoma of unknown origin	6 (6)
pancreatic cancer	43 (39)
gastric cancer	8 (8)
lung cancer	15 (14)
neuroendocrine tumor	11 (10)
colo-rectal cancer	8 (7)
biliary tumor	9 (7)
others	7 (4)
Liver cell carcinoma	3 (2)
Benign lesions	4 (4)

Table.

Results: 114 patients (mean age 68.05 years, range 32-88, 64 males) were included. Mean size of SLL was 25.0 mm (range 9-60 mm). Cytological needles were used in 43 cases (37.7%) [22-gauge in 19 cases and 25-gauge in 24]; and histological needles in 71 (62.3%) [19-gauge in 4 cases, 20-gauge in 5, 22-gauge in 37 and 25-gauge in 25]. An adequate sample for the cyto-histological evaluation was obtained in all cases (100%) after a mean of

1.4 passes (range 1-4). In 27 cases (23.7%) FNA samples were evaluated on-site by the pathologist. Table shows the final diagnosis and cases correctly diagnosed by FNA/FNB.

Sensitivity, specificity, and overall accuracy of EUS-guided tissue sampling was 89.1%, 100% and 89.5%, respectively. There was only one minor complication (self-limited mild bleeding at the puncture site).

Conclusion: EUS-guided tissue acquisition is a safe and accurate method for the cyto-histological diagnosis of SLL.

Disclosure: Julio Iglesias-Garcia: International advisor Pentax Medical, Itachi, Boston Scientific, Mediglobe

José Lariño Noia: International advisor Pentax Medical, Boston Scientific

J. Enrique Domínguez Muñoz: International advisor Boston Scientific.

P0938

USEFULNESS OF CONTRAST-ENHANCED ENDOSCOPIC ULTRASOUND (CH-EUS) TO GUIDE THE TREATMENT CHOICE IN SUPERFICIAL RECTAL LESIONS: A CASE SERIES

G. Gibiino¹, M. Sbrancia¹, C. Binda¹, C. Coluccio¹, L. Saragoni², R. Maselli³, A. Repici³, C. Fabbri¹

¹AUSL Romagna, Gastroenterology and Digestive Endoscopy Unit, Forlì-Cesena, Italy, ²Ospedale G.B. Morgagni-L. Pierantoni, U.O. Anatomia Patologica, Forlì, Italy, ³Ist. Clinico Humanitas Rozzano

Dept. of Gastroenterology, Dept. of Gastroenterology, Milano, Italy

Contact E-Mail Address: giulia.gibiino@gmail.com

Introduction: Large rectal lesions can conceal submucosal invasion and cancer nodules. Despite the increasing diffusion of high-definition endoscopes in the Western countries and the importance of an accurate morphological evaluation, a complete assessment in this setting can be challenging.

Endoscopic ultrasound (EUS) plays an established role in the locoregional staging of rectum cancer although with a tendency to an over-estimation of the loco-regional (T)-staging. However, there are still few data on the possible use of contrast-enhanced endoscopic ultrasound (CH-EUS), especially if this ancillary technique may increase the accuracy for predicting invasive nodules among large rectal lesions.

Aims & Methods: We performed a case series of consecutive large (≥20 millimeters) superficial rectal lesions assessed by CH-EUS.

Results: From January 2020 to December 2021 we evaluated eight cases with high-definition endoscopy, characterized by focal areas suggestive for V type according to Kudo Classification. All lesions corresponded to sessile or Granular Lateral Spreading Tumors (LST-G), mixed type or not granular (LST-NG) according to Paris Classification, with size ranging from 30 to 180 mm.

We performed EUS using II generation contrast agent.. Six cases, corresponding to invasive pattern at CH-EUS, were treated with surgery, confirmed as pT2 at final staging. Two cases, with non-invasive pattern at CH-EUS, underwent to curative endoscopic submucosal dissection (ESD) corresponding to pT1a tumors.

Conclusion: CH-EUS can provide additional information for the characterization of rectal superficial lesions with focal areas suggestive for invasive cancer, by improving the performance of EUS in T1 staging.

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P0939

SELECTIVE TISSUE SEPARATION IMPROVES DIAGNOSTIC YIELD OF EUS GUIDED TISSUE ACQUISITION

S. Akerkar¹, R.F. Havre^{1,2}, K.D.-C. Pham¹, Bergen Research Group for Advanced Gastrointestinal Endoscopy (BRAGE)

¹Haukeland University Hospital, Medicine, Bergen, Norway,

²University of Bergen, Department of Clinical Medicine, Bergen, Norway

Contact E-Mail Address: ramaker.birr@gmail.com

Introduction: Endoscopic Ultrasound-guided fine-needle aspiration (EUS-FNA) has been the primary method to obtain cellular material for cytopathological diagnosis in mural lesions, lymph nodes, and tumors along the GI tract¹.

The efficacy of EUS-FNA depends on the site, size, and characteristics of the target tissue as well as the experience of the endosonographer, and the availability of an on-site cytopathology service^{2,3}.

Fine-needle biopsy (FNB) needles are designed to take core samples. Even though the diagnostic yield might have improved with FNB needles, there is still a high miss rate⁴.

One of the challenges with EUS-FNA and FNB is the risk of either non-conclusive or false-negative results, and the procedure must be repeated to procure conclusive biopsy.

Aims & Methods: At our institution, we have previously prepared the tissue samples in 70% ethanol and 3-6 cellular smears that were preserved with fixation buffer spray. From 2018, however, we changed our approach by manually selectively separating the solid fragments of the specimens into formalin aldehyde for histology, and the non-solid materials in a methanol-based fixative for cytology, which also allows the creation of cell block. This manual selective tissue separation (STS) technique has not been previously reported for EUS-guided sampling. In this study, we compared patients who underwent EUS-FNA/FNB in 2017 and 2020. Patients who had cystic lesions were excluded from the study.

We retrospectively registered the relevant parameters from the electronic patient journal (EPJ) including the cytology and histology reports. The aim was to compare the diagnostic accuracy of EUS guided tissue sampling in solid lesions in two time periods before and after the introduction of STS and the methanol-based fixation agent.

Results: During 2017, we performed 117 EUS-FNA and FNB procedures out of which 97 (83%) were for solid lesions. In 2020, 120 out of 130 EUS-FNA and FNB procedures were for solid lesions (92%). The patient's average age in 2017 was 66.7 years, while it was 63.9 years in 2020.

Among patients in 2017, 36 (37.1%) were female and 61 (62.9%) were male while in 2020, 47 (39.2%) were female and 73 (60.8%) were male. In 2017, 32 (33%) procedures were performed using FNA needles while 64 (66%) used FNB needles. In 2020, 41 (34.2%) procedures were performed using FNA needles while 79 (65.8%) used FNB needles ($p=0.90$). The mean number of needle passes during EUS-FNA in 2017 was 2.56 (SD 0.89), while in 2020 it was 2.21 (SD 0.67) ($p=0.001$). Rapid on-site cytopathology service was available during 78 (67%) of procedures in 2017 and 108 (83%) of procedures in 2020 ($p>0.05$). In 2017, 66 out of 97 (68%) procedures provided accurate diagnosis, whilst in 2020, 100 out of 120 (83.3%) procedures were diagnostic ($p<0.02$).

Conclusion: Our analysis suggests that the STS technique and introduction of the new fixation agents have improved the diagnostic accuracy of EUS guided tissue sampling in solid lesions from 2017 to 2020.

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Disclosure: Khanh Do-Cong Pham is a consultant for Boston Scientific and Ambu, and a speaker for Taewoong and Olympus.

Roald Flesland Havre has received lecture fees from Bristol-Myers-Squib.

P0940

COMPARISON OF DIAGNOSTIC ACCURACY OF EUS GUIDED FINE-NEEDLE BIOPSY AND CYTOLOGY WITH ROSE IN PANCREATIC SOLID LESIONS (PSLS) USING NEWER GENERATION BIOPSY NEEDLES

S. Sundaram¹, U. Chhanchure¹, V. Seth¹, P. Patil¹, S. Mehta¹

¹Tata Memorial Hospital, Department of Digestive Diseases and Clinical Nutrition, Mumbai, India

Contact E-Mail Address: drsridharsundaram@gmail.com

Introduction: There have been significant advances in Endoscopic ultrasound guided tissue sampling, with better acquisition using biopsy needles. Whether Rapid On-site examination (ROSE) increases yield in patients who undergo biopsy has been a matter of debate. We aimed to compare yield of EUS guided biopsy with smear cytology with adequacy confirmed by ROSE, acquired using the same needle.

Aims & Methods: Consecutive patients with solid pancreatic lesions (PSLS) who underwent EUS-guided sampling of pancreatic solid lesions from January 2021 to December 2021 were included. Demographic details, details of site of lesion, size of lesion, number of passes, adequacy by ROSE, diagnosis as achieved by cytology and histopathologic assessment of core tissue were noted.

Those patients where ROSE was not performed or where core tissue acquisition was not done for histopathology were excluded from the analysis. EUS was performed by 2 experts having experience of more than 100 EUS procedures performed independently.

Sampling was done using 22G Acquire™ needle in all cases using slow stylet pull-through method, with patient either under conscious sedation or general anaesthesia. Minimum of 2 passes, one for ROSE and other for core tissue sampling were done. The first pass was given for ROSE to assess for adequacy. This sample was subsequently sent to cytology for diagnosis. If sample was adequate, additional passes were taken subsequently to acquire core tissue from the solid masses.

This sample was submitted for histopathologic assessment in formalin jars. The adequacy of core tissue was confirmed by Macroscopic On-site Evaluation (MOSE) of whitish core of more than 4 mm length. Final cytology and histopathology reports were compared for diagnostic accuracy. Statistics were performed using SPSS version 26.0 (IBM, Armonk, NY, USA).

Results: 110 patients underwent EUS guided sampling for pancreatic solid lesions during the study period. Of these, 7 patients either underwent only single pass for ROSE or core tissue acquisition without ROSE.

One hundred and three patients were included in the analysis during the study period (mean age 55.5 ± 12.7 years; 57.3% male). Majority of lesions were located in the head of pancreas (82.5%, 85/103) followed by body of pancreas (8.7%, 9/103). Mean largest dimension of lesions was 3.7±1.05 cm (Range 1.5 to 8.0 cm).

Final diagnosis was malignancy in 90 (adenocarcinoma-76, NET-10, SPEN-1, Lymphoma-3) with negative for malignancy in 13 (Autoimmune Pancreatitis-2, Tuberculosis-3). Median number of passes required were 3 (Range 2-6) (3 passes were needed in 33 (32.0%) patients; 4 passes in 31 (30.1%)). In 11 (10.6%) patients more than one pass was required for confirming adequacy on ROSE. Sensitivity and specificity for malignant PSLs for ROSE+cytology was 95.6% and 100% respectively. Final histopathology of core tissue could diagnose malignant PSLs with sensitivity and specificity of 95.6% and 100% respectively.

Comparison using McNemar Chi Square for paired nominal data showed no significant difference (p=1.0) between final HPR and ROSE+Cytology taken with FNB needle.

Conclusion: EUS FNB has high diagnostic accuracy in PSLs. ROSE may not increase diagnostic yield in solid pancreatic lesions sampled using newer generation EUS biopsy needles. Utility of ROSE should be reviewed considering added costs.

Disclosure: Nothing to disclose.

P0941

THE USE OF ANTITHROMBOTIC AND ANTICOAGULANT AGENTS DID NOT INCREASE THE BLEEDING RISK AFTER ENDOSONOGRAPHY (EUS)-GUIDED PUNCTURE

S. Bota¹, M. Razpotnik¹, M. Kutilek², C. Urak¹, G. Essler¹, J. Weber-Eibel¹, A. Maieron², M. Peck-Radosavljevic¹

¹Klinikum Klagenfurt am Wörthersee, Department of Internal Medicine and Gastroenterology (IMuG), Hepatology, Endocrinology, Rheumatology and Nephrology and Emergency Medicine (ZAE) with Centralized Endoscopy Service, Klagenfurt, Austria, ²University Hospital St. Pölten, Internal Medicine 2, St. Pölten, Austria

Contact E-Mail Address: bota_simona1982@yahoo.com

Introduction: Endoscopic ultrasound guided puncture is considered as high bleeding risk procedure.

Aims & Methods: Aim: compare the bleeding rate after EUS fine-needle aspiration (FNA) or biopsy (FNB) in different tumors according to the use of antithrombotic and anticoagulant agents.

Methods: Our bicentric retrospective study included EUS-FNA/FNBs performed between 01/2016-10/2021 in Klagenfurt and 11/2018-04/2021 in St. Pölten.

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 ≥ 1.5g/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.

According to newly updated ESGE guidelines, acetylsalicylic acid can be continued in the case of EUS-FNA/FNB, while clopidogrel should be discontinued seven days for procedure, warfarin five days, and DOACs three days before the intervention. Medication discontinued fewer days than recommended was classified as "ongoing".

Results: 618 EUS-FNA/FNB were assessed (Klagenfurt – 423 and St. Pölten – 195). FNB was performed in 47.4 % of cases.

EUS-FNA/FNB was performed for the following indications: solid pancreatic masses – 53.1%, pancreatic cysts – 21.1%, subepithelial gastrointestinal tumors – 12.1%, and other indications – 13.7%.

Bleeding occurred in 41 cases (6.6%) : 3 cases with major bleeding (0.5%) - immediate endoscopic treated without hemodynamic instability, and 6.1% minor bleedings.

The use of antithrombotic and anticoagulants was not associated with an increased bleeding risk regardless of the tumor type or use of FNB needles.

	All patients with antithrombotic and anticoagulant medication (n=161)	Ongoing medication (n=105)	Discontinued medication (n=56)	No medication (n=457)
Overall bleeding rate	6.8%	8.5%	5.3%	6.5%
Solid pancreatic tumors	9.9%	12.1%	9.1%	8.1%
Pancreatic cysts	2.6%	3.7%	0%	1.1%
FNB needle	7.9%	9.1%	6.2%	6.9%

Conclusion: The bleeding risk after EUS-FNA/FNB was similar in patients with or without antithrombotic and anticoagulant agents.

Disclosure: Nothing to disclose.

P0942

ENDOSCOPIC ULTRASOUND (EUS) STILL RELEVANT IN DIFFICULT PSEUDOACHALASIA WORKUP

C. Chia¹, J. Meenan², I. Koumoutsos², S. DeMartino²

¹Tan Tock Seng Hospital Dept. of Gastroenterology, Gastroenterology & Hepatology, Singapore, Singapore, ²St Thomas' Hospital, Gastroenterology, London, United Kingdom

Contact E-Mail Address: tzechris@gmail.com

Introduction: Pseudoachalasia is an infrequent secondary form of achalasia which can result from malignant or benign tumours, postoperative complications or paraneoplastic syndromes. Management can be vastly different between achalasia and pseudoachalasia, making it important to exclude the latter condition. Oesophago-gastro-duodenoscopy (OGD), high resolution manometry (HRM), barium oesophagram, CT scan and EUS play complementary roles to procure a diagnosis of achalasia and exclude pseudoachalasia.

This is one of the few studies that aims to evaluate the role of EUS in excluding pseudoachalasia for patients referred for achalasia workup.

Aims & Methods: Data was collected retrospectively from hospital electronic records over 7 years. Our study group comprised 77 patients (female=44, male=33) with a mean age of 62 years. All cases had a prior OGD and EUS performed. Only cases with a non-diagnostic OGD (including negative oesophageal biopsies) were included. Cases with obvious mass seen on OGD were excluded.

Work up included the following: (A) classic achalasia symptoms, (B) normal OGD, (C) positive HRM +/- barium for achalasia/gastro-esophageal junction outflow obstruction (GEJ-OO) and (D) had CT scan performed. Yield of excluding pseudoachalasia with addition of EUS was analysed in 4 groups: (1) A+B, (2) A+B+C, (3) A+B+D and (4) A+B+C+D.

Cases referred without information on manometry, barium or CT findings were excluded appropriately in the subgroup analysis. Surveillance was performed within 6-12 months to detect any missed cases of pseudoachalasia. Statistical analysis was performed using SPSS V20 using the McNemar Chi-Square and Cochran's Q.

Results: Almost all patients (98.7%) had dysphagia as one of the main symptoms. OGD was non-diagnostic in all cases. EUS was performed in all patients. Number of pseudoachalasia cases detected in Group (1)[n=77], Group (2)[n=53], Group (3)[n=38] and Group (4)[n=26] were 0, 0, 3 and 0 respectively. With addition of EUS, incremental detection of pseudoachalasia in these respective cohorts were 7.8% (p=0.031), 1.9% (p=NS), 0% (p=NS) and 0% (p=NS). EUS showed a sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV) of 85.7%, 100%, 100% and 98.6%.

There was only 1 case of pseudoachalasia that was not picked up which manifested 2 years later. Other modalities (B, C and D) complemented each other to give excellent values of sensitivity, specificity and NPV (Table 1).

Pseudoachalasia Detection	Sensitivity	Specificity	Positive Predictive Value (PPV)	Negative Predictive Value (NPV)
OGD (n=77) [95% C.I.]	0% [0.00-40.96%]	100% [94.87-100.00%]	NA	90.91% [82.16-96.27%]
HRM +/- barium (n=53) [95% C.I.]	100% [15.81-100.00%]	15.69% [7.02-28.59%]	4.44% [0.54-15.15%]	100% [63.06-100.00%]
CT scan (n=39*) [95% C.I.]	75% [19.41-99.37%]	97.14% [85.08-99.93%]	75% [19.41-99.37%]	97.14% [85.08-99.93%]
EUS (n=77) [95% C.I.]	85.71% [42.13-99.64%]	100.00% [94.87-100.00%]	100.00% [54.07-100.00%]	98.59% [92.40-99.96%]

Table 1.

Conclusion: In excluding pseudoachalasia, addition of EUS to a well complemented workup (typical symptoms, OGD, HRM and/or CT scan) may not yield statistically significant benefit. However, EUS demonstrated good sensitivity and excellent specificity, PPV and NPV for pseudoachalasia detection clinically and should be considered on a case-by-case basis especially in any diagnostic dilemma.

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Disclosure: None.

P0943

ENDOSCOPIC ULTRASOUND GUIDED CYSTOGASTROSTOMY IS TECHNICALLY FEASIBLE, SAFE AND EFFECTIVE IN TODDLERS AND SMALL CHILDREN

S. Sundaram¹, P. Patil¹, S. Mehta¹

¹Tata Memorial Hospital, Department of Digestive Diseases and Clinical Nutrition, Mumbai, India

Contact E-Mail Address: drsridharsundaram@gmail.com

Introduction: Endoscopic ultrasound guided cystogastrostomy (EUS-CG) is the intervention of choice for management of peripancreatic fluid collections (PFCs).¹ A previous study suggested role of EUS-CG in management of PFCs in children between 9 and 18 years of age.²

No previous data on feasibility, safety and efficacy of EUS-CG in toddlers and small children. We aimed to evaluate the safety and efficacy of EUS-CG in toddlers and small children.

Aims & Methods: Retrospective review of prospectively maintained endoscopy database was done for children ≤8 years of age referred for endoscopic management of PFCs between January 2021 to January 2022. Children who underwent percutaneous or surgical intervention for management of PFCs were excluded. Details of demographics, underlying chronic pancreatitis, type of PFC, size and site of PFC, mode of drainage (plastic stents or Biflanged metal stent (BFMS)), technical success, adverse events

and clinical success. EUS-CG was performed by endoscopist (SS) with experience of over 500 EUS procedures performed independently. All EUS procedures were performed using standard linear echoendoscope (GIF UCT180, Olympus, Tokyo, Japan) with 19G needle (Expect needle, Boston Scientific, USA) for aspiration.

To achieve drainage, double pigtail plastic stents (DPPS) (Cook Medical, USA) of 7 Fr 5 cm were used. Nagi Stent (14 mm X 20 mm) (Taewoong Medical, South Korea) was used as BFMS as indicated. Technical success was defined as successful placement of plastic or BFMS with drainage of cyst contents confirmed endoscopically. Clinical success was defined as reduction in size of PFC to <2 cm size on follow up imaging. Adverse events were graded as per standard ASGE lexicon.

Results: Six children were screened for EUS-CG, and 5 underwent EUS-CG (Mean age 6.2 years, Range 4-8 years, 3 females). Persistent abdominal pain was the most common symptom (80%) followed by vomiting (40%). Underlying chronic pancreatitis was evident in 1 patient.

Three patients had pseudocyst while 2 had Walled off pancreatic necrosis (WOPN). Of these, one patient had recurrent pseudocyst after surgical cystogastrostomy. Site of the PFC was body in 4 patients and tail of pancreas in 1 patient. Mean largest dimension of PFC was 8.1 cm (Range 7.2-10.6 cm). Nagi stent was placed in 2 patients and DPPS in 3 patients. Technical success was achieved in 100%. No moderate or severe adverse events were reported.

One patient developed persistent fever after drainage of WOPN which was managed with intravenous antibiotics. Clinical success was achieved in 4 (80%) patients. One patient had spontaneous extrusion of plastic stent with persistence of small collection of 4 cm size.

All patients underwent MRCP subsequently at 3-4 weeks with evidence of disconnected pancreatic duct (DPD) seen in 3 patients (of whom 1 had spontaneous extrusion of plastic stent). Of patients with DPD, exchange to DPPS was done in 2 patients and stent exchange was not feasible in one patient. Stent removal could be done in 2 patients.

Conclusion: EUS guided cystogastrostomy using standard linear echoendoscope is safe and effective in toddlers and small children and should be the procedure of choice for drainage of PFCs.

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Disclosure: Nothing to disclose.

P0944

THE RISK OF MALIGNANCY OF DIAGNOSTIC CATEGORIES DEFINED BY PAPANICOLAOU SOCIETY OF CYTOPATHOLOGY SYSTEM IN EUS-FNA SAMPLING OF SOLID PANCREATIC LESIONS

B. Vasas¹, R. Bor², Z. Bősze², A. Fabian², T. Tóth², A. Balint², Á. Milassin², P. Bacsur², M. Rutka², T. Resál², K. Farkas², T. Molnár², Z. Szepes²

¹University of Szeged, Department of Pathology, Szeged, Hungary,

²University of Szeged, First Department of Medicine, Szeged, Hungary

Contact E-Mail Address: vasas.bela@gmail.com

Introduction: The aim of the standardized diagnostic categories defined by Papanicolaou Society of Cytopathology (PSC) System is to facilitate the communication between pathologists and other members of the multidisciplinary team involved in the management of pancreatic cancer. Furthermore, it provides information about the risk of malignancy.

Aims & Methods: This observational cohort study retrospectively enrolled all consecutive patients with solid pancreatic lesions who underwent endoscopic ultrasound-guided fine-needle aspiration (EUS-FNA) sampling in University of Szeged from 2014 to 2021. The predictive value of diagnostic categories defined by PSC System was determined by histologic outcome and/or clinical follow-up.

Results: A total of 522 EUS-FNA sampling of solid pancreatic lesions was performed during the study period, in which the initial diagnosis based on the EUS morphology was benign in 50 cases and malignant in 472 cases. The diagnostic accuracy of EUS-FNA was 79.12% with 78.21% sensitivity, 93.55% specificity and 99.41% positive predictive value. The risk of malignancy was 100% for “malignant” and 100% for “suspicious for malignancy” categories. In 21 cases, follow-up data was not available in “non diagnostic” and “atypical” categories, which were excluded from the analysis. The proportion of malignancy in these categories was 50.82% and 86.20%, respectively. There were no cases in the “neoplastic: benign” category. The final diagnosis in the “neoplastic: other” category was ductal adenocarcinoma in 3 cases, solid pseudopapillary neoplasm in 3 cases, low grade neuroendocrine tumor in 12 cases and IPMN in 7 cases. Based on this, the risk of malignancy was 72.00%.

Conclusion: Our data confirmed that the “non diagnostic” category does not provide any information about the lesion being sampled. The “atypical” category represents some diagnostic uncertainty, however a high risk of malignancy should be considered. The “neoplastic: other” category by definition contains premalignant lesions and low-grade malignancies which could cause confusion in the interdisciplinary communication, therefore, the reclassifying of this category would be beneficial.

Disclosure: No conflict of interest.

P0945

ROLE OF NOVEL MOTORIZED SPIRAL ENTEROSCOPY IN THE EVALUATION OF SMALL BOWEL DISEASES: A SYSTEMATIC REVIEW AND META-ANALYSIS

Z. Nabi¹, J. Samanta², R. Chavan¹, J. Dhar³, R. Talukdar¹, D.N. Reddy¹

¹Asian Institute of Gastroenterology, Gastroenterology, Hyderabad, India, ²Post Graduate Institute of Medical Education and Research, Gastroenterology, Kolkata, India, ³Post Graduate Institute of Medical Education and Research, Gastroenterology, Chandigarh, India

Contact E-Mail Address: zaheernabi1978@gmail.com

Introduction: Device assisted enteroscopy is an established tool for the evaluation and treatment of various small bowel diseases. Recently, motorized spiral enteroscopy (MSE) has been introduced. Preliminary data suggest safety and efficacy of MSE for the evaluation of small bowel diseases.

Aims & Methods: In this systematic review and meta-analysis, we aim to analyze the performance of MSE for evaluation of small bowel diseases. Literature search was performed in Embase, PubMed, Cochrane database for studies evaluating MSE between Jan 2010 to July 2021. Primary outcome of the study was rate of pan-enteroscopy by antegrade or bidirectional routes. Secondary outcomes included technical success, depth of maximum insertion, procedure duration, diagnostic yield and adverse events.

Results: 10 studies (382 patients, 179 males) were included in the review. Procedures included antegrade in 276, retrograde in 38 and combined in 51 patients. Pooled rate of technical success was 95.6% (95% CI 92.8% - 97.4%; $I^2=0$). Overall, the pooled rate of total enteroscopy rate was 45.9% (95% CI 21.5%-72.5%; $I^2=90.7\%$), by antegrade route in 25.8% (95% CI

12.1%-46.6%; $I^2=82.8\%$) and combined route in 71.3% (95% CI 47.9%-87.1%; $I^2=60.5\%$) of cases. Mean depth of maximum insertion by antegrade and retrograde routes were 444.1 cm (95% CI 381.5-506.7; $I^2=94.9\%$) and 232.8 cm (95% CI 132.5 to 333.2; $I^2=95.4\%$) cm, respectively. Pooled mean duration for antegrade MSE was 43.1 (95% CI 38.6-47.6; $I^2=84.5\%$) minutes and retrograde route was 36.5 (95% CI 28.9-44.1; $I^2=78.1\%$) minutes. Overall, diagnostic yield was obtained in 65.9% patients (95% CI 60.8 - 70.7%; $I^2=72\%$). Pooled rates for all and major adverse events were 17.4% (95% CI 11.7%-25.1%; $I^2=49.5\%$) and 3% (95% CI 1.5% -5.9%; $I^2=0$), respectively.

Conclusion: MSE is safe and effective tool for the evaluation of small bowel disorders. Pan-enteroscopy is possible in more than two-third of patients by combined route with minimal adverse events and relatively shorter procedure duration.

Disclosure: Nothing to disclose

	Single balloon enteroscope	Double balloon enteroscope	Spiral enteroscope	Motorized spiral enteroscope
Total enteroscopy rates (%)	15 to 25	40 to 60	8	3 to 100
Depth of maximal insertion (antegrade), cm	204 to 258	200 to 346	175 to 262	395 to 530
Procedure duration, min	46 to 96	42 to 105	43 to 55	25 to 62
Diagnostic yield (%)	43 to 53	42 to 61	33 to 69	25 to 80
Adverse events (%)	0 to 23	0 to 24	0 to 23	0 to 28
Advantages	Shorter procedure time, easy to use	Higher depth of maximum insertion, extensively evaluated in studies	Short procedure time	Shorter procedure time, high pan-enteroscopy rates
Limitations	Lower depth of maximum insertion	Long procedure duration	Low depth of maximum insertion, two operators required	Limited data on safety, requirement of general anaesthesia

Table. Comparison of available device assisted enteroscopy techniques.

P0946

EFFICACY AND SAFETY OF CONTINUOUS INTRAVENOUS MIDAZOLAM INFUSION AND PETHIDINE HYDROCHLORIDE IN DOUBLE-BALLOON SMALL INTESTINE ENDOSCOPY: A MULTICENTER RANDOMIZED CONTROLLED TRIAL

T. Hamada¹, Y. Sakakibara², T. Kuwai¹, R. Kusunoki¹, T. Mannami³, T. Wakatsuki³, T. Toyokawa⁴, S. Katsushima⁵, N. Esaka⁵, A. Kanda⁶, M. Shimada⁷, M. Kuramochi⁸, S. Hamada⁹, H. Fujii¹⁰, T. Kagaya¹¹, N. Watanabe¹², Y. Sasaki¹³, T. Uraoka¹⁴, K. Mabe¹⁵, K. Kubo¹⁵, M. Kato¹⁵, E. Mita², N. Harada⁹

¹National Hospital Organization Kure Medical Center and Chugoku Cancer Center, Department of Gastroenterology, Kure, Japan, ²National Hospital Organization Osaka National Hospital, Department of Gastroenterology, Osaka, Japan, ³National Hospital Organization Okayama Medical Center, Department of Gastroenterology, Okayama, Japan, ⁴National Hospital Organization Fukuyama Medical Center, Department of Gastroenterology, Fukuyama, Japan, ⁵National Hospital Organization Kyoto Medical Center, Department of Gastroenterology, Kyoto, Japan, ⁶National Hospital Organization Higashi-ohmi General Medical Center, Department of Gastroenterology, Higashi-ohmi, Japan, ⁷National Hospital Organization Nagoya Medical Center, Department of Gastroenterology, Nagoya, Japan, ⁸National Hospital Organization Saitama Hospital, Department of Gastroenterology, Saitama, Japan, ⁹National Hospital Organization Kyushu Medical Center, Department of Gastroenterology, Clinical Research Institute, Fukuoka, Japan, ¹⁰National Hospital Organization Fukuokahigashi Medical Center, Department of Gastroenterology, Koga, Japan, ¹¹National Hospital Organization Kanazawa Medical Center, Department of Gastroenterology, Kanazawa, Japan, ¹²National Hospital Organization Mie Chuo Medical Center, Department of Gastroenterology, Mie, Japan, ¹³National Disaster Medical Center, Department of Gastroenterology, Tokyo, Japan, ¹⁴National Hospital Organization Tokyo Medical Center, Department of Gastroenterology, Tokyo, Japan, ¹⁵National Hospital Organization Hakodate National Hospital, Department of Gastroenterology, Hakodate, Japan

Contact E-Mail Address: damaha_2@yahoo.co.jp

Introduction: Double-balloon small intestine endoscopy is longer in duration and more painful than other endoscopic procedures despite the use of high-dose sedatives and analgesics. A combination of midazolam and pethidine hydrochloride is normally used.

However, the current method of intermittent midazolam administration by giving additional doses during body movements fluctuates the blood concentration of midazolam and is not sufficient to provide the necessary sedation and analgesia.

Aims & Methods: The efficacy and safety of 'continuous intravenous midazolam plus pethidine hydrochloride' (new group) with those of 'intermittent midazolam plus pethidine hydrochloride' (standard group) was compared with a prospective, randomised, controlled trial conducted by 14 centres of the National Hospital Organization Gastroenterology Research Group.

Both groups were sedated with a single intravenous dose of 2.5 mg midazolam at the beginning of the examination. The continuous midazolam infusion was adjusted at 2.5–6.0 mg/h to maintain appropriate sedation levels in the new group. The standard group added 2.5 mg midazolam as needed during body movements if sedation was insufficient.

There were sedation evaluators and anaesthesia personnel along with the endoscopist, but patient assignment was only disclosed to the anaesthesia personnel. Ramsay sedation scale (RSS) was used to assess the sedation status. An RSS score of 3–4 was defined as adequate.

Results: From May 2020 through September 2021, 76 patients were enrolled; 39 were assigned to the new group and 37 to the standard group. Discontinuations prior to drug initiation (one case in each group) were excluded from the analysis. This resulted in a total of 74 patients in the analysis population (FAS, PPS and safety analysis population); 38 in the new group and 36 in the standard group.

The primary endpoint was the mean (standard deviation) rate of adequate sedation of 0.637 (0.315) for the new group and 0.609 (0.272) for the standard group, with an estimated difference (new group – standard group) of 0.024, 95% CI = –0.111–0.160, $p = 0.721$.

The percentage of physical movements requiring treatment interruption was 7.9% (3/38) in the new group and 25.0% (9/36) in the standard group ($p = 0.091$). In terms of surgeon satisfaction, the percentage of patients who wanted to receive the same sedation on the day of examination was 89.5% (34/38) in the new group and 97.2% (35/36) in the standard group ($p = 0.392$).

The percentage of test discontinuation was 5.3% (2/38) in the new group and 2.8% (1/36) in the standard group ($p = 1.000$). The median (range) pethidine dose per hour (mg/hr) was 52.2 (28.6–112.5) in the new group and 48.9 (27.2–116.7) in the standard group ($p = 0.287$). The median (range) midazolam dose per hour (mg/hr) was 8.4 (1.1–21.7) in the new group and 5.7 (1.6–19.1) in the standard group ($p = 0.003$).

Conclusion: The new group had fewer body movements that required interruption, but advantage over the standard group was not established. Continuous infusion might serve as an alternative for sedation in some patient populations, particularly those having difficulty with sedation, owing to its acceptable safety profile.

Disclosure: No conflict of interest.

P0947

HIGHER LEVELS OF OPIOID ANALGESIA AND SEDATION ARE REQUIRED TO MAINTAIN ADEQUATE PATIENT COMFORT AND IMPROVE PROCEDURE SUCCESS IN DEVICE ASSISTED ENTEROSCOPY. IS CONSCIOUS SEDATION ENOUGH?

C. Walker¹, F. O'Hara^{1,2}, R. Connaughton¹, S. Anwar¹, R. Ballester¹, B. Ryan¹, A. O'Connor¹, S. O'Donnell¹, N. Breslin¹, D. McNamara^{1,2}

¹Tallaght University Hospital, Gastroenterology Department, Dublin 24, Ireland, ²Trinity College Dublin, Trinity Academic Gastroenterology Group, School of Medicine, Dublin, Ireland

Contact E-Mail Address: walkerca@tcd.ie

Introduction: Device assisted enteroscopy (DAE) enables identification, biopsy and therapeutic intervention of small bowel pathology. The joint position statement by BSG, JAG and RCoA highlight patient intolerance as an important factor in procedure success and recommend considering deep sedation for protracted and complex procedures, including DAE. While ESGE guidelines from 2018 suggest the choice and level of sedation employed should be guided by patient, procedure, and hospital factors. To this end, we assessed sedation requirements and outcomes for DAE compared to other standard and interventional endoscopic procedures.

Aims & Methods: Our aim was to compare conscious sedation and analgesia requirements for DAE with other standard and interventional endoscopy procedures.

A single centre retrospective comparison study was undertaken. Elective DAE's from 2018 – 2021 identified from our endoscopy database were included. Comparative endoscopic procedures were randomly selected

over the same time period. Cases performed under general anaesthesia or on inpatients were excluded. Patient demographics, procedure type, sedation and analgesia dosages, Modified Gloucester Comfort Scores (CS) (range 1-5), and DAE outcomes were documented. Data was compared between groups with a t-test or Fisher's exact test as appropriate.

Results: In all 786 cases were included; 200 OGD's, 200 Anterograde DAEs (ADAE), 62 Retrograde DAEs (RDAE), 124 Colonoscopies and 200 ERCP's. All cases were performed under conscious sedation with a combination of IV midazolam and fentanyl. Overall mean age was 61.3 years (range 20-90) and 49% (n=386) were male. Demographics were similar between groups, other than for age in the RDAE group, who were younger (mean 54 years, $p < 0.02$).

The mean midazolam dose was significantly higher for ADAEs 5.3mg versus OGDs 2.1mg, $p < 0.0001$. Similarly, mean midazolam dose in RDAE 5.0 mg was higher than for colonoscopy 2.7mg, $p < 0.0001$. More midazolam was also employed for DAEs versus ERCPs 5.2mg and 4.7mg respectively, $p = 0.032$. Of note DAEs and ERCPs required above the maximum recommended 5mg dose; 35% ADAE, 29% RDAE, ERCPs 29% compared to 0.5% of OGDs and 1.6% of colonoscopies, $p < 0.0001$.

There was also a significantly higher fentanyl requirement for both ADAE and RDAE compared to OGD and colonoscopy groups, 68.7mg v 30.6mg and 71.9mg v 42.1 mg respectively, $p < 0.0001$. Again, mean fentanyl dose for DAEs was significantly more than for ERCP, 69.2mg v 63.0mg, $p = 0.02$.

Overall reported comfort was adequate and similar for all procedures (1.1 OGD, Colonoscopy, 1.3, ERCP - 1.3, ADAE - 1.2, RDAE - 1.3).

However, increased midazolam and fentanyl use was associated with more discomfort. CS 1 versus CS 2, 3.6mg and 50mg versus 5mg and 67.1mg, respectively, $p < 0.0001$.

Overall, the success rate based on indication for DAE was acceptable 69% (n=181) and was higher for ADAE 74% (n=147) versus RDAE yield 53% (n=33), $p < 0.002$. Similarly mean depth of insertion was higher for ADAE V RDAE, 180cm v 75.4cm, $p < 0.0001$. Higher levels of sedation use was associated with increased depth of insertion and procedure success, $P < 0.001$.

Conclusion: More opioid and benzodiazepine agents are required to maintain acceptable patient comfort and to allow for adequate depth of insertion and therapeutic intervention in DAE compared to other diagnostic and interventional endoscopies. Where available deeper levels of sedation could offer both a significant procedural advantage and improved patient reported outcomes.

Disclosure: Nothing to disclose.

P0948

TWO DECADES OF CAPSULE ENDOSCOPY: INDICATIONS, DETECTION, COMPLETION AND RETENTION RATES

P. Cortegoso Valdivia¹, K. Skonieczna-Żydecka², A. Elosua González³, M. Sciberras⁴, S. Piccirelli^{5,6}, M. Rullan Iriarte³, T. Tabone⁴, K. Gawel⁷, A. Stachowski⁸, A. Leminski⁹, W. Marlicz^{7,10}, I. Fernández-Urién¹¹, P. Ellul⁴, C. Spada^{5,12}, M. Pennazio¹³, E. Toth¹⁴, A. Koulaouzidis^{15,16,17,18}

¹University Hospital of Parma, University of Parma, Gastroenterology and Endoscopy Unit, Parma, Italy, ²Pomeranian Medical University, Department of Biochemical Sciences, Szczecin, Poland, ³Hospital García Orcóyen, Gastroenterology Unit, Estella, Spain, ⁴Mater Dei Hospital, Division of Gastroenterology, Msida, Malta, ⁵Fondazione Poliambulanza Istituto Ospedaliero, Digestive Endoscopy Unit and Gastroenterology, Brescia, Italy, ⁶Fondazione Policlinico Universitario A. Gemelli IRCCS, Università Cattolica del Sacro Cuore, Rome, Italy, ⁷Pomeranian Medical University, Department of Gastroenterology, Szczecin, Poland, ⁸Pomeranian Medical University, Department of Human Nutrition and Metabolomics, Szczecin, Poland, ⁹Pomeranian Medical University, Department of Urology and Urological Oncology, Szczecin, Poland, ¹⁰Endoklinika, Centre for Digestive Diseases, Szczecin, Poland, ¹¹University Hospital of Navarra, Department of Gastroenterology, Pamplona, Spain, ¹²Università Cattolica del Sacro Cuore, Digestive Endoscopy Unit, Rome, Italy, ¹³City of Health and Science University Hospital, University of Turin, University Division of Gastroenterology, Turin, Italy, ¹⁴Skåne University Hospital, Lund University, Department of Gastroenterology, Malmö, Sweden, ¹⁵OUH Svendborg Sygehus, Department of Medicine, Svendborg, Denmark, ¹⁶University of Southern Denmark (SDU), Department of Clinical Research, Odense, Denmark, ¹⁷OUH, Surgical Research Unit, Odense, Denmark, ¹⁸Pomeranian Medical University, Department of Social Medicine and Public Health, Szczecin, Poland

Contact E-Mail Address: akoulaouzidis@hotmail.com

Introduction: Capsule endoscopy (CE) is a widespread modality for a non-invasive evaluation of the gastrointestinal (GI) tract. Several CE models were introduced throughout the last two decades. In this systematic review we evaluated CE performance measures such as completion, detection, and retention rates.

Aims & Methods: Available literature through August 2021 was screened for papers regarding all capsule types: small bowel, double-headed capsule for the colon or PillCam® Crohn's capsule, magnetically-controlled capsule endoscopy, esophageal capsule and patency capsule. Primary outcomes included detection (DR), completion (CR) and capsule retention rates (RR). A sub-analysis on the outcomes was performed regarding CE main indications such as obscure GI bleeding (OGIB), known/suspected Crohn's disease (CD), celiac disease (CeD), neoplastic lesions (NL) and clinical symptoms (CS).

Results: 328 original articles were included in the study, involving 86,930 patients who underwent CE. The most common indication was OGIB (n=44,750), followed by CS (n=17,897), CD (n=11,299), NL (n=4,989) and CeD (n= 947). Small bowel CE was the most used capsule type (236 studies). DR, CR and RR overall were, respectively, 59%, 89.6% and 2%. According to specific indications, DR, CR and RR were: OGIB (55%, 90.6%, 2%), CD (66%, 86.5%, 4%), NL (63%, 78.2%, 1%), CeD (52%, 94%, 6%), CS (62%, 92.8%, 2%).

No significant difference was seen in the pooled lesion detection per indication group according to capsule type, although the highest DRs were seen with PCC and CCE.

No statistically significant difference was seen in CR, regarding the two most common indications (OGIB and CD, 90.6% and 86.5% respectively), even in the subgroup analysis per capsule type. The overall RR was low (2%), in line with previous literature results. The high value seen in CeD (6%) might be explained by the low number of studies (only 6) providing heterogeneity of the analysis.

Indications	Detection rate (DR)	Completion rate (CR)	Retention rate (RR)
OGIB	55%	90.6%	2%
CD	66%	86.5%	4%
NL	63%	78.2%	1%
CeD	52%	94.0%	6%
CS	62%	92.8%	2%
All indications	59%	89.6%	2%

Conclusion: Overall pooled DR, CR and RR were acceptable for all CE types, with no statistically significant difference. CE confirmed its substantial role in the detection of GI pathology, expanding the scope in the last years thanks to technological advancements, with acceptable rates for a complete examination.

Disclosure: Nothing to disclose.

P0949

SMARTPILL™ WIRELESS MOTILITY CAPSULE ASSESSMENT OF INTRA- AND INTER-INDIVIDUAL VARIABILITY OF SPECIFIC GASTRIC PH RANGES FOLLOWING A LOW-FAT, LOW-CALORIE MEAL: IMPLICATIONS FOR DRUG DELIVERY

H.M. Fadda¹, P.M. Hellström², D.-L. Webb²

¹Butler University, Department of Pharmaceutical Sciences, College of Pharmacy and Health Sciences, Indianapolis, United States, ²Uppsala University, Gastroenterology & Hepatology Unit, Medical Sciences, Uppsala, Sweden

Contact E-Mail Address: dominic-luc.webb@medsci.uu.se

Introduction: Food can alter drug bioavailability through gastric pH changes. Gastric pH can have a significant effect on pH-dependent dissolution of ionizable drugs and enteric delivery systems, including formulations for the next generation of orally ingested peptides, which continue to suffer from poor bioavailability.

Aims & Methods: The aim was to investigate time spent at different pH ranges during a low fat, low calory breakfast, conditions under which medications could be consumed. Along with time within distinct gastric pH ranges, variability was studied. Healthy subjects (n=20) from local population were recruited for 3 visits. Exclusion criteria were: acute or chronic abdominal pain, dysphagia, gastric bezoars, strictures, fistulas, bowel obstructions, diverticulitis, celiac disease, Crohn's disease, ulcerative colitis or proctitis, inflammatory or stenotic gastrointestinal changes, previous GI surgery (except for appendectomy), implanted electromechanical or cardiac pacemaker devices or medications shown to influence gastrointestinal (GI) motility and transit time (prokinetics, antidiarrheals, antiemetics, laxatives) as well as NSAIDs. Participants should refrain from alcohol or smoking and were limited to 5 cups of coffee/day throughout the study. Subjects were fasted overnight. In the morning, they ingested a light, mixed, standardized meal for 10 min consisting of two egg whites, buttered toast and jelly (260 kcal: 3% fat, 21% protein and 76% carbohydrate of which ~3% was fiber). SmartPill™ wireless motility capsule (WMC) was then ingested. This was twice repeated (3 visits total). Gastric phase pH was sorted into pH <2, 2-3, 3-4, 4-5 and >5. All visits and all subjects were pooled to determine median (25-75th percentiles) in min. Data was then

stratified for inter- and intra-subject variability, which were calculated as robust coefficient of variation% (RCV%), which is median absolute deviation / median x 100.

Results: Of 60 possible visits, pH data was obtained for 53. Reference values for gut transit times in these subjects have been published (1). Gastric emptying time was median 176 (137-205) min, mostly spent at pH <2, 111 (67 – 163) min. Following a drop of pH <2, some recordings revealed an upward rebound in the middle of the gastric phase to pH >2, which again dropped below pH 2 prior to when the WMC was expelled from the stomach. This occurred in 2 of the 3 visits in some subjects. Therefore, simple measurements of time to drop to a specific pH can be misleading. This legitimized sorting the gastric phase pH data into time spent within different pH ranges.

Minutes at pH 2-3 and 3-4 were similar: 17 (5.7 – 35.6) and 18 (7.2 - 29.3). Minutes at pH 4-5 was 9 (1.3 - 20.6) and at pH >5 0.7 (0 - 4.4). Inter-subject RCV% was 49% for pH <2, 89% for pH 2-3, 54% for pH 3-4, 97% for pH 4-5 and 148% for pH >5. Intra-subject RCV% was 30% for pH <2, 57% for pH 2-3, 71% for pH 3-4, 106% for pH 4-5 and 144% for pH >5. Variability was less consistent at higher pH ranges, with main differences explained by skewness in inter-subject values, albeit much less time was spent at these pH ranges, particularly pH >5. Of 53 total visits, 16 (30%) never attained pH >5 (i.e., time = 0 min), impacting variability values.

Conclusion: Inter-subject variability can be twofold higher than intra-subject variability, especially in the pH<2 range, where most of the gastric phase is spent under light meal conditions. The data obtained differs from other published values with large, high fat meals. The present data is pertinent, since a substantial number of medicines may be taken in the morning with a light breakfast.

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Disclosure: The authors have no conflicts of interest.

P0950

DIAGNOSTIC ACCURACY OF CAPSULE ENDOSCOPY READING ASSISTED BY ARTIFICIAL INTELLIGENCE FOR EXPERT READERS: INTERIM ANALYSIS OF A SINGLE CENTER EXPERIENCE

S. Piccirelli^{1,2}, A. Bizzotto¹, E.V. Pesatori^{1,2}, D. Salvi^{2,1}, E. Tettoni^{1,2}, N. Belluardo^{2,1}, C. Spada^{2,1}

¹Fondazione Poliambulanza Istituto Ospedaliero, Department of Medicine, Gastroenterology and Endoscopy, Brescia, Italy,

²Università Cattolica del Sacro Cuore, Fondazione Policlinico Universitario A. Gemelli IRCCS, Rome, Italy

Contact E-Mail Address: stefania.piccirelli@gmail.com

Introduction: Artificial Intelligence (AI) promises to revolutionize the field of capsule endoscopy by reducing reading time while maintaining high diagnostic accuracy. Preliminary results show that Convolutional Neural Network (CNN)-based algorithms demonstrate promising diagnostic accuracy in detection of small bowel lesions with relevant reduction of reading time.

Aims & Methods: Primary aim of this study was to compare the diagnostic accuracy of AI-assisted reading with standard reading, when both are performed by expert readers (>500 cases), in detection of significant pathology of the small bowel. Secondary aim was to compare mean reading time of both reading modalities.

A consecutive series of 20 patients who performed Small Bowel Capsule Endoscopy (SBCE) (NaviCam® SB System, Ankon, China) from July to November 2021 at Fondazione Poliambulanza Hospital was prospectively enrolled. All capsule examinations were evaluated by an expert reader according to the standard of care (i.e. ESGE standards). A second blinded

expert reader reviewed all videos in the “AI-assisted” modality (ProScan™, Intelligent Reading Support). In case of discordant results between AI and Standard Reading (SR) a panel of experts was used to resolve the discrepancies. Main diagnoses (suspected SB neoplasia or high potential bleeding lesions -P2 lesions using Saurin classification) reported by each reader were compared, considering SR as the gold standard. Mean reading time of the two readers was also measured and compared.

Results: Of 20 patients (13 females, mean age 69 ± 12) who underwent SBCE, 19 patients had a complete SB examination and were included in the interim per-patient analysis (in 1 patient the capsule remained in the stomach for the entire recording). Both standard and AI-assisted readings detected small bowel pathology in 15 patients while 4 patients had negative examination, with an overall match of main diagnoses reported by two readers. Sensitivity, specificity, positive and negative predictive values of AI-based reading compared to SR were 100%. Mean SB reading time in SR and AI-assisted modality were $41.25 \text{ min} \pm 14.14$ and $4.75 \pm 2.86 \text{ min}$, respectively ($p < 0.0000001$).

Conclusion: AI-assisted CE reading showed 100% diagnostic accuracy in detection of significant small bowel pathology with a significant reduction of reading time.

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Disclosure: Nothing to disclose.

P0951

ROLE OF ARTIFICIAL INTELLIGENCE IN SMALL BOWEL CAPSULE ENDOSCOPY TRAINING

S. Piccirelli^{1,2}, A. Bizzotto¹, E.V. Pesatori^{1,2}, D. Salvi^{1,2}, E. Tettoni^{1,2}, N. Belluardo^{1,2}, C. Spada^{1,2}

¹Fondazione Poliambulanza Istituto Ospedaliero, Department of Medicine, Gastroenterology and Endoscopy, Brescia, Italy,

²Università Cattolica del Sacro Cuore, Fondazione Policlinico Universitario A. Gemelli IRCCS, Rome, Italy

Contact E-Mail Address: stefania.piccirelli@gmail.com

Introduction: Reading of small bowel capsule videos still represents the main limitation since it requires time and prolonged attention. Training in capsule endoscopy is also critical for its time consumption and the number of capsules that make a reader “proficient”. In this scenario, Artificial Intelligence in Small Bowel Capsule Endoscopy (SBCE) might represent a key strategy not only in clinical use but also in a training setting.

Aims & Methods: The primary aim of this study was to measure the inter-observer agreement among novices and experts when both perform standard or AI-assisted SBCE reading. The secondary aim was to evaluate reading time with or without the assistance of AI in both young and expert readers.

10 videos of patients who performed SBCE (NaviCam® SB System, Ankon, China) from July to September 2021 at Fondazione Poliambulanza Hospital were retrospectively evaluated by 2 experts (>500 cases) and 4 novices (<5 cases). Readers were randomized to blindly review videos in standard modality (1 expert reader -E1- and 2 novices -T1 and T2), or with the assistance of Artificial Intelligence (ProScan™, Intelligent Reading Support), (1 expert reader -E2- and 2 novices -T3 and T4). Findings were classified according to the Saurin classification. The agreement between experts and novices was evaluated only for P2 lesions in a per-patient analysis using Cohen's kappa statistic.

Results: 10 SBCE videos of patients (30% males, mean age 68, SD 13) referred for suspected small bowel bleeding were evaluated. At per-patient analysis, expert readers reported the same main diagnoses (100% inter-observer agreement). Inter-observer agreement between novices and experts resulted from moderate to substantial. Mean reading time was also evaluated (see the table below). Standard reading time between experts and novices was comparable.

Conversely, AI-assisted reading time was significantly shorter in experts than in novices. ($p < 0.005$, 95% IC). Overall, the AI-assisted reading time for both expert and novices was significantly shorter when compared to standard reading. ($p < 0.005$, 95% IC).

	Cohen's K	Mean reading time +/- SD
Expert 1 – SR	1	43.7 ± 10.97
Expert 2 – AI	1	4 ± 1.49
Trainee 1 – SR	1	42.1 ± 9.8
Trainee 2 – SR	0.58	40 ± 6.6
Trainee 3 – AI	0.61	14 ± 4.35
Trainee 4 – AI	0.61	10.1 ± 2.96

Conclusion: In a training setting, these preliminary data suggest that artificial intelligence significantly reduces the reading time of non-expert readers without affecting the overall accuracy and the agreement with expert readers. Moreover, AI may have a minor impact on reading time in CE training with respect to that measured for expert readers.

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Disclosure: Nothing to disclose.

P0952

EFFICIENCY OF THE CAPSULE ENDOSCOPY, ARE THE QUALITY CRITERIA OF THE ESGE MET? EXPERIENCE IN A CENTER

M.d.M. Díaz Alcázar¹

¹Hospital Universitario Clínico San Cecilio, UGC Aparato Digestivo, Granada, Spain

Contact E-Mail Address: mmardiazalcasar@gmail.com

Introduction: The European Society of Gastrointestinal Endoscopy (ESGE) and United European Gastroenterology (UEG) have indicated as a high priority the need to establish quality benchmarks in endoscopic procedures. To this end, in 2019, the ESGE published a guide with quality improvement initiatives in small bowel endoscopy.¹

Aims & Methods: The aim of this study was to assess whether an endoscopy unit met the quality recommendations in capsule endoscopy procedures.

A retrospective descriptive study. Review of capsule endoscopy procedures performed during 2021 and comparison with minimum and objective quality standards.

Results: We performed 81 capsule endoscopy examinations. Compliance with quality criteria and comparison with standards are summarized in Table 1.

Domain	Compliance	Minimum standard	Target standard	Compliance (yes/no)
Indication according to ESGE guideline	78,82%. In anemia 59,52%	≥95%	≥95%	No
Rate of adequate bowel preparation	70,37%	≥95%	≥95%	No
Identify retention risk and prior evaluation with Patency®	Patency® not available	≥95%	≥95%	Not valuable
Complete cecal or stomal visualization	82,72%	≥80%	≥95%	Yes (minimum)
Lesion detection rate	81,93%	≥50%	≥50%	Yes
Timing of capsule for overt bleeding	100%	≥90%	≥90%	Yes
Reading speed	Not registered	≥90%	≥95%	Not valuable
Appropriate referral for enteroscopy	59,09%	≥75%	≥90%	No
Capsule endoscopy retention	2,47%	<2%	<2%	No

Table 1. Quality criteria for capsule endoscopy procedures

Conclusion: 1. The indication for capsule endoscopy should be adequate to increase efficiency and avoid work overload. Moreover, adequate indication prevents unnecessary procedures with the risk of complications. In our series, this criterion is not met, probably because some examinations due to anemia are not appropriate. Before indicating a capsule endoscopy for iron-deficiency anemia, a complete evaluation, including gastric and duodenal biopsies, is important.

2. Currently, the assessment of preparation is based on subjective judgments. The use of purgatives is also unclear. In our center we use simethicone and we recommend maintaining 2 hours of fasting and 4 hours without solids after taking the capsule. 7 hours without solids could be evaluated to improve the cleanliness.

3. Patency® capsule has proven useful in assessing the risk of retention. Its availability would reduce this complication.

4. The capsule endoscopy is a diagnostic procedure. If lesions are found, the enteroscopy should be considered, and the recommendation should be included in the capsule report.

5. It is important to know the quality standards and analyze their compliance to make improvements in order to provide quality assistance.

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Disclosure: Nothing to disclose.

P0953

REANALYSIS OF NEGATIVE SMALL BOWEL CAPSULE ENDOSCOPY BY DEEP CONVOLUTIONAL NEURAL NETWORK MODEL IMPROVED DIAGNOSTIC YIELD AND COULD CHANGE THE OUTCOME

K. Choi¹, H.H. Lee¹, W.Y. Lee², D. Park³, S. Lee^{3,4,5}, D.Y. Cheung¹, B. Lee⁶, Y.-S. Cho⁶, J.I. Kim¹, M. Choi⁶

¹Yeouido St. Mary's Hospital, College of Medicine, The Catholic University of Korea, Division of Gastroenterology, Department of Internal Medicine, Seoul, Korea (Republic of), ²Seoul St. Mary's Hospital, College of Medicine, The Catholic University of Korea, Department of Pediatrics, Seoul, Korea (Republic of), ³Pohang University of Science and Technology (POSTECH), Department of Mechanical Engineering, Pohang, Korea (Republic of), ⁴Pohang University of Science and Technology (POSTECH), Graduate School of Artificial Intelligence, Pohang, Korea (Republic of), ⁵Institute of Convergence Research and Education in Advanced Technology, Yonsei University, Seoul, Korea (Republic of), ⁶Seoul St. Mary's Hospital, College of Medicine, The Catholic University of Korea, Division of Gastroenterology, Department of Internal Medicine, Seoul, Korea (Republic of)

Contact E-Mail Address: choiks123@catholic.ac.kr

Introduction: Although several studies showed the usefulness of artificial intelligence to identify abnormalities in small bowel capsule endoscopy (SBCE) images, few have proven actual clinical usefulness.

Aims & Methods: We aimed to examine whether meaningful results could be obtained when reanalyzing negative SBCE video with a deep convolutional neural network (CNN) model. We retrospectively collected clinical data of patients who received SBCE at Yeouido and Seoul St. Mary's hospital between February 2018 and September 2019. All SBCE videos read as negative were reanalyzed with the CNN algorithm developed in our previous study.¹

Meaningful findings including angioectasia or ulcer were finally decided after reviewing the CNN-selected images by two gastroenterologists (KSC and HHL).

Results: A total of 113 (35.8%) among 316 SBCE videos were read as negative or non-specific. After reviewing with AI, meaningful findings were found in 70 (61.9%) videos. Red spot or angioectasia were 80 in 42 videos, and erosions or ulcers were 87 in 44 videos. Diagnosis of 9 patients (8.0%) was changed.

During a mean follow-up of 15.8 months, rebleeding occurred in 20.5% (16/78) of overt GI bleeding patients. Rebleeding rate was 23.5% (12/51) of patients with meaningful findings and 14.8% (4/27) of patients without meaningful findings, respectively (Table 1. P = 0.36). 8 patients received additional small bowel examinations such as 2nd SBCE or small bowel enteroscopy. When reanalyzing 1st SBCE with AI, the prognosis could be altered in 3 patients (37.5%).

	Meaningful finding (-) group	Meaningful finding (+) group
Rebleeding (+)	12 (23.5 %)	4 (14.8%)
Rebleeding (-)	39 (76.5 %)	23 (85.2%)
Total	51	27

Table 1. The Rebleeding rate in Overt GI bleeding.

Conclusion: Our CNN algorithm additionally detected meaningful findings in negative SBCE videos, which were probably missed by humans. It is expected that SBCE image reading by deep CNN could be used to compensate for human error and improve patient outcomes.

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P0954

IS VIDEO CAPSULE ENDOSCOPY SUPERIOR TO CT-ENTEROGRAPHY IN ASSESSING SMALL INTESTINAL PATHOLOGY IN OCCULT GASTROINTESTINAL BLEEDING FOLLOWING NEGATIVE UPPER ENDOSCOPY AND COLONOSCOPY? A DIAGNOSTIC TEST ACCURACY META-ANALYSIS

M. Yaghoobi¹, J. Tan¹, Y.T.A. Alshammari¹

¹McMaster University, Division of Gastroenterology, Hamilton, Canada

Contact E-Mail Address: yaghoobi@mcmaster.ca

Introduction: Both CT-enterography (CTE) and video capsule endoscopy (VCE) are used in identifying small intestinal pathology in patients with occult gastrointestinal bleeding (OGIB) following normal upper gastrointestinal endoscopy and colonoscopy. Identifying accurate diagnostic accuracy including the sensitivity and specificity of these two modalities, which we aimed at determining by using Cochrane methodology, is crucial for healthcare decision making.

Aims & Methods: A comprehensive electronic search was performed for studies on CTE and/or VCE using double balloon enteroscopy (DBE) as the reference standard. Literature search, data extraction and quality assessment were done by two independent reviewers. Cochrane methodology was used to perform a diagnostic test accuracy meta-analysis. Indices of diagnostic accuracy of CTE and VCE were calculated. Cochrane tool was used to assess risk of bias. We used STATA version 16.0 using bivariate mixed-effects regression framework to calculate sensitivity, specificity, diagnostic odds ratio (DOR), positive and negative likelihood ratios.

Results: Twenty-one studies on VCE and 11 on CTE were included with no visual evidence of publication bias. Six of these studies were head-to-head comparison of CTE and VCE using DBE as reference standard. Positivity rate was 56% for VCE and 33% for CTE. Sensitivity was 0.82 (0.75-0.88) and 0.58 (0.34-0.78) for VCE and CTE, while specificity was 0.62 (0.42-0.77) and 0.89 (0.81-0.94), respectively. The positive likelihood ratio was 2.16 (1.33-3.51) for VCE and 5.44 (2.81-10.51) for CTE while the negative likelihood ratio was 0.28 (0.19-0.41) for VCE and 0.47 (0.27-0.82) for CTE.

Overall, DOR was 7.67 (3.53-16.61) for VCE and 11.48 (4.02-37.70) for CTE (p =non-significant). In sensitivity analysis of only head-to-head studies, CTE showed a sensitivity of 0.50 (0.21-0.77), specificity of 0.89 (0.75-0.96) and DOR of 8.08 (0.65-15.50) as compared to 0.79(0.58-0.91), 0.59 (0.24-0.87) and 5.46 (0-12.7) for VCE, respectively.

Conclusion: Neither VCE nor CTE is a perfect test in identifying etiology of OGIB in small intestine. VCE provided better sensitivity while CTE ensured superior specificity. Our results remained robust in sensitivity analysis. Cost-effectiveness analysis is recommended to further elaborate on practicality of these findings, meanwhile, clinicians should choose the appropriate modality depending on whether better sensitivity or specificity is required in each clinical scenario.

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P0955

NON-INVASIVE PAN-ENTERIC EVALUATION IN CROHN'S DISEASE – USEFULNESS OF CAPSULE ENDOSCOPY IN UPSTAGING AND CHANGING DISEASE MANAGEMENT

J.P. Laranjeira Correia¹, M.M. Estevinho¹, E. Afecto¹, A. Ponte¹, A. Rodrigues¹, R. Pinho¹, T. Freitas¹

¹Centro Hospitalar de Vila Nova de Gaia/Espinho, Gastroenterology, Vila Nova de Gaia, Portugal

Contact E-Mail Address: joaopaulo_laranjeira@hotmail.com

Introduction: Pan-enteric capsule endoscopy (PCE) allows a non-invasive assessment of endoscopic healing, which has been associated with improved long-term outcomes in inflammatory bowel disease. We intended to evaluate the impact in clinical practice of PCE studies in patients with established and suspected Crohn's disease (CD).

Aims & Methods: A retrospective analysis of all consecutive PCE studies performed in a tertiary centre between March 2018 and February 2022 in patients with established or suspected CD was undertaken. The Capsule Endoscopy Crohn's Disease Activity Index (CECDALic) was used in patients with established CD; this score was compared with clinical features (using the PRO2 questionnaire) and biochemical markers (using C-reactive protein). The percentage of disease upstaging and change in medical management after PCE was also evaluated. Univariate and multivariate binary logistic regression analyses were applied to identify independent predictive factors of treatment intensification.

Results: Overall, 67 PCE studies were included - 26(38.8%) for suspected and 41(61.2%) for established CD. CD was confirmed in 8 patients in whom the diagnosis was suspected (32%). Concerning patients with established CD, median CECDALic was 8 (IQR 14), median C-reactive protein was 4.2 (IQR 6.3) mg/L and median PRO-2 score was 0 (IQR 1).

No significant association between CECDALic and PRO2 score ($rs=0.182$, $p=0.261$) nor C-reactive protein ($rs=0.159$, $p=0.327$) was identified. PCE upstaged Montreal Classification in 6 (14.6%) patients, changed disease management in 14 (34.1%) and resulted in treatment intensification in 12 (29.3%). CECDALic score was an independent predictor of treatment intensification ($p=0.02$).

On the other hand, disease location and behaviour, presence of L4 disease, PRO-2 score, and C-reactive protein were not.

Conclusion: This study corroborates the usefulness of PCE in assessing mucosal activity in CD, which was the only independent predictor of treatment intensification, as well as the role of this technique for appropriate disease staging.

Disclosure: Nothing to disclose.

P0956

COLON CAPSULE ENDOSCOPY: PREDICTORS OF INADEQUATE BOWEL PREPARATION

A.I. Ferreira^{1,2,3}, T. Lima Capela^{1,2,3}, M. Freitas^{1,2,3}, C. Arieira^{1,2,3}, S. Xavier^{1,2,3}, P. Boal Carvalho^{1,2,3}, B.J.F. Rosa^{1,2,3}, M.J. Moreira Basto^{1,2,3}, J. Berkeley Cotter^{1,2,3}

¹Hospital Senhora da Oliveira – Guimarães, Gastroenterology Department, Guimarães, Portugal, ²Life and Health Sciences Research Institute (ICVS), School of Medicine, University of Minho, Braga, Portugal, ³ICVS/3B's, PT Government Associate Laboratory, Guimarães/Braga, Portugal

Contact E-Mail Address: tiagolimacapela@gmail.com

Introduction: The most important factors in achieving an adequate colon capsule endoscopy (CCE) study are bowel cleansing and capsule excretion during the CCE battery time.

Aims & Methods: The aim of this study was to evaluate demographic and clinical factors associated with inadequate bowel preparation in patients undergoing CCE, predicting the need to adjust bowel preparation regimens. A retrospective single-center study including consecutive adult patients undergoing CCE during a 2-year period was performed. Patients' demographic and clinical data, including comorbidities, were recorded, as well as quality of bowel preparation according to CC-CLEAR^a. Patients with insufficient data were excluded.

Results: A total of 86 patients undergoing CCE were analysed. The most common indication for CCE was incomplete screening colonoscopy. CCE was incomplete in 28% of patients. Bowel preparation was adequate (good or excellent) in 55 patients (64%) and it was excellent in 26 patients (31%). In 29 patients (35%), bowel preparation was inadequate. Smoking history was associated with 5.8 times higher risk of inadequate bowel preparation ($p=0.001$; OR 5.8; 95% CI [1.9–17.9]).

Additionally, diabetes and smoking significantly prevented the achievement of an excellent bowel preparation in the CCE: the odds of having sub-optimal (non-excellent) preparation were 5 times higher in diabetic patients ($p=0.029$; OR 5.0; 95% CI [1.1–23.3]) and 4.6 times higher in active or former smokers ($p=0.040$; OR 4.6; 95% CI [1.0–21.7]).

Conclusion: Smoking history and diabetes were associated with sub-optimal (non-excellent) bowel preparation, with smoking having a greater influence and being a risk factor for inadequate bowel preparation. In these patients, adjustments may be considered aiming to improve bowel preparation regimens.

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Disclosure: Nothing to disclose.

P0957

CAPSULE ENDOSCOPY WITH ARTIFICIAL INTELLIGENCE ASSISTED TECHNOLOGY: AI IN CLINICAL PRACTICE

F. O'Hara^{1,2}, D. McNamara^{1,2}, C. Walker¹

¹Tallaght University Hospital, Gastroenterology, Dublin, Ireland,

²Trinity Academic Gastroenterology Group, Clinical Medicine, Dublin, Ireland

Contact E-Mail Address: fintan.ohara@gmail.com

Introduction: Capsule endoscopy (CE) has revolutionized the management of small bowel (SB) diseases owing to its convenience and non-invasiveness. However, capsule reading is a time-consuming and often tedious process with average reading times in the literature ranging between 30–120 minutes.

The use of artificial intelligence (AI) in CE is an attractive solution for reducing reading time by removing redundant images and simplifying the identification of intestinal landmarks and suspicious abnormalities.

While previous studies have demonstrated impressive sensitivity and specificity in created datasets of capsule images, real-world data is lacking.

OMOM[®] HD Capsule (Jinshan group) introduced in 2020 includes Smartscan technology which includes redundancy deletion, lesion detection, and classification software.

Aims & Methods: Our aim was to evaluate the OMOM HD Smartscan software in a real-world setting against experienced capsule readers.

The OMOM[®] HD Capsule was employed prospectively over a 4-week period in unselected patients presenting to our unit for CE. Procedures were performed as per standard departmental protocols.

Recordings were then read by 2 separate modalities; (i) "Standard reading mode" (SR) which was reading at a 10-fps single image mode which was deemed the current gold standard and (ii) "Smartscan reading mode" (SS) which was read at 5fps after image processing by AI-assisted technology. A findings report was generated separately for each reading technique. For each study the following were documented and compared:

- Reading time,
- Intestinal landmark identification,
- Bowel preparation (Brotz Score), and d) pathology.

The reading time required for examination of the data by each method was recorded using a stopwatch. Data was analysed using SPSS software.

Results: In this pilot study, 25 cases have been analysed to date. The mean age was 51 years (18–74); 74% were men. All patients completed the procedure uneventfully. Complete visualization of the SB was achieved in 96% ($n=24$) of patients. No capsule retention was recorded.

44% ($n=11$) of studies detected significant pathology.

The indications for procedure were occult gastrointestinal bleeding 52% ($n=13$), suspected Crohn's disease 40% ($n=10$), and Crohn's disease assessment in 8% ($n=2$).

The mean SB reading time was significantly shorter using SS vs SR (2.5min vs 27.3min, $P < 0.001$).

Evaluation of adequate bowel cleansing by the Brotz score correlated moderately between the two reading methods with agreement in only 44% ($k = 0.6$).

Recognition of the intestinal landmarks by the software was poor, with an average discrepancy between SS and SR of ± 86 min (range ± 9 to 543min) for first duodenal image and ± 132 min (range ± 23 to 237min) for first caecal image.

There was excellent agreement between both modalities for lesion detection with 100% correlation for positive and negative studies. While a per lesion analysis ($n = 321$) also showed excellent correlation ($k = 0.997$). The only lesions not recorded by SV were 2 small angiodysplasias in an otherwise positive study.

Conclusion: Correlation between OMOM HD SmartView technology and expert reader for detection of pathology is excellent. However, recognition of intestinal landmarks is poor and assessment of bowel preparation is unreliable. With recognition of these limitations by the operator Smartscan can significantly improve reading time in CE without negatively affecting pathology recognition and diagnostic yield.

Disclosure: Nothing to disclose.

P0958

CAPSULE ENDOSCOPY: AUTOMATIC IDENTIFICATION AND DIFFERENTIATION OF SMALL BOWEL LESIONS WITH DISTINCT HEMORRHAGIC POTENTIAL USING A CONVOLUTIONAL NEURAL NETWORK

J. Afonso¹, M.J. Mascarenhas Saraiva¹, T. Ribeiro¹, P. Cardoso¹, H. Cardoso¹, A.P. Andrade¹, J. Ferreira², G. Macedo¹

¹Centro Hospitalar Universitário São João, Gastroenterology, Porto, Portugal, ²FEUP - Faculdade de Engenharia da Universidade do Porto, Porto, Portugal

Contact E-Mail Address: tiagofcribeiro@outlook.com

Introduction: Capsule endoscopy (CE) has a decisive role on the approach to patients with suspected small bowel disease. However, reading CE exams is a time-consuming, error prone and monotonous task and so, artificial intelligence tools may be helpful in the CE videos analysis. In this pioneer work, we aimed to develop a CNN-based model for identification and differentiation of multiple small bowel lesions and their classification according to their hemorrhagic potential.

Aims & Methods: We developed, trained, and validated a denary CNN based on CE images. Each frame was labeled according to the type of lesion (lymphangiectasia, xanthomas, ulcers, erosions, vascular lesions, protruding lesions, and blood) by three experts in CE. The hemorrhagic potential was assessed by Saurin's classification: P0 – lesions without bleeding potential; P1 – lesions with uncertain bleeding potential; P2 – lesions with high bleeding potential; P3 – luminal blood. A training dataset was used for development of the model (80% of the full image dataset). The CNN's prediction was compared to the experts' labeling. The performance of the network was evaluated using an independent dataset (20% of the full image dataset). The performance of the CNN was measured by the area under the receiving operating characteristic curve (AUROC), sensitivity, specificity, positive and negative predictive values (PPV and NPV, respectively).

Results: A total of 53555 CE images were included from 1229 patients. The model had an overall accuracy of 99%, a sensitivity of 88%, a specificity of 99%, a PPV of 87% and NPV of 99% for detection of multiple small bowel abnormalities and respective classification of bleeding potential.

Conclusion: We developed and tested a CNN-based model for automatic detection of multiple types of small bowel lesions and classification of the respective bleeding potential. This system may improve the diagnostic yield of CE for these lesions and overall CE efficiency.

Disclosure: Nothing to disclose.

P0959

VIDEO CAPSULE ENDOSCOPY IN PATIENTS WITH SURGICALLY ALTERED PROXIMAL SMALL BOWEL IS ASSOCIATED WITH LONGER TRANSIT TIMES, INADEQUATE PREPARATION AND REDUCED DIAGNOSTIC YIELD

T. Thurm^{1,2}, M. Shnell^{1,2}, L. Deutsch (Mlynarsky)^{2,1}

¹Tel Aviv Sourasky Medical Center, Gastroenterology and Liver Diseases, Tel-Aviv, Israel, ²Tel Aviv University, Sackler School of Medicine, Tel-Aviv, Israel

Contact E-Mail Address: tamarth@tlvmc.gov.il

Introduction: Video capsule endoscopy (VCE) is an effective, noninvasive modality for small bowel (SB) investigation. Its usage in patients with prior SB surgical interventions is rising. However, data in patients with altered SB anatomy regarding diagnostic yield and feasibility are lacking.

Aims & Methods: Our aim was to evaluate and compare safety and efficacy of VCE among patients with surgically altered proximal SB anatomy, patients with other SB resections and the normal anatomy (non-surgical) patients.

This is a retrospective study of prospectively maintained database. All consecutive VCEs of patients ≥ 18 years (03/2018-02/2022) were included. All patients received SB preparation protocol based on low residue diet followed by liquid diet and a 12 hour fast as instructed by the manufacturer (PillCam®, Given imaging, Israel). The cohort was divided into three groups: 1. Patients with surgically altered SB anatomy (e.g. gastric bypass, single anastomosis gastric bypass, pancreaticoduodenectomy (Whipple procedure) and bilroth II gastrojejunostomy); 2. Other SB resections (e.g. segmental SB resection, ileocectomy, right hemicolectomy, ileal pouch anal anastomosis (IPAA) and ileostomy); 3. Controls without gastrointestinal surgery. Patients with any history of other gastrointestinal surgery were excluded. Diagnostic yield, VCE completion rate and transit times were compared between groups.

Results: A total of 1121 VCEs were performed. Ten repeated VCEs, and 45 studies of patients with prior non-SB gastrointestinal surgery were excluded. Twenty-one patients with altered SB anatomy and 55 patients with other SB resections were compared to 990 controls. Age was similar between the groups (53.8 ± 14.1 y, 50.5 ± 20.1 y and 52.4 ± 20.9 y respectively,

$p=0.842$). Endoscopic insertion of the SB capsule according to physician's discretion was significantly more common in patients with altered SB (47.6%) compared to resected SB (3.6%) and controls (4.3%, $p<0.001$). The prevalence of clinically significant VCE findings was the highest among patients with resected SB (61.1%) and the lowest among patients with altered SB (28.6%, controls - 41.9%, $p=0.009$ between groups). Adequate SB preparation and visualization was significantly lower in altered SB (47.6%) compared to similar rates among resected SB (72.7%) and controls (75.9%) respectively, ($p=0.011$). Moreover, altered SB (vs. controls) was an independent risk factor for inadequate preparation in a logistic regression adjusted for gender, age and endoscopic placement (OR 2.846, 95%CI 1.133-7.145, $p=0.05$). Study completion rates (cecal or colon documentation) were comparable (altered SB - 95.2%, resected SB - 94.5% and controls - 98.3%, $p=0.102$). However, SB transit time was significantly longer in altered SB and comparable between SB resection and controls (308 ± 110 min, 252 ± 111 min and 249 ± 94 min, $p=0.006$ and $p=0.843$ respectively).

Conclusion: In patients with surgically altered proximal SB anatomy, VCE is as safe as in controls or patients with other resections of SB. However, longer SB transit times and inadequate SB preparation may result in reduced diagnostic yield. Patients with altered SB anatomy might benefit from tailored preparation protocol prior to VCE.

Disclosure: Author Liat Deutsch, is consultant for "Given Imaging", yet the company was not involved in the study in any way.

P0960

VIDEO CAPSULE ENDOSCOPY STUDIES IN PATIENTS WITH DIABETES MELLITUS ARE CHARACTERIZED BY INADEQUATE PREPARATION AND LONGER TRANSIT TIMES

N. Akerman¹, N. Fliss-Isakov^{2,1}, T. Thurm^{2,1}, O. Shibolet^{2,1}, L. Deutsch (Mlynarsky)^{2,1}

¹Tel-Aviv University, Sackler School of Medicine, Tel-Aviv, Israel, ²Tel Aviv Sourasky Medical Center, Gastroenterology and Hepatology, Tel Aviv, Israel

Contact E-Mail Address: Liatml@tlvmc.gov.il

Introduction: Type 2 Diabetes Mellitus (DM) is a global epidemic that poses a significant challenge to health systems around the world. Its incidence has been rising in the last decades. Gastrointestinal motility disorders are common among patients with T2DM. Data on the safety and efficacy of video capsule endoscopy (VCE) among patients with T2DM is still lacking.

Aims & Methods: This was a retrospective study of a prospectively maintained database in order to evaluate safety and efficacy of VCE among patients with DM compared to patients without DM. All consecutive VCEs of patients' ≥ 35 years, performed between 03/2018-03/2022 were included. Patients with and without DM were compared regarding diagnostic yield, cleansing score and transit times (TT).

Results: A total of 1184 VCEs were performed during study period while 512 patients were excluded due to: age < 35 ($n=339$) previous intestinal surgery ($n=121$), endoscopic placement ($n=31$), technical malfunction ($n=13$) and repeated studies ($n=8$). Out of 672 included patients, 189 patients reported the diagnosis of DM (28.1%, DM group) and 483 patients were defined as controls (without DM).

Fifty DM patients (26.5%) were treated with insulin, 22 (11.6%) patients were treated with glucagon-like peptide 1 (GLP-1) agonist medications and 159 (84.1%) with other oral anti-diabetic medications.

Only one patient in the control group was treated with GLP-1 agonist. Patients with DM were older than those without DM (70.4 ± 9.6 vs. 58.8 ± 15.1 years, respectively, $p<0.001$). The prevalence of medications and co-mor-

bidities, potentially effecting intestinal motility in the entire cohort was rare: Parkinson's disease 0.6%, connective tissue disease 0.6%, multiple sclerosis 0.4% ($p=0.07$ between groups), prescribed narcotics were comparable between patients with and without DM (0.5% vs. 1.6%, $p=0.296$). VCE completion rates (cecal documentation) were similar between DM and controls (98.4% vs. 99.0%, respectively, $P=0.553$). No capsule retention (>2 weeks) occurred in the entire cohort.

Angioectasia and active bleeding were more common among patients with DM compared to those without DM (28.3% vs. 19.7%, $p=0.02$ and 10.9% vs. 6.2% $p=0.04$), yet ulcers were significantly less common (20.1% vs 34.6%, $p<0.001$). Gastric TT was similar between patients with and without DM (37.5 ± 45.5 vs. 34.3 ± 48.6 minutes= 0.42) while small bowel TT was longer (261.8 ± 95.6 vs. 244.9 ± 98.4 , $p=0.04$) and reported bowel movement frequency was lower ($1.42\pm 1.15/\text{day}$ vs. $1.74\pm 1.73/\text{day}$, $p=0.008$).

Inadequate visualization due to poor preparation was more prevalent among patients with DM compared to those without DM (31.2% vs. 23.4%, $p=0.04$). Moreover, insulin-users had higher rates of inadequate preparation compared to DM without insulin (44.0% vs. 26.6%, $p=0.006$).

In a multi-variate analysis adjusted for age, gender and bowel movements frequency, diagnosis of DM was not independently associated with inadequate preparation. However, insulin usage was significantly associated with inadequate preparation (OR 2.477, 95%CI 1.335-4.596, $p=0.004$ adjusted for age, gender and bowel movements frequency). The association was not seen for patients with DM without insulin ($p=0.675$ vs. patients without DM).

Conclusion: Higher rates of inadequate preparation, longer small bowel transit time and reduced bowel movements were observed among patients with DM compared to patients without DM. DM treated with insulin was positively associated with inadequate preparation for VCE. Future studies should focus on personalized protocols for pre-VCE preparation and post-swallowing acceleration.

Disclosure: The corresponding author, Liat Deutsch, is consultant for "Given Imaging", yet the company was not involved in the study in any way. All other authors have nothing to declare.

P0961

AUTOMATED PROMPTS RESULT IN HIGH PROKINETIC USE WITHOUT IMPROVING COLON CAPSULE PERFORMANCE

C. Costigan¹, R. Bourke¹, D. McNamara¹

¹Tallaght University Hospital, Gastroenterology, Dublin, Ireland

Contact E-Mail Address: conorcostigan92@gmail.com

Introduction: Colon capsule endoscopy (CCE) relies on timed small bowel and colonic boosters to ensure passage through the gastrointestinal tract resulting in complete colonic visualisation. Prokinetics are recommended for delayed gastric transit (>30 minutes) and can be detected by either direct visual assessment (DVA) or an automated (Alert 0) system.

Aims & Methods: The aim was to compare the impact of DVA & Alert 0 assessments on CCE performance.

CCE cases were sequentially assigned to either DVA or automated (Alert 0) gastric transit assessment. Patient demographics, metoclopramide use and CCE key performance measures were documented and compared between groups using Chi² and t-tests as appropriate.

Results: In all 71 patients were recruited (38 DVA and 33 (Alert 0), 66% ($n=47$) were female, mean age was 60 years. Demographics were similar between groups. Overall CCE completion rate was 76% and diagnostic yield was 66%. In all 36% ($n=23$) had delayed gastric transit and received metoclopramide. CCE Completion rates were the same in both groups (76%). Diagnostic yield was statistically similar in both groups (72% vs 55%).

Significantly more patients in the Alert 0 cohort received Metoclopramide (64% Alert 0 versus 19% DVA, $p<0.0001$, OR 9.6, 95% CI 2.9936 to 30.7858). Notably, Metoclopramide use had no significant impact in mean colonic transit times (210 mins vs 193 mins), SB transit times (100 mins vs 97 mins), nor was there any difference in CCE completion rates (70 % v 76%).

Conclusion: This study demonstrates an increase in Metoclopramide use with automated gastric transit assessment, which does not improve CCE completion, and questions the early use of prokinetics in CCE.

Disclosure: Nothing to disclose.

P1042

THE ARTIFICIAL INTELLIGENCE-ASSISTED SMALL BOWEL CAPSULE ENDOSCOPY (TANTALUS), MULTICENTRE STUDY – AI IN CAPSULE ENDOSCOPY WELL WITHIN OUR REACH!

X. Xie¹, Y. Xiao¹, J.-J. Li¹, Q.-Q. Yang¹, X. Peng¹, X.-B. Nie¹, J.-Y. Zhou¹, Y.-B. Zhao¹, H. Yang¹, X. Liu¹, E. Liu¹, Y.-Y. Chen¹, Y.-Y. Zhou¹, C.-Q. Fan¹, J.-Y. Bai¹, X.-Y. Zhao¹, H. Lin¹, A. Koulaouzidis^{2,3}, S.-M. Yang¹

¹The 2nd Affiliated Hospital, the Third Military Medical University, Gastroenterology, Chongqing, China, ²Kirurgisk Afdeling A, Sygehus, SATC-C/CICA, Svendborg, Denmark, ³University of Southern Denmark (SDU), Clinical Research, Odense, Denmark

Contact E-Mail Address: akoulaouzidis@hotmail.com

Introduction: Reading small-bowel capsule endoscopy (SBCE) is a tedious task for clinicians^{1,2}; a new method should be applied to solve this issue and free clinical time. Artificial intelligence (AI) algorithms seem to perform well here^{3,4}.

Aims & Methods: We aimed to evaluate the performance of a Convolutional Neural Network (CNN) algorithm (*SmartScan*)-assisted reading in the setting of real-life clinical care. 5,825 SBCE video examinations (comprising 295,314,067 images) performed in 51 Chinese medical centres were collected. 2,927 SBCE examinations from 29 medical centres were used to train *SmartScan* to detect 17 categories of CE structured terminology (CEST) findings. *SmartScan* was later validated in 2,898 SBCEs collected from 22 medical centres.

Eight specialist gastroenterologists read all 2,898 SBCEs with both Conventional Reading (CR) and *SmartScan*-Assisted Reading (SSAR). If finding(s)/results by both types of reading in a patient were concordant, the result was taken as the Combined Agreed Comparator (CAC) for that case. In discordant cases, the consensus result by three expert readers was taken as the CAC for the case.

Main Outcomes & Measures: The detection rate and efficiency of CEST findings detected by SSAR and CR were compared. The missed findings of CEST were also added to the evaluation. This study was registered in the Chinese Clinical Trial Registry (reg no. ChiCTR2100042455).

Results: SSAR achieved an overall higher detection rate (79.30%) for CEST findings compared to CR (70.67%). From a total of 6,084 SB findings, SSAR detected 95.89%, significantly higher than CR (76.10%). SSAR achieved an overall higher sensitivity (98.80%), for the 17 CEST subtypes of findings, 10.75% higher than CR (88.05%). With SSAR, the number of images requiring review per SB CE video was reduced to 779.17 ± 337.18 min, with reading time shortened to 5.37 ± 1.51 min.

Conclusion: A commercially available CNN algorithm (*SmartScan*) can increase the detection rate of SB findings while drastically reducing SBCE reading times.

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P0962

EVALUATION OF SPLEEN STIFFNESS IN HEALTHY POPULATION: A VIBRATION-CONTROLLED TRANSIENT ELASTOGRAPHY STUDY

H.T. Kani¹, Ç. Keklikkiran¹, I. Ergenç¹, Y. Yilmaz¹

¹Marmara University School of Medicine, Gastroenterology, Istanbul, Turkey

Contact E-Mail Address: htkani@yahoo.com

Introduction: Vibration-controlled transient elastography (VCTE) is an accurate technique that has an increasing use. In recent years, VCTE was started to use in predicting spleen stiffness (SS). Portal vein pressure and flow have an impact on SS and in previous studies it was used to predict portal hypertension, esophageal varices.

Aims & Methods: Our aim was to evaluate the SS measurements in healthy population and its correlation with age, sex, liver stiffness measurement (LSM), continued attenuation parameter (CAP) and body mass index (BMI). We enrolled healthy volunteers who were agreed to participate to the study and collected age, sex, smoking history, alcohol consumption, body mass index before the VCTE procedure. Liver and spleen elastography were performed to all patients by VCTE.

Results:

All Patients (n=82)	
Sex	
Female (n%)	49 (59.8%)
Male (n%)	33 (40.2%)
Age (years) (mean ± SD)	37.80 ± 11.13
BMI (kg/m²) (mean ± SD)	26.67 ± 5.12
Tobacco use (n%)	
Current smoker	16 (19.5%)
Ex-smoker	17 (20.7%)
Non-smoker	49 (59.8%)
Alcohol consumption (n%)	38 (46.3%)
LSM (kPa) (median, min – max)	4.40 (2.10 – 75.00)
CAP (dB/m) (mean ± SD)	231.78 ± 51.93
SS(kPa) (median, min – max)	18.35 (7.20 – 80.10)

A total of 97 participants were enrolled to the study, 15 patients were excluded and 82 patients included for the final analysis. There was no significant difference in SS, liver stiffness measurement LSM, CAP and BMI

between females and males. There was no correlation between age and SS. There was a weak correlation between SS and LSM, SS and CAP and no correlation was found between SS and BMI.

Conclusion: SS had a weak correlation with LSM and CAP but not with BMI, age and sex. There is no extra-large probe use in SS measurement and it was a challenge in participants with increased submucosal fat thickness. Multiple and repeatable studies needed to set an accurate cut-off point and evaluate the factors that impact on SS in healthy individuals.

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Disclosure: Nothing to disclose.

P0963

EUS-GUIDED HEPATICOGASTROSTOMY: CLINICAL OUTCOMES AND COMPLICATIONS. EXPERIENCE OF A MAIN FRENCH REGIONAL HOSPITAL

H. El Moufid^{1,2}, E. Siegel¹, P. Claude¹, G. Bors¹, S. Husson-Wetzel¹

¹Groupe Hospitalier Mulhouse et Sud-Alsace, Gastro-Entérologie, Mulhouse, France, ²Hôpital Cheikh Zayd, Gastro-Entérologie, Rabat, Morocco

Contact E-Mail Address: elmoufid.houda@gmail.com

Introduction: Hepaticogastrostomy guided by echo-endoscopy (HG) represents an option for the management of obstructive jaundice, as an alternative to surgery or percutaneous drainage, after failure or impossibility of endoscopic retrograde drainage. The technical success rate of this technique is higher than 90% in most studies.

Aims & Methods: The aim of this study is to evaluate the efficacy and morbidity of EUS guided hepatico-gastric drainage in our center.

Single-center retrospective study. All patients with malignant tumor pathology who required hepatico-gastrostomy drainage between June 2015 and December 2021 were included. Anatomical, technical, and clinical characteristics were studied. Technical (stent placement) and clinical success (clinico-biological improvement of angiocholitis and jaundice), as well as complications were considered.

Results: A total of 34 patients were included (16F/18M, mean age 72 years, range 40-96). Obstructive jaundice was caused in all patients by malignant disease (pancreatic cancer in 41%, liver metastasis 20%, cholangiocarcinoma 17%, gall bladder carcinoma 11%, biliary compression by carcinoid nodules 5% and Ampulloma 2%).

The stenosis was localized at the hilar level in 17 cases (50%), at the hepato-cojejunal anastomosis in 2 (5%) and at the choledochal level in 15 patients (44%).

The indication was failure of ERCP in 13 cases (38%), tumor duodenal stenosis in 8 cases (23%), presence of a duodenal stent in 5 cases (14%), incomplete left biliary drainage in 5 cases (14%), and altered post-surgical anatomy (post gastrectomy or whipple surgery) in 4 cases (11%).

Hepatico-gastrostomy were performed after punctures with 19-gauge needles, drilling of the tract using the 6, 7, 8, or 10F cystotome in 22, 2, 1, and 9 patients respectively, and placement of 8 cm semi-covered metal stent in 28 cases (82%), Completely covered 8cm metal stent in only 1 case (2.9%), semi-covered 10 cm metal stent in 3 cases (8.8%), and double semi-covered 8cm metal stent in 2 cases (5.8%).

Technical success was achieved in 33 cases (97%) after a median follow-up of 19.5 weeks (0.1-84). Among these 33 patients, 10 (30%) presented a complication: infectious syndrome (4/10, 40%), obstruction (3/10, 30%), migration (2/10, 20%) and hemorrhage (2/10, 20%). No choleperitoneum occurred.

The clinical success is 81% with a reduction of Bilirubin rate day 7 of more than 50% obtained in 19 cases (57%), a reduction of Bilirubin between 20-49% obtained in 8 cases (24%). Improvement of angiocholitis at 72 hours post-drainage in 16 cases (47%). 16 (47%) patients had received chemotherapy after drainage.

The reintervention rate was 15%. Mortality related to the procedure was 2.9% (Hemorrhagic shock).

Conclusion: Hepaticogastrostomy guided by echo-endoscopy is an interesting alternative for neoplastic obstructive jaundice. The complication rate, particularly infectious, seems high (12%), but this can be explained by the large proportion of patients with complex hilar stenosis, often multi-drained with chronic bacterial contamination of the bile ducts.

Disclosure: Nothing to disclose.

P0964

SELF-EXPANDABLE METALLIC STENTS FOR PALLIATION OF MALIGNANT DYSPHAGIA - EFFICACY AND SAFETY

F. Bordalo Ferreira¹, M.A. Rafael¹, L. Carvalho Lourenço¹, A.M. Oliveira¹, R. Carvalho¹, D. Horta¹

¹Hospital Professor Doutor Fernando Fonseca, Gastroenterology, Amadora, Portugal

Contact E-Mail Address: filipamvpbferreira@gmail.com

Introduction: Esophageal self-expandable metallic stent (SEMS) placement allows for oral feeding in patients with dysphagia caused by malignant esophageal stenosis, contributing for a significant improvement of quality of life in these patients.

Aims & Methods: We performed a single-center retrospective study which evaluated the results of esophageal SEMS placement for malignant dysphagia palliation, between 2015 and 2021, with a maximum follow-up (FUP) of 3 years.

Results: Sixty-two (62) patients who underwent esophageal SEMS placement for malignant dysphagia palliation were included. Malignant esophageal stenosis was often caused by esophageal or gastroesophageal junction neoplasms (81%), followed by lung origin (15%). A total of 72 esophageal SEMS were placed, with high technical (100%) and clinical (94%) success. Previous dilatation was performed in 7% of the procedures. Complication rate was 3%, which included intra-procedural bleeding (1%), stent migration into the stomach (1%) and aorto-esophageal fistula (1%). The latter two were late complications (3 and 4 months after the procedure, respectively) and occurred in patients on chemotherapy.

Thirty percent (30%) of all patients were on chemotherapy during or after the procedure. Tumor ingrowth causing recurrence of dysphagia occurred in 15% of the patients (median interval of 7.5 months) and was resolved by placement of additional SEMS (the maximum number of stents per pa-

tient was 4). Median FUP time was 3 months (interquartile range of 2-6 months). Survival rate was 82% at 1 month, 56% at 3 months, 29% at 6 months, 23% at 1 year e 16% at 3 years.

Conclusion: These results reinforce that esophageal SEMS placement for palliation of malignant dysphagia is an effective and safe procedure, with a low rate of complications.

Disclosure: Nothing to disclose.

P0965

RISK FACTORS FOR REFRACTORY BENIGN ESOPHAGEAL STRICTURES

A. Sair¹, S. Mrabti¹, A. Benhamdane¹, T. Addajou¹, R. Berraida¹, S. Sentissi¹, E. ilham¹, F. Rouibaa¹, A. Benkirane¹, H. Seddik¹

¹The Military Teaching Hospital of Rabat, Gastroenterology II Department, Rabat, Morocco

Contact E-Mail Address: asmae-sr@hotmail.fr

Introduction: Endoscopic dilatation remains the mainstay of therapeutic management of benign esophageal strictures, expressed primarily as dysphagia, which can significantly impair quality of life. They can be caused by various disorders or lesions of the esophagus.

Aims & Methods: Our aim is to report the results of dilatation, as well as the different risk factors of refractory benign esophageal strictures.

This is a retrospective descriptive and analytical study of 33 patients with benign esophageal stenosis who underwent esophageal dilation between 2016 and 2021. Refractory (or recurrent) stenosis was defined as the inability to maintain esophageal caliber at 14 mm diameter over 5 dilatation sessions, or the inability to maintain satisfactory luminal diameter for 4 weeks once a 14 mm diameter was achieved.

Results: Of the 33 patients who underwent dilatation for benign esophageal strictures, 38.7% had refractory strictures. The mean age was 50 ± 20.9 years with a male predominance of 66.7% and a sex ratio (M/F) of 2.9. All patients had dysphagia and 45.5% had chronic gastroesophageal reflux disease (GERD). Endoscopy revealed low stenosis in 65.6%, medium in 15.6% and high in 18.8%. 50% had peptic stenosis, 31.3% achalasia, 9.4% anastomotic, 6.3% Schatzki ring and 3.1% caustic.

78.8% of the stenoses were dilated by balloon and 21.2% by candles with a mean dilatation caliber of 18.8 ± 6.8 mm.

After univariate analysis, refractory stenoses were associated with the presence of a peptic stenosis (p=0.002) and dilatations of caliber less than 16 mm (p=0.012), after multivariate analysis only peptic stenosis was associated with refractory stenoses (p=0.034).

Conclusion: In our series, refractory stenosis was present in 38.7%. Peptic stenosis was statistically significantly associated with refractory oesophageal stenosis.

Disclosure: Nothing to disclose.

P0966

ENDOSCOPIC STRICTUROTOMY VERSUS ENDOSCOPIC BALLOON DILATION FOR THE TREATMENT OF INTESTINAL STRICTURES IN CROHN'S DISEASE

G. Casanova¹, A. Giordano¹, M. Urpi¹, J. Llach¹, M. Escapa¹, I. Ordás², B. Caballol Oliva², A. Fernández-Clotet², A. Gines¹, M.G. Fernández-Esparrach¹, E. Ricart², B. González-Suárez¹

¹Hospital Clínic de Barcelona, Endoscopy Unit, Gastroenterology Department, Barcelona, Spain, ²Hospital Clinic de Barcelona, Inflammatory Bowel Disease Unit, Gastroenterology Department, Barcelona, Spain

Contact E-Mail Address: gscasanova@clinic.cat

Introduction: Endoscopic stricturotomy with needle-knife (STK) is a recently introduced therapy for the treatment of intestinal strictures in Crohn's disease (CD). Data on its efficacy and safety are scarce as well as comparative studies with other techniques.

Aims & Methods: **Aim:** To compare the efficacy and safety of STK with endoscopic balloon dilation (EBD).

Methods: A prospective cohort of CD patients undergoing STK from July 2019 to April 2022 were compared with a retrospective cohort of patients treated with DEB using Propensity Score Matching to ensure similar demographic and clinical characteristics. Patients with up to 3 intestinal strictures were included. Technical success (passage of endoscope through the stricture after endoscopic treatment), clinical success (remission of abdominal pain), surgery-free survival rate and adverse events after 1-year follow-up were described.

Results: A total of 13 patients treated with STK (median age 38 years, IQR 31-44) and 13 with DEB (median age 47 years, IQR 38-58) were included. There were no significant differences in technical success between the two treatment groups (69.2 vs 84.6%, $p=0.645$). No differences were detected in surgery-free survival rate (76.9% vs 92.3%, $p=0.593$), however clinical success at 1 year was higher in STK group (61.5 vs 23%, $p=0.04$). No early or late major adverse events were detected during follow-up with both techniques.

Conclusion: Present data show that STK has similar efficacy and safety rates as DEB after 1-year follow-up. Clinical success at 1 year was higher in STK group.

Disclosure: Nothing to disclose.

P0967

A NATIONWIDE, MULTICENTER, PROSPECTIVE COHORT OF ENDOSCOPIC ULTRASOUND-GUIDED GASTROENTEROSTOMY IN PATIENTS WITH MALIGNANT GASTRIC OUTLET OBSTRUCTION

Y.-T. Kuo¹, J.-H. Chen², S.-C. Liao³, J.-C. Lin⁴, C.-K. Sun⁵, M.-C. Tsai⁶, C.-H. Wu⁷, C.-Y. Yang⁸, M.-Y. Lin⁹, C.-L. Hsieh¹⁰, H.-P. Wang¹¹

¹National Taiwan University Hospital, Department of Integrated Diagnostics & Therapeutics, Taipei, Taiwan, ²Taipei Tzu Chi Hospital, Department of Internal Medicine, Taipei, Taiwan, ³Taichung Veterans General Hospital, Department of Internal Medicine, Taichung, Taiwan, ⁴Tri-Service General Hospital, Department of Internal Medicine, Taipei, Taiwan, ⁵Shin Kong Wu Ho-Su Memorial Hospital, Department of Internal Medicine, Taipei, Taiwan, ⁶Chung Shan Medical University Hospital, Department of Internal Medicine, Taichung, Taiwan, ⁷Mackay Memorial Hospital Taitung Branch, Department of Internal Medicine, Taitung, Taiwan, ⁸China Medical University Hospital, Department of Internal Medicine, Taichung, Taiwan, ⁹National Cheng Kung University Hospital, Department of Internal Medicine, Tainan, Taiwan, ¹⁰National Taiwan University Hospital Hsin-Chu Branch, Department of Internal Medicine, Hsin-Chu, Taiwan, ¹¹National Taiwan University Hospital, Department of Internal Medicine, Taipei, Taiwan

Contact E-Mail Address: sfstruck@gmail.com

Introduction: Surgical gastrojejunostomy and enteral self-expanding metal stents are efficacious for the management of malignant gastric outlet obstruction (GOO) but limited by high complication rates and short-term efficacy. As such, EUS-guided gastroenterostomy (EUS-GE) has emerged as an attractive procedure to treat patients with GOO as an alternative to surgery and enteral self-expanding metal stents. We aimed to prospectively assess clinical outcomes and safety of EUS-GE for the management of gastrointestinal obstruction in Taiwan.

Aims & Methods: Patients who underwent EUS-GE between July 2020 and April 2022 as part of a prospective multicenter registry at ten academic centers in Taiwan were included.

Technical success was defined as successful placement of a lumen-apposing metal stent (LAMS). Clinical success was defined as the ability of the patient to tolerate an oral diet or clinical symptom relief. Post-procedural adverse events were recorded.

Results: This prospective study included 52 patients, of whom 32 (61.5%) were male and 34 (65.4%) were diagnosed as pancreatic cancer. 22 patients (95.7%) receiving EUS-GE for the palliation of malignant gastric outlet obstruction. The mean procedural time was 53.4 minutes.

Technical and clinical success was achieved in 51 patients (98.1%) and 50 (96.2%), respectively. The mean change in the gastric outlet obstruction scoring system (GOOSS) after EUS-GE was 2.2. During a mean follow-up of approximately 100 days, 3 patients (5.8%) need reintervention. Adverse events, including bleeding and migration, occurred in 3 patients (6.3%).

Conclusion: EUS-GE is an emerging and minimally invasive procedure that has efficacy and safety comparable with those of current therapies for the management of malignant gastric obstruction.

Disclosure: No Any Conflict of Interest.

P0968

PERCUTANEOUS CHOLECYSTOSTOMY FOR ACUTE CALCULOUS CHOLECYSTITIS AN OBSERVATIONAL STUDY FROM A SINGLE INSTITUTE

K. Abdelsaid¹, B. Jayasanakar¹, M. Hassan¹, M. Jeilani¹, H. Ali¹

¹Maidstone and Tunbridge Wells NHS Trust, General Surgery, Tunbridge Wells, United Kingdom

Contact E-Mail Address: Kirolos.Abdelsaid@nhs.net

Introduction: Although percutaneous cholecystostomy (PC) is generally accepted as a bridge to definitive therapy for acute cholecystitis (AC), which remains cholecystectomy, some patients did not undergo cholecystectomy primarily due to contraindications to surgery. Here, we aimed to audit our clinical practice from a single institute.

Aims & Methods: The study included one hundred fifty-three patients who presented with Acute Cholecystitis and were initially managed with a Percutaneous Cholecystostomy tube. In addition, the proportion of patients who did not undergo subsequent LC and their characteristics were analysed.

Period: January 2016 till December 2021

Characteristics of patients who did not undergo subsequent LC were analysed.

Results: 27% (41/153) of the study cohort underwent LC, while the remaining patients (n=112) did not receive any surgical intervention. 22/122(20%) were presented with AC and coexisting hepatobiliary malignancy.

The mean age of the remaining patients (n=90) was 75±13 years, and the median length of drain insertion of those patients was 40 days.

The majority (57%) was presented with severe AC, while 8% had AC with adjacent liver abscess.

55% of those patients did not develop any further attacks of AC after PC removal, while 25% were deemed unfit for surgery.

The rest of the patients (20%) either refused the operation or died before LC.

The American Society of Anaesthesiologists (ASA) score was IV in 9% of patients (8/90).

15% (13/90) experienced post PC complications, including blocked stent, pain or cellulitis around the tube.

The 60-day mortality rate of patients who did not undergo LC was 11% (10/90).

Conclusion: The majority of AC patients treated initially with PC did not undergo subsequent LC. PC in high surgical risk patients with AC could be considered a definitive treatment.

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Disclosure: Nothing to disclose.

P1044

EFFECT OF AN AUTOMATED FLEXIBLE ENDOSCOPE CHANNELS BRUSHING SYSTEM ON IMPROVING THE REPROCESSING QUALITY: A PROSPECTIVE, RANDOMIZED CONTROLLED STUDY

R. Shang¹, J. Liu¹, H. Yu¹

¹Renmin Hospital of Wuhan University, Department of Gastroenterology, Wuhan, China

Contact E-Mail Address: riddle@whu.edu.cn

Introduction: Qualified reprocessing, of which meticulous channels brushing is the most crucial step, is essential for the prevention and control of endoscopy-associated infections. However, channels brushing is often omitted in practice, due to the pressure of endoscope turnover, the lack of reprocessing technicians and weak supervision.

Aims & Methods: This single-center, prospective, randomized controlled study aimed to evaluate the effect of an automated flexible endoscope channels brushing system (AECBS) on reducing bioburden and improving the quality of endoscope reprocessing.

This study was conducted, between Nov 24, 2021 and Jan 22, 2022, at Renmin Hospital of Wuhan University, China. Eligible endoscopes were randomly allocated to the auto group (channels brushed by AECBS) or the manual group (channels brushed manually), with sampling and culturing after high-level disinfection and drying. The primary endpoint was the positive rate of cultures for endoscopes.

Results: 204 endoscopes in the auto group and 205 in the manual group were eventually analyzed. The positive rate of cultures was significantly lower in the auto group than in the manual group (15.2% vs 23.4%, relative risk 0.649 [95% CI 0.432-0.976]; p=0.035).

Conclusion: AECBS could reduce the endoscope bioburden and improve the reprocessing quality. It has great potential to replace manual channels brushing and lower the risk of endoscopy-associated infections, providing a new idea for the optimization of reprocessing protocols.

Disclosure: Nothing to disclose.

Poster presentations

Surgery

Poster Presentations Surgery

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P0969

FIRST EXPERIENCE OF ENDOSCOPIC STENTING OF THE MAIN PANCREATIC DUCT IN PATIENTS WITH PANCREATIC FLUID COLLECTIONS AFTER PANCREAS TRANSPLANTATION

Y. Teterin¹, S. Suleymanova¹, I. Dmitriev¹, P. Yartcev¹¹Sklifosovsky Research Institute for Emergency Medicine, Endoscopy, Moscow, Russian Federation**Contact E-Mail Address:** shabi_s@mail.ru

Introduction: One of the most common complications after pancreas transplantation are pancreatic fluid collections (PFCs), which are often complicated not only by infection and subsequent disfunction of the pancreatoduodenal graft (PDG), but also with a rather high mortality rate of recipients. Drainage is not always effective and often requires repeated open surgical interventions, which worsens the outcome of the surgery. Percutaneous drainage of PFCs combined with endoscopic stenting of the main pancreatic duct of the pancreatoduodenal graft (MPDPDG) showed high efficiency in the treatment of PFCs.

Aims & Methods: From 01.01.2012 to 31.12.2021 at the Sklifosovsky Research Institute for Emergency Medicine were performed 64 transplantations of PDG. In 11 cases (17.2%), the early postoperative period was complicated by the formation of PFCs.

Of these, 7 patients underwent percutaneous drainage of pancreonecrosis with high efficiency and did not required additional methods of treatment. In the remaining 4 patients, drainage was ineffective and was an indication for endoscopic stenting of the MPDPDG. They were the ones who made up the study group.

Among them were 3 men and 1 woman. The mean age of the patients was 36,4 years. PFCs in these patients formed on days 1, 12, 18, and 47 after PDG transplantation. We used a gastroscope to stent the MPDPDG, due to anatomical features of the location of the duodenoduodenal anastomosis after PDG transplantation.

Through the endoscope channel was performed selective catheterization of the MPDPDG, using a catheter and a guidewire, followed by its contrasting with a water-soluble contrast agent. Due to the extravasation of the contrast, was determined the localization of the defect in the PDG duct system.

After that, a plastic pancreatic stent with a diameter of 7 Fr. and a length of 7 cm. was installed along guidewire. The stent was installed in such a way that its proximal edge completely covered the defect zone, and the distal one was determined in the intestinal lumen.

Results: In all patients PDG pancreaticography revealed extravasation of a contrast in the area of the isthmus and body of the pancreas, which required stenting of the MPDPDG. In 1 (25%) case, the patient had a dislocation of the stent into the intestinal lumen (III degree according to Clavien-Dindo (2009)). This patient underwent repeated endoscopic stenting of the MPDPDG.

On average 23 days after endoscopic stenting of the MPDPDG, the drainage tubes were removed and after approximately 40 days all patients were discharged in a satisfactory condition with follow-up endocrinologist and surgeon consultation. Pancreatic stents were removed after 6 months $\pm$ 7 days.

Conclusion: Endoscopic stenting of the main pancreatic duct of the donor pancreas is by far the most highly effective and minimally invasive method in the treatment of PFCs after transplantation of the pancreatoduodenal complex.

Disclosure: Nothing to disclose.

P0970

RISK FACTORS AND TREATMENT STRATEGIES OF DELAYED GASTRIC EMPTYING AFTER LAPAROSCOPIC PANCREATODUODENECTOMY

Y. Liu¹, J. Kong², T. Wang², J. Liu¹¹Shandong University, Department of Liver Transplantation and Hepatobiliary Surgery, Shandong Provincial Hospital, Jinan, China, ²Shandong Provincial Hospital Affiliated to Shandong First Medical University, Department of Liver Transplantation and Hepatobiliary Surgery, Jinan, China**Contact E-Mail Address:** dr1027188507@163.com

Introduction: With the development of laparoscopic technology and instruments, laparoscopic pancreaticoduodenectomy (LPD) has been applied in the surgical treatment of pancreatic head tumors, periampullary tumors and lower common bile duct tumors in an increasing number of medical centers.

However, LPD takes a long time, excises many organs, involves accurate perivascular anatomy and complex digestive tract reconstruction techniques, and has a high incidence of postoperative complications. Delayed gastric emptying (DGE) is one of the most common postoperative complications of LPD, with an incidence of up to 30%. The mechanism of DGE is still unclear. At present, there is still a lack of effective strategies for DGE prevention and treatment.

Aims & Methods: To explore the risk factors and key points of management of delayed gastric emptying (DGE) after laparoscopic pancreaticoduodenectomy (LPD), the clinical data of 832 patients who underwent LPD in the Department of Liver Transplantation and Hepatobiliary Surgery, Shandong Provincial Hospital Affiliated to Shandong First Medical University between March 2017 and November 2021 were analyzed retrospectively. According to the occurrence of DGE, patients were divided into DGE group and non-DGE group. The clinical characteristics between the two groups were compared, the risk factors for DGE were analyzed, and the effects of various treatment strategies were evaluated.

Results: A total of 194 (23.3%) patients developed DGE after LPD. Patients in the DGE group had a significantly higher rate of preoperative hypoalbuminemia and incidence of other kinds of postoperative complications. Multivariate logistic regression analysis showed that preoperative hypoalbuminemia, intraoperative blood transfusion and intra-abdominal infection were independent risk factors for DGE; furthermore, intraoperative blood transfusion, postoperative pancreatic fistula and bile leakage were the main risk factors for the development of grade B and C DGE. The modified surgical strategy, which put the gastrojejunal anastomosis in the input loop of the jejunum, could reduce the incidence of DGE.

Sixty-two patients developed grade B and C DGE, 48 of whom had intra-abdominal infection combined with stomal leakage. Among them, 42 patients underwent abdominal puncture drainage, 6 received continuous internal negative pressure flushing and drainage, and all of them recovered rapidly after treatment.

Conclusion: Treatment of preoperative hypoalbuminemia, rational gastrojejunum anastomosis, controlling intra-abdominal infection and reducing the occurrence of stomal leakage could reduce the incidence of DGE after LPD. Drainage is vitally important for the treatment of grade B and C DGE patients who have intra-abdominal infection combined with stomal leakage.

Disclosure: Nothing to disclose.

P0971

ENDOSCOPIC OVERSTITCH SUTURE OF PARIETAL LEAKS AFTER GASTROINTESTINAL COMPLEX RESECTIONS IS FEASIBLE, SAFE AND REDUCE THE NEED FOR HOSPITALIZATION

G. Grande¹, H. Bertani¹, S. Cocca¹, F. Pigò¹, S. Mangiafico¹, R. Salvatore¹, M. Lupo¹, G. Pontillo¹, R. Conigliaro¹
¹Azienda Ospedaliero Universitaria of Modena, Gastroenterology and Digestive Endoscopy Unit, Modena, Italy

Contact E-Mail Address: grande.giuseppe@aou.mo.it

Introduction: Endoscopic submucosal dissection (ESD) and endoscopic full thickness resection (EFTR) are recognized as useful advanced techniques for the treatment of pre-neoplastic, neoplastic and sub-epithelial lesions of the gastrointestinal tract.

However, complication rate and the need for hospitalization still remain a matter of discussion. The application of suturing devices have been suggested as an option to prevent complications and reduce hospital stay.

Aims & Methods: The aim of our study was to analyse the feasibility and safety endoscopic Overstitch suturing devices applied after large and deep ESD and EFTR. The secondary aim was to evaluate the efficacy of suturing system to reduce hospital stay and complication rate.

From September 2020 to April 2022 (in Covid-19 pandemic era) all consecutive patients sutured with Apollo SX Overstitch after complex resections were prospectively enrolled. Feasibility, complications, hospital stay were analyzed.

Results: Seventeen patients (8 female, mean 78, range 48-89) were enrolled; lesions were located in the stomach (3), in the rectum (9), in the sigmoid colon (3), in the descending colon (2). Final diagnosis were 1 occludent sub-epithelial lesion, 10 HGD/T1 (sm1) and 4 T1 (sm2/3) or T2 cancer. Eleven patients were treated with ESD (10 as outpatients) whereas 6 underwent eFTR, 5 of them as inpatients during uneventful medium hospital stay of 4.7 days (range 4-6).

Overstitch suture was feasible in all the lesions, and all locations. No major complications occurred. One minor complications (descending colon luminal stenosis) occurred and was successfully treated with temporary placement of covered metal stent.

Conclusion: Endoscopic overstitch system is safe and a useful tool to close large wall defect after ESD/EFTR

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Disclosure: Nothing to disclose.

P0972

COMPARISON BETWEEN LAPAROSCOPIC AND OPEN APPROACHES FOR SECOND COLORECTAL RESECTION AFTER COLECTOMY OR PROCTECTOMY

H. Nozawa¹, K. Sasaki¹, K. Murono², S. Emoto¹, S. Ishihara¹
¹University of Tokyo, Department of Surgical Oncology, Tokyo, Japan, ²University of Tokyo, Department of Surgical Oncology, Tokyo, Japan

Contact E-Mail Address: hiroanozawa@yahoo.co.jp

Introduction: Past randomized controlled trials demonstrated that a laparoscopic approach provides several benefits in patients who undergo colon or rectal surgery without jeopardizing oncological outcomes. Laparoscopic approach in second colorectal surgery in such patients is considered more challenging than that in surgery-naïve patients because of potential intra-abdominal adhesion, resulting in an elevated risk of unexpected trauma [1].

Unfortunately there is a paucity of studies comparing outcomes of laparoscopic and open approaches for second primary colorectal lesions after colectomy or proctectomy.

Aims & Methods: The current study is aimed to compare the surgical outcomes of laparoscopic vs open resection of the colorectum after colectomy or proctectomy. Among patients with colorectal disease who underwent surgery between 2008 and 2021 at our hospital, we selected 73 consecutive patients who had previous colorectal surgery for this retrospective study. Here, reoperation aimed at managing complications of preceding colorectal surgery, e.g. anastomotic leakage or stenosis, or bowel obstruction, local resection of tumors near the anus, and surgical cases of familial adenomatous polyposis or inflammatory bowel disease were excluded.

Based on the second surgery approach (laparoscopic or open), patients were divided into the Lap group (n=38) or Op group (n=35). Patients' baseline characteristics and surgical outcomes, such as operative time, blood loss, first bowel movement, postoperative complications, and survival were compared between the groups.

Categorized data were compared by the chi-squared or Fisher's exact test, whereas continuous variables were compared by the unpaired t or Wilcoxon's test. Kaplan-Meier methods were used to estimate survival curves. The log rank test was used to examine the difference in OS between patients in the Lap and Op groups.

Results: Four patients (11%) required conversion to open surgery in the Lap group; all of these patients had received open surgery for the first colorectal lesion. The median volume of blood loss was 50 ml in the Lap group and 210 ml in the Op group (p=0.0003). The median time to first bowel movement was shorter in the Lap group than the Op group (2.7 days vs 3.5 days, p=0.004). The operative time, frequencies of postoperative complications, and overall survival were similar between the groups.

Variable		Lap (n=38)	Op (n=35)	p-value
Interval from previous colorectal surgery, month	Mean ± SD	121 ± 100	122 ± 110	0.98
Resection including previous anastomosis		13 (34%)	14 (40%)	0.61
Operative time, min	Mean ± SD	321 ± 152	279 ± 139	0.22
Blood loss, ml	Median (IQR)	50 (15-403)	210 (125-420)	0.0003
Time until first bowel movement, day	Mean ± SD	2.7 ± 1.1	3.5 ± 1.2	0.004
Complications	Any Grade 2-	11 (29%)	13 (37%)	0.46

SD standard deviation, IQR interquartile range.

Table 1. Perioperative parameters according to second surgical approach.

Conclusion: Laparoscopic surgery was safe and beneficial for selected patients undergoing second colorectal resection after colectomy or proctectomy in terms of blood loss and bowel function recovery without affecting other outcomes. Encouragingly, there were no conversion cases when considering patients who had undergone preceding colorectal surgery via a laparoscopic approach presumably owing to less intraabdominal adhesion [2-4]. Our findings need to be verified using a larger number of patients in multiple institutes.

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Disclosure: No conflict of interest.

P0973

A FRENCH MULTICENTRIC PROSPECTIVE STUDY OF SURGICAL TREATMENT OF HEMORRHOIDAL DISEASE WITH RADIO FREQUENCY

J.-M. Rouillon¹, A. Laurain², D. Bouchard³, P. Petit⁴, A. Liddo⁵, B. Vinson-Bonnet⁶, A. Venara⁷, J.-M. Didelot⁸, G. Bonnaud⁹, A. Senejoux¹⁰, T. Higuero¹¹, P. Delasalle¹², A.-L. Tarrerias¹³, F. Devulder¹⁴, A. Castinel¹⁵, C. Thomas¹⁶, H. Pillant-Lemoult², C. Favreau-Weltzer³, L. Abramowitz²
¹Polyclinique Montréal, Gastroenterology, Carcassonne, France, ²Clinique Blomet, Paris, France, ³Maison de Santé Protestante, Bagatelle, Bordeaux, France, ⁴Cabinet de Proctologie, Saint-Herblain, France, ⁵Clinique de la Victoire, Tourcoing, France, ⁶CHI de Poissy-Saint Germain en Laye, Poissy, France, ⁷CHU Angers, Chirurgie Viscérale, Angers, France, ⁸Cabinet de Gastro-Entérologie, Montpellier, France, ⁹Clinique Ambroise Paré, Toulouse, France, ¹⁰Centre Hospitalier Privé Saint-Grégoire, Rennes, France, ¹¹Cabinet de Proctologie, Beausoleil, France, ¹²Clinique du Palais, Grasse, France, ¹³Clinique du Trocadéro, Paris, France, ¹⁴Polyclinique Reims-Bezannes, Reims, France, ¹⁵Cabinet de Proctologie, Bordeaux, France, ¹⁶Hôpital Saint-Joseph, Paris, France

Contact E-Mail Address: rouillon.gastro11@gmail.com

Introduction: Hemorrhoidal disease is benign but can decrease the quality of life of patients. Hemorrhoidectomy according to Milligan Morgan is an effective surgery method but often has a long and painful postoperative course. Also, “minimally invasive” procedures are currently being developed.

The use of a radio frequency current allowing the destruction of the internal hemorrhoidal tissue is a recent technique, little evaluated, and only in monocentric studies.

The objective of this multicenter study was to prospectively evaluate the efficacy and tolerance of radiofrequency in patients suffering from internal hemorrhoidal disease.

Aims & Methods: Patients with isolated internal hemorrhoidal disease had radiofrequency surgery (Rafaelo®) under general or spinal anesthesia. Patients were evaluated at 1, 3, 6 and 12 months after surgery. The primary endpoint was the change in the HEMO-FISS-QoL score at month 3 (vali-

dated score to assess the impact of hemorrhoidal disease on quality of life via a self-administered questionnaire [1]). The secondary endpoints were the changes of this score at 1, 6 and 12 months, the evolution of symptoms, complications, scores of postoperative pain and duration of work interruption.

Results: Between January 2019 and March 2021, 129 patients (69% males, median age 49 years) were included in 16 French centers for minimally invasive procedure. The hemorrhoidal disease initial grades were, respectively, grade 1 in 2%, grade 2 in 41%, grade 3 in 54% and grade 4 in 3% of patients. The median joules delivered per patient was 3925 with a median operating time of 15 minutes.

Three months after surgery, the median of the HEMO-FISS-QoL score dramatically and significantly decreased from 15.8/100 to 0/100 ($p < 0.0001$) with a median score remaining at 0/100 at M6 and M12. There was also a significant decrease at month 3 in the rates of patients reporting bleeding (21% vs 84%, $p < 0.001$), prolapse (34% vs 91.3%, $p < 0.001$) and anal discomfort (median 0/10 vs. 5/10, $p < 0.0001$). The median work interruption was 4 days. The median maximum scores of postoperative pain were 1.7/10, 0.4/10, 0/10 and 0/10 at weeks 1, 2, 3 and 4, respectively. A total of respectively 32%, 25%, 12% and 3% of patients consumed level 2 analgesics during weeks 1, 2, 3 and 4. Opioids were administered in 8.5% of patients, most often due to postoperative external hemorrhoidal thrombosis.

At year 1, only 7 patients (5%) had to be re-operated, all using the Milligan and Morgan technique.

Three patients (2.3%) had postoperative hemorrhage, one of which had to have hemostasis under general anesthesia. Patients on DOACs (4 patients) or antiplatelet agents other than aspirin (3 patients) did not have any bleeding complications.

Three patients (2.3%) had dysuria requiring urinary catheter, 2 had abscess, 2 a fecal impaction. A patient was operated for an anal fissure. Finally, 10 patients (7.7%) presented postoperative external hemorrhoidal thrombosis.

Regarding patient satisfaction, 86% of patients would agree to repeat the same procedure if necessary and 80% would recommend it to those around them.

Conclusion: The “minimally invasive” surgical treatment of internal hemorrhoidal disease by radiofrequency can significantly improve the quality of life of patients and their symptoms at 1 year. Postoperative pain was not significant in most cases and the work interruption short.

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P0974

MANAGEMENT OF SUPERFICIAL GASTROINTESTINAL NEOPLASTIC LESIONS ASSOCIATED WITH SEVERE SUBMUCOSAL FIBROSIS - ENDOSCOPIC SUBMUCOSAL DISSECTION TO THE RESCUE!

R. Mendo¹, A. Mascarenhas¹, C. O'Neill¹, A.R. Franco¹, I. Simao¹, P. Barreiro¹, C. Chagas¹

¹Centro Hospitalar Lisboa Ocidental, Gastroenterology, Lisbon, Portugal

Contact E-Mail Address: mendorui@gmail.com

Introduction: Endoscopic submucosal dissection (ESD) is a technically complex and demanding procedure that allows for the *en bloc* removal of gastrointestinal epithelial neoplasms regardless of size. Previous resection/manipulation, surgery or radiotherapy prior to ESD are associated with severe submucosal fibrosis, greatly enhancing the complexity of the procedure. Nevertheless, little is known about the outcomes of these patients that undergo ESD.

Aims & Methods: We retrospectively analysed, in a single center, consecutive patients that underwent ESD for gastrointestinal lesions previously subjected to resection or ablation therapy, surgery or radiotherapy, using our prospectively collected database. Short and long-term outcomes were evaluated, including efficacy, safety and complications associated with ESD in these patients.

Outcomes and complications were compared between groups. High local-risk resection was considered if piecemeal resection and if positive horizontal margin for the presence of dysplasia or carcinoma (HM1d and HM1c, respectively).

High-risk resection was defined if R1 resection or in the presence of R0 resection associated with poor prognostic histopathologic findings, defined by lymphovascular invasion, poorly differentiated carcinoma, or if deep submucosal invasion, defined as >200 µm for squamous cell cancer, >500 µm for Barrett's or gastric adenocarcinoma and >1000 µm for colorectal adenocarcinoma.

Results: From all ESD performed (n=605), 40 lesions (6.6%) had undergone previous manipulation (esophageal, n=3; gastric, n=5; colon, n=4; rectal, n=28). Previous endoscopic mucosal resection (EMR) was the most common cause of prior manipulation (65%, n=26), followed by surgery (15%, n=6), radiotherapy (5%, n=2) and ESD (5%, n=2); 10% (n=4) had prior manipulation by more than one technique. Complete procedure was achieved in 97.5% of cases (n=39), with *en bloc* resection rate of 80% (n=32), and curative resection (R0) of 51.3% (n=20).

For non-curative resected lesions, 68.4% (n=13), there was a high local-risk resection (piecemeal resection, n=7; HM1, n=6) and 31.6% (n=6) were high-risk resection. Three cases (50%) of high-risk resected lesions were submitted to surgery. Local recurrence was 5% (n=2), that were successfully retreated endoscopically. Complication rate was 12.5% (n=5) (bleeding 7.5%, n=3; perforation 5%, n=2) all successfully treated during the procedure. Mean follow-up time was 842 ± 513 days (mean ± standard deviation).

Conclusion: Lesions typically associated with severe submucosal fibrosis are associated with a lower rate of *en bloc* and of curative resection. However, ESD was associated with a high efficacy treatment rate with a good safety profile, making this minimal invasive treatment a first-line therapy in the management of superficial gastrointestinal neoplastic lesions associated with severe submucosal fibrosis.

Disclosure: Nothing to disclose.

P0975

DEVELOPMENT OF A NEW 3D PRINTED ENDOSCOPIC GRASPING INSTRUMENT

B. Sudarevic¹, J. Troya¹, K.H. Fuchs¹, A. Hann¹, A. Meining¹

¹University Hospital Würzburg, Interventional and Experimental Endoscopy (InExEn), Internal Medicine II, Würzburg, Germany

Contact E-Mail Address: sudarevicboban@gmail.com

Introduction: The constant flow of innovative ideas regarding interventional endoscopic procedures and instruments requires a quick response from the side of developers and engineers to create prototypes following these ideas. Early testing of new ideas allows for early selection of those ideas and instruments, which may have a high potential of becoming successful in future clinical practice. Using 3D printing technology may assist in the production of prototypes.

Aims & Methods: The aim of this study is the use of 3D printing technology to develop and produce a new endoscopic grasping instrument.

The design of the "new grasper" was developed at an initial conference between gastroenterologists, engineers, and endoscopic surgeons, listing the wished features of such a new instrument. The instrument should be designed for endoscopic procedures in the upper and lower GI tract. It should have a superior grasping surface and force to provide a safe grip.

The engineers created a 3D printed prototype, which could be quickly produced and subsequently tested by the involved endoscopists, who could determine the flaws and limitations.

Furthermore, versions 2.0 and 3.0 were developed and tested regarding the following criteria: maneuverability, grasping and pulling abilities, force measurements, and durability.

Results: The new 3D-printed graspers provide improved maneuverability compared to traditional endoscopic instruments with an increased working radius by its steering capacity of 220 degrees and could be advanced and withdrawn as well as angulated towards a lesion within a median 120-sec resp. 70 sec. It can be rapidly produced and assembled in the endoscopic laboratory. The correlation between rigidity and flexibility was sufficient, while the pulling force was 7.85 Newton (conventional instrument 7.68N).

Conclusion: 3D-printed grasping instruments show sufficient stability and grasping force for the tasks in interventional endoscopic procedures. In addition, the 3D printed graspers provide improved maneuverability. In the future, they may be customized to special patients or tasks, medically necessary in an individualized patient approach.

Disclosure: Nothing to disclose.

Poster presentations
COVID-19 / Health economics / Digitalisation
in GI / Education In GI / Gender and diversity

Poster Presentations

COVID-19 / Health economics / Digitalisation in GI / Education In GI / Gender and diversity

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P0976

GUT MICROBIOME TO REDUCE CARBON EMISSION

H.S. Bozkurt¹

¹Maltepe University, Gastroenterology, Istanbul, Turkey

Contact E-Mail Address: sancarb79@gmail.com

Introduction: It is estimated that the total waste generated during all endoscopic procedures alone performed in the USA annually would weigh 38 000 metric tons (equivalent of 25 000 passenger cars) and the net waste mass would increase by 40% if all endoscopic procedures were performed with single-use endoscopes (1). It is worth noting that more than 100 million endoscopic procedures are performed yearly in around the world. New approaches are needed to reduce global warming and increase the protection of petroleum-based scopy devices. We aimed to reveal the bio-hybrid biomaterial that we obtained as a result of the combination of probiotic bifidobacteria which have carbon binding/reducing properties (2) with sodium alginate.

Aims & Methods: In these study which was designed in Yıldız Technical University / Istanbul, bio-hybrid films were produced by using both *Bifidobacterium animalis subsp. lactis* BB-12 probiotic strain and *Bifidobacterium infantis* in combination with sodium alginate (SA), which demonstrates biocompatibility and facilitated gelation properties in aerobic atmospheric condition. Bio-hybrid films were characterized by using different methods.

Results: Based on the spectroscopic and mechanical analysis, it was found that mechanical strength increased in films produced by adding *Bifidobacterium infantis* in SA while this increase was relatively lower as compared to those containing *Bifidobacterium animalis subsp. lactis* BB-12 as crosslinking ratio increases. Besides, bacteria contained in bio-hybrid films increased the percentage of amorphous zone of SA in SA/bacteria films, which reduced the crystallinity ratio. This indicated that crystalline chains contained in the structure of SA are degraded by probiotic bifidobacteria.

Conclusion: "Mechanical properties" are crucial for biodegradable and/or non-biodegradable materials used in tissue engineering applications. Biohybrid biofilm that contains probiotic bifidobacteria and SA structures coated endoscopy devices and sets can be a pioneering approach to reduce carbon emissions, as well as to prevent secondary infections and increase device protection (3). This is the first study to demonstrate the usability of bifidobacterium as a biomaterial.

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P0977

ADALIMUMAB IN CROHN'S DISEASE AND ULCERATIVE COLITIS IN SPAIN

J.A. Schoenenberger-Arnaiz¹, J.M. Martínez-Sesmero², C. Crespo-Diz³, M. Cerezales⁴, M. Guigini⁵

¹Regió Sanitària de Lleida, Pharmacy Service, Lleida, Spain,

²Hospital Clínico San Carlos, Pharmacy Service, Madrid, Spain,

³Área Sanitaria Pontevedra e O Salnés, Pharmacy Service, Pontevedra, Spain, ⁴Axentiva Solutions SL, Oviedo, Spain,

⁵Fresenius Kabi España, S.L.U, Barcelona, Spain

Contact E-Mail Address: jas.lleida.ics@gencat.cat

Introduction: Gastrointestinal immune-mediated inflammatory diseases are chronic conditions generally causing abdominal pain and diarrhoea (sometimes bloody)^{1,2} among other symptoms, which entail a high burden for patients and society.

In Spain, Crohn's disease (CD) and ulcerative colitis (UC) are the most frequent gastrointestinal immune-mediated inflammatory diseases, with a joint prevalence of 0.78%³ affecting about 370,000 people.

With the introduction of biological treatments, such as adalimumab (ADA), there has been an improvement in the clinical outcomes for patients with moderately to severely active CD and UC who have had an inadequate response with, lost response to, or were intolerant to 1st line therapy⁴.

However, until biosimilars arrived, the high cost of biologics was a barrier to its prescription⁵. Cost-effectiveness analysis can be a useful tool in decision-making for the treatment of these pathologies.

Aims & Methods: Our objective was to assess the cost-effectiveness of ADA and its clinical alternatives in CD and UC in Spain.

All the effectiveness information for ADA (biosimilar) and its comparators (infliximab, tofacitinib, ustekinumab, and vedolizumab) was gathered using a PICO-S-T strategy. Two reviewers evaluated the inclusion of the studies and assessed their quality using PRISMA-NMA Checklist.

A cost-effectiveness model was built based on meta-analyses (direct or indirect) conducted between 2018-2021. Cost data (€2021) was obtained from Spanish drug cost datasets⁶ and literature review⁷.

Effectiveness was measured as the number needed to treat (NNT) versus (vs) placebo (PLC) to achieve clinical remission according to Crohn's disease activity index (CDAI) for CD or Mayo Score for UC.

Efficiency score was cost per NNT vs. PLC to achieve clinical remission according to CDAI or Mayo Score. The model was designed from a hospital perspective (only direct costs) with a 1-year time horizon.

With all this information, a cost-effectiveness analysis between ADA and the suitable alternatives was performed. A deterministic and probabilistic sensitivity analysis (PSA) was also carried out.

Results: Two meta-analyses, one for CD⁸ and one for UC⁹, met the inclusion criteria and both fulfilled 91% of the 32 points on the PRISMA-NMA Checklist items.

For CD, no statistically significant differences were seen in NNT to achieve clinical remission according to CDAI between infliximab, ADA, ustekinumab, and vedolizumab. The annual cost for ADA was 5,230€ vs 5,351€ - 10,714€ for the other treatments. As no effectiveness difference was seen, a cost minimization analysis was performed. Therefore ADA, was the most cost-effective treatment.

For UC, there were no statistically significant differences in NNT to achieve clinical remission, according to Mayo score, between infliximab, ADA,

tofacitinib, and vedolizumab. Annual cost for ADA was between 121€ - 5,484€ less expensive than the other treatments. Therefore, ADA was the most cost-effective treatment.

We performed a sensitivity analysis for both pathologies, obtaining similar results. In the deterministic sensitivity analysis, ADA was the best option with average and maximum discounts. In the PSA, ADA was the best option in 63% of the cases.

Conclusion: According to our model, ADA was the most cost-effective option for the treatment of CD and UC in Spain.

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M Cerezales works as a consultant in Axentiva Solutions S.L., a consultancy firm working for several pharmaceutical companies.

MA Guigini works for Fresenius Kabi España, S.A.U.

P0978

UNMET MEDICAL NEEDS IN SHORT BOWEL SYNDROME WITH INTESTINAL FAILURE IDENTIFIED FROM A QUALITATIVE SURVEY OF PATIENTS AND HEALTHCARE PROVIDERS

D. Wolin¹, K. Kosa¹, N.N. Youssef², L. Zografos¹

¹RTI Health Solutions, Research Triangle Park, United States,

²VectivBio, Basel, Switzerland

Contact E-Mail Address: nader.youssef@vectivbio.com

Introduction: Short bowel syndrome with intestinal failure (SBS-IF) is a complex and heterogeneous malabsorptive disorder. The burdensome current standard of care includes parenteral support (PS), symptomatic management, and the first-generation daily glucagon-like peptide-2 (GLP-2) analogue.

Aims & Methods: In an effort to identify perception of current treatment and unmet needs in the GLP-2 era, pilot qualitative interviews were conducted with healthcare providers (HCPs) and patients treated with tedu-

glutide. Participants (N=22; 11 patients, 5 physicians, 3 nurses, 3 dieticians) were recruited based on SBS-IF diagnosis for patients and number of SBS-IF patients for HCPs. Interview material was reviewed and exempted by institutional review board and included topics of patient experience with SBS-IF, PS and current treatment, as well as preferences for future treatments.

Results: Mean age of the 11 patients was 42.5 years (range 27-75). The majority was female (n=6), non-Hispanic White (n=8), either unemployed or receiving disability (n=7), and at least some college education (n=8). Mean time since diagnosis was 10.7 yrs (range 0.25-54). Mean length of remaining colon was 11.1 inches (0-27). Six patients had stoma. All patients had received teduglutide with a mean duration of 11.4 months (range 0.5-42). Of the 11 patients, 4 discontinued teduglutide due to end of clinical trial, allergic reaction, abdominal cramps, and intestinal blockage. Separately, 4 of the 11 patients reported no noticeable change with teduglutide treatment, while others reduced or eliminated PS, improved digestion/absorption, decreased output, improved overall wellbeing, and had more energy. The challenges reported by patients with current first generation GLP-2 treatment included suboptimal efficacy, self-injection, injection preparation, and tolerability (abdominal pain). Patients wanted future GLP-2 medications to further reduce or eliminate PS, earlier onset of action, decrease injection frequency, prefilled syringe, different mode of administration, improve overall wellbeing, and reduce bowel emptying frequency. The 11 HCPs indicated the current challenges with GLP-2 as adverse effects, increased monitoring required, and insurance/reimbursement issues. HCPs would like to see improved efficacy, less side effects, more flexibility with diet and ease of administration.

Conclusion: Progress has been made in the treatment of SBS-IF patients with first generation GLP-2 analogue. However, notable limitations and challenges still exist, including the need for daily injections, pre-mixing procedures, and suboptimal tolerability and efficacy in certain patients. Patients perceived the lack of efficacy as one of the most important challenges with current GLP-2, while physicians identified adverse events as limiting. These observations from HCPs and patients indicate the continued significant opportunities for further improvement in the management of SBS-IF.

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P0979

USEFULNESS OF ENZYMATIC CLEANING IN A THERMOSTATIC CHAMBER FOR ENDOSCOPE CLEANING: A MULTICENTER PROSPECTIVE STUDY

A. Nakanishi¹, T. Toyokawa¹, Y. Sakakibara², E. Mita², Y. Takahashi³, K. Kubo⁴, K. Mabe⁴, N. Watanabe⁵, H. Hamada⁶, R. Kusunoki⁷, T. Kuwai⁷, T. Wakatsuki⁸, T. Mannami⁸, A. Fujimoto⁹, T. Uraoka⁹, T. Hayashi¹⁰, N. Esaka¹¹, S. Katsushima¹¹, A. Kanda¹², A. Takazoe¹³, H. Saito¹³, M. Shimada¹⁴, T. Kagaya¹⁵, Y. Sasaki¹⁶, H. Fujii¹⁷, S. Uehara¹⁸, N. Ara¹⁹, B. Chin²⁰, E. Masuda²¹, M. Kato⁴, S. Nakazuru², N. Harada²²

¹National Hospital Organization Fukuyama Medical Center, Gastroenterology, Fukuyama, Japan, ²National Hospital Organization Osaka National Hospital, Gastroenterology and Hepatology, Osaka, Japan, ³National Hospital Organization Hokkaido Cancer Center, Gastroenterology, Sapporo, Japan, ⁴National Hospital Organization Hakodate National Hospital, Gastroenterology, Hakodate, Japan, ⁵National Hospital Organization Mie Chuo Medical Center, Gastroenterology, Tsu, Japan, ⁶National Hospital Organization Higashihiroshima Medical Center, Gastroenterology, Higashihiroshima, Japan, ⁷National Hospital Organization Kure Medical Center and Chugoku Cancer Center, Gastroenterology, Kure, Japan, ⁸National Hospital Organization Okayama Medical Center, Gastroenterology, Okayama, Japan, ⁹National Hospital Organization Tokyo Medical Center, Gastroenterology and Hepatology, Tokyo, Japan, ¹⁰National Hospital Organization Shikoku Medical Center for Children and Adults, Gastroenterology, Zentsuji, Japan, ¹¹National Hospital Organization Kyoto Medical Center, Gastroenterology, Kyoto, Japan, ¹²National Hospital Organization Higashi-ohmi General Medical Center, Gastroenterology, Otsu, Japan, ¹³National Hospital Organization Asahikawa Medical Center, Gastroenterology, Asahikawa, Japan, ¹⁴National Hospital Organization Nagoya Medical Center, Gastroenterology, Nagoya, Japan, ¹⁵National Hospital Organization Kanazawa Medical Center, Gastroenterology, Kanazawa, Japan, ¹⁶National Disaster Medical Center, Gastroenterology, Tokyo, Japan, ¹⁷National Hospital Organization Fukuokahigashi Medical Center, Gastroenterology, Fukuoka, Japan, ¹⁸National Hospital Organization Takasaki General Medical Center, Gastroenterology, Takasaki, Japan, ¹⁹National Hospital Organization Sendai Medical Center, Gastroenterology, Miyagi, Japan, ²⁰National Hospital Organization Nanao National Hospital, Gastroenterology, Nanao, Japan, ²¹National Hospital Organization Osaka Minami Medical Center, Gastroenterology, Kawachinagano, Japan, ²²Clinical Research Institute, National Hospital Organization Kyushu Medical Center, Gastroenterology, Fukuoka, Japan

Contact E-Mail Address: isinakau.arika.609039@gmail.com

Introduction: Several recent outbreaks of infection with carbapenem-resistant Enterobacteria associated with duodenoscope use have forced endoscopists to reassess the risk of infection transmission related to endoscopic procedures. The manual component of reprocessing appears to be the most prone to errors. Immersion cleaning in an enzyme detergent solution is very useful, and the removal ability is independent of human involvement. In addition, the usefulness of adenosine triphosphate (ATP) as an indicator to determine the endoscope cleaning effectiveness has been reported in recent years.

Aims & Methods: This study aimed to evaluate the usefulness of enzymatic cleaning using a thermostatic bath containing ATP. This prospective cohort study was conducted at 22 facilities in Japan between January 2019

and March 2021. Endoscope types included gastroscope, colonoscope, duodenoscope, echoendoscope, and enteroscope. The primary endpoint was the amount of ATP in the suction-biopsy channels after manual cleaning. For duodenoscopes, the amount of ATP in the elevator guide-wire channel was also evaluated.

The secondary endpoints were the bacteria detection rate in endoscopes, re-cleaning rate, and relationship between years of endoscope use and ATP levels. The recleaning rate was defined as the percentage of endoscopes with an ATP content ≥ 200 relative light units (RLUs) in the endoscope channel after a single cleaning.

There was no specification for the thermostatic chamber used in this study, but a neutral or alkaline enzyme detergent diluted at 0.5–1% was used, and the temperature of the enzyme detergent was controlled at approximately 40°C. ATP testing was performed on the rinsates using the CleanTrace Water/Swab ATP test (3M Co, Maplewood, Minn), and ATP RLUs were determined using a handheld luminometer.

Results: A total of 489 endoscopes were registered during the study period, and the amount of ATP in 5979 samples was assessed. The mean $\pm$ standard deviation amount of ATP (RLU) suction-biopsy channels of total endoscopes, gastroscopes, colonoscopes, duodenoscopes, echoendoscopes, and enteroscopes before and after the introduction of the thermostatic chamber was 135.3 ± 1092.7 and 40.2 ± 123.0 , 124.2 ± 423.0 and 36.1 ± 64.1 , 48.7 ± 176.3 and 20.7 ± 33.1 , 386.6 ± 3714.0 and 45.7 ± 56.2 , 425.1 ± 746.9 and 189 ± 437.0 , and 103.1 ± 386.6 and 45.3 ± 56.2 , respectively. The ATP levels after cleaning were significantly lower for all endoscopes except enteroscopes ($p < 0.0001$). The bacterial detection rate and recleaning rate improved significantly from 7.5% to 3.2% and 11.9% to 2.1%, respectively, after the introduction of the thermostatic chamber ($p < 0.001$). The amount of ATP in the elevator guidewire channels of duodenoscopes improved from 731.5 ± 3754.9 RLU to 484.6 ± 2966.8 RLU. Despite the significant decrease after the introduction of the thermostatic chamber, the amount of ATP in the elevator guide-wire channels remained high. No correlation was found between the number of years the endoscope was used and amount of ATP.

Conclusion: Enzymatic cleaning using a thermostatic chamber significantly decreased the amount of ATP, bacteria detection rate, and recleaning rate. However, the amount of ATP in the elevator guidewire channels of duodenoscopes was high, suggesting the need for special care when cleaning duodenoscopes.

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P0980

FATIGUE IMPROVEMENT CORRELATES WITH REDUCTIONS IN WORK PRODUCTIVITY IMPAIRMENT AND RELATED INDIRECT COST IN PATIENTS WITH CROHN'S DISEASE: POST HOC ANALYSIS OF PHASE 3 RISANKIZUMAB INDUCTION TRIALS

E. Louis¹, J. Panés², S. Ghosh³, B. Siegmund⁴, W.-J. Lee⁵, H. Deng^{6,7}, K. Kligys⁸, J. Kalabic⁹, E.V. Loftus¹⁰

¹CHU Liège and Liège University, Gastroenterology, Liège, Belgium,

²Hospital Clínic Barcelona, Gastroenterology, Barcelona, Spain,

³University College Cork, APC Microbiome Ireland, Birmingham,

Ireland, ⁴Charité - Universitätsmedizin Berlin, Med. Klinik m.S.

Gastroenterologie, Infektiologie und Rheumatologie, Berlin,

Germany, ⁵AbbVie Inc, North Chicago, United States, ⁶AbbVie Inc.,

North Chicago, United States, ⁷University of Illinois at Chicago,

Pharmacy Systems Outcomes and Policy, Chicago, United States,

⁸AbbVie, North Chicago, United States, ⁹AbbVie Deutschland

GmbH & Co., KG, Ludwigshafen, Germany, ¹⁰Mayo Clinic College of

Medicine, Division of Gastroenterology and Hepatology, Rochester,

United States

Contact E-Mail Address: sugghosh@gmail.com

Introduction: Patients with Crohn's disease (CD) frequently experience fatigue,¹ which may reduce quality of life and work productivity, thereby contributing to patient and societal costs. Few studies have analyzed the indirect cost burden associated with fatigue; this analysis used Phase 3 clinical trial data in patients with CD to assess this relationship.

Aims & Methods: The study used pooled 12-week data from patients with moderate to severe CD who received risankizumab (600 mg or 1200 mg IV) or placebo in ADVANCE and MOTIVATE. Patients completed Functional Assessment of Chronic Illness Therapy-Fatigue (FACIT-F) and Work Productivity and Activity Index (WPAI) questionnaires at Baseline and Week 12. All risankizumab or placebo IV treated patients with non-missing values were analyzed. Correlation between FACIT-F and WPAI was assessed by Pearson correlation. Mean change from Baseline to Week 12 in WPAI was assessed and stratified by quartiles of the mean change from Baseline FACIT-F scores. The linear relationship between improvements from baseline in FACIT-F and WPAI Overall Work Impairment (OWI) was assessed; results from the regression analyses were used to calculate cost savings based on corresponding WPAI scores and average hourly wages in the US and Europe. Annualized cost savings were determined in patients who achieved a clinically meaningful improvement (≥ 9 -unit increase) in FACIT-F and compared between patients who achieved or did not achieve a FACIT-F score $>$ normative value (>40) at Week 12.

Results: Mean age (standard deviation) of patients was 38.4 (13.3) years and 53.1 percent were male in the study population. Moderate correlation was observed between FACIT-F and all four domains of WPAI (Pearson coefficient range -0.55 to -0.30, $P < 0.0001$) at Week 12. Greater improvements in WPAI scores from Baseline were consistently observed among patients with greater mean change from Baseline scores in FACIT-F (Table) at Week 12. A ≥ 9 -unit change from Baseline in FACIT-F at Week 12 corresponded to a 12% reduction in OWI, which resulted in 4.8 hours of improved work productivity per week and an annualized cost savings per person of \$7,749 in US and €7,117 in Europe. Patients with a normative FACIT-F score of >40 at Week 12 had a corresponding reduction in OWI score of 29%, resulting in 12 hours less work impairment per week and an annualized cost savings per person of \$18,726 in US and €17,199 in Europe.

Conclusion: A significant correlation was observed between fatigue and work productivity in the induction trials of risankizumab. Early clinically meaningful improvements, as well as achieving fatigue normality, were associated with improvements in work productivity that lead to substantial indirect cost savings.

	FACIT-F <2		2≤ FACIT-F <9		9≤ FACIT-F <17		FACIT-F ≥17		P-value
Work time missed	146	7.5 ± 32.5	133	-0.7 ± 25.6	162	-3.2 ± 30.1	185	-18.4 ± 36.7	<0.0001
Overall work impairment	146	2.5 ± 27.3	133	-11.0 ± 26.3	162	-20.8 ± 29.2	185	-37.5 ± 31.3	<0.0001
Impairment while working	130	-1.4 ± 21.9	121	-14.1 ± 22.6	147	-23.3 ± 23.5	160	-35.7 ± 26.1	<0.0001
Activity impairment	303	-3.0 ± 23.0	310	-13.3 ± 22.5	300	-23.7 ± 23.7	341	-41.9 ± 26.7	<0.0001

Data are n and mean change ± standard deviation. P-value derived from analysis of covariance (ANOVA).

Table. Mean change in WPAI Stratified by Mean Change in FACIT-F Scores from Baseline to Week 12.

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P0981

A RETROSPECTIVE STUDY COMPARING THE USE OF THE AGE, BLOOD TESTS AND COMORBIDITIES (ABC) SCORE TO PREDICT 30-DAY MORTALITY IN ACUTE UPPER AND LOWER GI BLEEDING WITH CURRENT SCORES USED AT MATER DEI HOSPITAL

G. Costa¹, F. Mercieca¹, M. Aquilina², N. Azzopardi³

¹Mater Dei Hospital, Msida, Malta, ²University of Edinburgh, Deanery of Molecular, Genetic and Population Health Science, Edinburgh, United Kingdom, ³Mater dei Hospital, Gastroenterology, Msida, Malta

Contact E-Mail Address: glenncosta110@gmail.com

Introduction: Gastrointestinal (GI) bleeding is a common problem that medical practitioners encounter in both the emergency department as well as the primary care setting⁽¹⁾.

During assessment, it may be difficult to distinguish between upper GI bleeding (UGIB) and lower GI bleeding (LGIB). Ideally, clinicians should use a single score for both acute UGIB and LGIB. This was recommended in the recent 2015 UK National Confidential Enquiry into Patient Outcome and Death (NCEPOD) report on GI bleeding⁽²⁾.

Accurate and early stratification of mortality risk could allow targeted management that may improve outcome.

Aims & Methods: The purpose of this study was to assess and compare the performance of the Age, Blood tests and Comorbidities (ABC) score⁽³⁾ in predicting 30-day mortality in acute UGIB/LGIB against established scores including the Glasgow Blatchford score (GBS), Oakland, Rockall and AIMS65 scores.

The salient data of 137 patients presenting with GI bleeding at Mater Dei Hospital Malta between July 2018 and July 2020 were recorded. Patients who developed UGIB or LGIB while already inpatients were excluded.

UGIB was defined as presentation with coffee-ground vomiting, melaena or haematemesis. LGIB was defined as presentation with fresh red blood (haematochezia) or clots per rectum, maroon-coloured stool or blood mixed in with stool.

Patient demographics, investigations (blood tests, parameters), comorbidities, medications and management (including endoscopy) were obtained using the Mater Dei Hospital electronic database and the patients' medical notes. The risk scores were then calculated using the data collected.

All cause 30-day mortality, ASA score, transfusion requirements and the need for surgical/endoscopic interventions were used as the primary outcome measures to classify patients as being in high/low risk of mortality. The ABC score's performance in both UGIB/LGIB was compared with existing scores by calculating the area under receiver operating characteristic curve (AUROCs), sensitivities, specificities and outcome among patients classified as low risk and high risk. Statistical analysis was carried out using the pROC R package,⁽⁴⁾ with the AUROCs compared using DeLong's method⁽⁵⁾

Results: After statistical analysis, the ABC score showed a clear AUROC improvement over all the other scores in LGIB, most of which were also statistically significant, with a p-value less than 0.05. It is clear that the LGIB is significantly more discriminative than all other standard scores for the LGIB case.

In the UGIB case, the ABC score AUROC continued to show improvement over all other scores. However, the statistical significance of this higher AUROC is much weaker, which means that the ABC score is at least as capable as other scores in classifying high/low risk UGIB patients, but not necessarily more discriminative.

Conclusion: An accurate diagnosis of location of bleeding cannot always be made on presentation. The discriminative performance of existing scores for prediction of mortality in patients with GI bleeding is relatively poor.

From this study we can conclude that the ABC score is a reliable tool which can be used as a single metric for all GI bleed cases.

It has shown good performance in predicting mortality and stratifying patients into high or low risk of death.

Furthermore, the ABC score shows superior performance to other standard metrics in the majority of LGIB and some of the UGIB cases.

The clinical application of this score should improve patient management as well as produce more accurate prognostic information for both clinician and patient.

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P0982

INFORMED CONSENT FOR GASTROINTESTINAL ENDOSCOPY: RESULTS OF A SURVEY ON CURRENT PRACTICES IN MEMBER SOCIETIES OF THE EUROPEAN SOCIETY OF GASTROINTESTINAL ENDOSCOPY

G. Tziatzios¹, J. Gauci², K. Triantafyllou³, S.M. Everett⁴

¹Attikon University General Hospital, Hepatogastroenterology Unit, Second Department of Internal Medicine – Propaedeutic, Research Institute and Diabetes Center, Medical School, National and Kapodistrian University of Athens, "Attikon" University General Hospital, Athens, Greece, ²Department of Gastroenterology, Leeds Teaching Hospitals NHS Trust, Leeds, United Kingdom, ³Attikon University General Hospital, Hepatogastroenterology Unit, Second Department of Propaedeutic Internal Medicine, Medical School, National and Kapodistrian University of Athens, "Attikon" University General Hospital, Athens, Greece, ⁴Leeds Teaching Hospitals NHS Trust, Dr., Hemel Hempstead, United Kingdom

Contact E-Mail Address: g_tziatzios@yahoo.gr

Introduction: Obtaining valid informed consent prior to endoscopic procedures is considered a fundamental requirement in most countries. We aimed to understand current practice, guidance and regulations in each member nation of the European Society of Gastrointestinal Endoscopy (ESGE) with the intention of informing the need for, and content of a ESGE Position Statement on Consent.

Aims & Methods: A dedicated 12-item, web-based survey assessing practices regarding the process of informed consent prior to gastrointestinal endoscopy was anonymously disseminated to two leading representatives of each member society of the ESGE.

Results: Forty-six (47.4%) representatives from 32/50 (64.0%) societies responded. The process of obtaining informed consent prior to any endoscopic procedure is a prerequisite in all countries, and this is usually recorded in writing (93.8%, n=30).

The legal age above which an individual can provide informed consent varies from 14 years (10.9%) to 18 years (65.6%, n=21). Whilst endoscopists in most countries are routinely required to assess the patient's capacity to provide informed consent (65.6%, n=21), an official legal definition of capacity is in place in only 43.8% (n=14).

In situations where the patient lacks capacity, the appropriate path will be determined by the patient's next of kin or the caring medical team in 43.8% and 21.9% of countries respectively.

National guidance on consent, either from specialist or general medical governing bodies, is not available in more than half (56.3%, n=18) of countries. Relevant case law or legislation is available in only 18.8% of countries (n=6), whilst the remainder were not aware of any such documentation. The development of ESGE guidance on the process of informed consent prior to endoscopy was deemed valuable by most participants (95.7%, n=44). Popular key areas proposed by respondents included the level of information provided to patients about adverse events and risk/benefit ratios, process for consent in emergency situations and assessment of capacity.

Conclusion: Although the process of obtaining informed consent prior to endoscopy is commonplace among ESGE member states, there is a wide variation in practice with national guidance frequently not available. The development of ESGE guidance may allow for standardization of approach but will need to account for variations in national legislature.

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P0983

REASONS FOR CHOICE OF ADVANCED THERAPIES (BIOLOGICS AND JAKIS) FOR THE TREATMENT OF ULCERATIVE COLITIS IN EUROPE

G. O'Neill¹, F. Hennessy¹, S. Barlow¹, J. Kumar², F. Brellier², F. Sheikh², K. Davé²

¹Adelphi Real World, Bollington, United Kingdom, ²Bristol Myers Squibb, Princeton, United States

Contact E-Mail Address: grace.oneill@adelphigroup.com

Introduction: Many factors influence treatment choices in ulcerative colitis (UC). Currently approved advanced treatments (ATs) for moderate-to-severe UC include biologics and small molecules (Janus kinase inhibitors [JAKis] and sphingosine 1-phosphate receptor modulators) and it is important to understand how those therapies are chosen.

Aims & Methods: We assessed reasons for choice of biologics and JAKis using data collected September 2020–March 2021 in France, Germany, Italy, Spain, and the United Kingdom by the Adelphi Disease Specific Programme for UC (1), a point-in-time survey of gastroenterologists (GIs) and patients. GIs provided demographics, clinical characteristics, and treatment history for 7 consecutive UC patients and an additional 2 patients receiving JAKis. Mann-Whitney U test, t-test, and Fisher's exact test were used to compare patients on biologics with those on JAKis.

Results: The study included 253 GIs and 1030 patients on biologics and 503 on JAKis. Patients had a mean age of 40 years (SD 13.33) and mean disease duration of 6 years (SD 5.8); over half were male (biologics, 54%; JAKis, 58%). JAKis were more commonly given as third-line or greater therapy (73%) vs biologics (45%). Patients on JAKis had more severe disease at initiation (biologics, 40%; JAKis, 50%). GIs chose ATs mainly because of efficacy; however, a significantly higher proportion of patients were receiving biologics because of safety and access ($P<0.05$), and JAKis were more often chosen for mode of administration ($P<0.05$).

Only 37% of patients receiving biologics were deemed suitable to receive JAKis but were not switched because GIs either wanted to exhaust other treatment options first, had safety concerns, or there were formulary restrictions (Table).

	Biologic (n=1030)	JAKi (n=503)	P value
Number of treatment lines, mean (SD) ¹	2.5 (1.1)	3.2 (1.3)	<0.0001
Number of AT lines, mean (SD)	1.3 (0.6)	2.2 (1.0)	<0.0001
Severity at initiation of AT, n (%)			
Mild	14 (1.4)	8 (1.6)	0.0009
Moderate	602 (58.5)	246 (48.9)	
Severe	414 (40.2)	249 (49.5)	
Reasons for choice of AT, n (%)			
Efficacy	1017 (98.7)	494 (98.2)	0.4922
Safety/tolerability	537 (52.1)	187 (37.2)	<0.0001
Treatment administration and monitoring	374 (36.3)	347 (69.0)	<0.0001
Access/cost	423 (41.1)	143 (28.4)	<0.0001
Areas of improvement for AT, n (%)			
Efficacy	631 (61.3)	220 (43.7)	<0.0001
Safety/tolerability	340 (33.0)	270 (53.7)	<0.0001
Treatment administration and monitoring	402 (39.0)	47 (9.3)	<0.0001
Access/cost	224 (21.8)	147 (29.2)	0.0015
Suitable candidate for JAKi, n (%)	380 (36.9)	–	–
Suitable candidate for biologic, n (%)	–	165 (32.8)	–
Top 3 reasons for not receiving a JAKi, n (%) (n=380)			
Prefer to exhaust other treatment options	175 (46.1)		
Safety factors ²	94 (24.7)		
Formulary restrictions	86 (22.6)		
Top 3 reasons for not receiving biologic, n (%) (n=165)			
Prefer to exhaust other treatment options		41 (24.9)	
Does not want to go to an infusion center		40 (24.2)	
Patient dislikes injections/ infusions		37 (22.4)	

¹Treatment line includes any combination of 5-ASA, steroids, immunomodulators and AT.

²Safety factors include 'Concerns regarding: infection, malignancy, and blood clots' and 'other safety/side effect concerns.'

Table. GI-reported clinical and treatment characteristics of patients with UC receiving biologics and JAKis

Conclusion: GIs treating patients with UC largely prescribed JAKis as third-line or later treatment and identified a greater need for JAKis with improved safety; biologics with improved efficacy and treatment administration overall were identified as needed. These data point to a need for additional AT options that address efficacy, safety, and administration unmet needs and facilitate treatment choice.

References:

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P0984

CLINICAL AND HEALTH OUTCOMES ASSOCIATED WITH TREATMENT SEQUENCES FOR MODERATE-TO-SEVERE ULCERATIVE COLITIS

M.C. Dubinsky¹, S. Rivolo², M. Suryavanshi³, A. Ambavane², N. Agnihotri², C. Franco-Villalobos², M.T. Osterman³, K. Gupte-Singh³
¹Icahn School of Medicine at Mount Sinai, Department of Pediatrics and Medicine, New York City, United States, ²Evidera, Inc., London, United Kingdom, ³Bristol Myers Squibb, Princeton, United States

Contact E-Mail Address: marla.dubinsky@mssm.edu

Introduction: Clinical guidelines recommend various treatments for moderate-to-severe ulcerative colitis (UC), including anti-TNFs (infliximab, adalimumab) and other advanced therapies (vedolizumab, tofacitinib, ustekinumab). Ozanimod (OZA), a selective oral sphingosine-1-phosphate receptor modulator, was recently approved for UC.

Aims & Methods: Given the availability of multiple treatment classes, the aim of this study was to evaluate the optimal sequencing of available treatments to control UC disease activity and delay the need for treatment switching. A patient-level simulation was developed to predict changes in Mayo score, based on patients' baseline characteristics and treatment received, and consequent clinical outcomes (response, remission, relapse) at the end of the induction and maintenance phases, associated with 3 lines (1st line [1L], 2nd line [2L], 3rd line [3L]) of UC treatment. The modeled sequences evaluated OZA either replacing the current 1L treatments or shifting them to 2L, across multiple 1L treatment baskets (Table). On each line, patients could switch to the subsequent line because of either relapse or adverse events. The average time spent on each line of treatment and the overall life-years (LYs) and quality-adjusted life years (QALYs) were estimated over patient lifetime and discounted at 3% annually.

Multivariate risk equations were developed for OZA outcomes based on the phase 3 TRUENORTH randomized controlled trial. Matching adjusted indirect treatment comparison was conducted for the comparators vs. OZA using published randomized controlled trial data stratified by prior anti-TNF exposure. Due to data gaps, the reduction in comparator efficacy post exposure to non-anti-TNFs was assumed to be 50% of the reduction observed post anti-TNF exposure for all treatments. In scenario analysis, two scenarios with 0% and 25% reduction post non-anti-TNFs exposure for all treatments were evaluated. Further extensive scenario analyses were conducted to test alternative input sources, clinical assumptions, or shorter time horizon.

Results: OZA was associated with higher or similar 1L QALYs (2.00 years [yrs]) and 2L QALYs (1.62-1.79 yrs) compared to all other treatment scenarios in all baskets evaluated (1L: 0.91-2.01, 2L: 0.66-1.73 yrs) (Table). The overall QALYs (16.46-16.67 yrs) and 1L-3L QALYs (4.33-5.76 yrs) were similar for all sequences. Testing alternative scenarios of 25% and 0% reduction in efficacy after non-anti-TNFs exposure favored OZA starting sequences, leading to comparable or higher 1L-3L QALYs in comparison to all other sequences in the study (1L-3L QALYs difference: 0.00-0.69 yrs). The results were robust across all other sensitivity analyses performed.

Conclusion: This study found that positioning OZA as either 1L or 2L therapy was associated with improved time on treatment and QALYs in 1L and 2L compared to most of the advanced treatments baskets considered, primarily driven by OZA efficacy.

Disclosure: Simone Rivolo, Male, Evidera Inc. London, UK; Apoorva Ambavane, Female, Evidera Inc. London, UK; Conrado Franco-Villalobos, Male, Evidera, Inc. London, UK; and Neeharika Agnihotri, Female, Evidera Inc. London, UK are employed by Evidera, a company that received fees from Bristol Myers Squibb, Princeton, NJ, USA.

Marla Dubinsky, Female, Icahn School of Medicine at Mount Sinai, NY, received fees for consulting from Bristol Myers Squibb.

Manasi Suryavanshi, Female, BMS Princeton; Mark Osterman, Male, BMS Princeton; and Komal Gupte-Singh, Female, BMS Princeton are employees and shareholders of Bristol Myers Squibb.

1L* Treatments	2L* Treatments	3L* Treatments	1L QALYs	2L QALYs	Total 1-3L QALYs	Total QALYs
Anti-TNFs ADA 54%, IFX 46%	OZA	TOF (25%) + UST (25%) + VDZ (50%)	1.48	1.72	4.82	16.52
OZA	Anti-TNFs		2.00	1.15	4.77	16.51
Anti-TNFs + VDZ ADA 36%, IFX 31%, VDZ 33%	OZA	TOF (50%) + UST (50%)	1.94	1.64	5.55	16.63
OZA	Anti-TNFs + VDZ ADA 36%, IFX 31%, VDZ 33%		2.00	1.43	5.44	16.61
Anti-TNFs + VDZ + UST ADA 33%, IFX 28%, VDZ 30%, UST 9%	OZA	TOF (50%) + UST (50%)	2.01	1.62	5.62	16.64
OZA	Anti-TNFs + VDZ + UST ADA 33%, IFX 28%, VDZ 30%, UST 9%		2.00	1.47	5.48	16.62
Anti-TNFs + VDZ + UST ADA 33%, IFX 28%, VDZ 30%, UST 9%	OZA	TOF (50%) + UST (50%)	2.01	1.50	5.47	16.62
OZA	Anti-TNFs + VDZ ADA 13%, IFX 29%, VDZ 58%		2.00	1.73	5.76	16.67
ADA	OZA	TOF (25%) + UST (25%) + VDZ (50%)	0.91	1.79	4.37	16.47
OZA	ADA		2.00	0.66	4.33	16.46
ADA	Anti-TNFs + VDZ + UST VDZ 46%, IFX 24%, UST 30%	TOF	0.91	1.55	5.26	16.57
90% ADA + 10% OZA			1.03	1.58	5.38	16.59

Abbreviations: 1L-1stline, 2L-2nd line, 3L-3rd line, ADA-adalimumab, IFX-infliximab, OZA-ozanimod, TOF-tofacitinib, UST-ustekinumab, VDZ-vedolizumab

*Market share for treatment mix are taken from US-based chart audit study

Table.

P0985

IMPACT OF TREATMENT SWITCH ON CLINICAL OUTCOMES IN CROHN'S DISEASE PATIENTS IN THE UNITED STATES AND 5 EUROPEAN COUNTRIES (FRANCE, GERMANY, ITALY, SPAIN, UK)

M. Sanon¹, J. Kershaw², S. Kachroo³, S. Barlow², T. Hoops¹, D. Naessens⁴, C. Willey⁵

¹Janssen Global Services, Horsham, United States, ²Adelphi Real World, Cheshire, United Kingdom, ³Janssen Scientific Affairs, Horsham, United States, ⁴Janssen Pharmaceutica NV, Beerse, Belgium, ⁵College of Pharmacy, University of Rhode Island, Department of Pharmacy Practice, Kingston, United States

Contact E-Mail Address: jim.kershaw@adelphigroup.com

Introduction: Crohn's disease (CD) is a chronic inflammatory bowel condition that requires lifelong management. Cycling through ineffective treatments can have adverse impacts on patients; however, there remains limited data on how treatment switches affect patients with inflammatory bowel disease (IBD).

Aims & Methods: This study aimed to evaluate the impact of treatment switch on clinical symptoms and functional impairment. Data from the Adelphi Real World IBD Disease Specific Programme™, a real-world, point-in-time survey of Gastroenterologists (GEs) and their consulting CD patients in the United States, France, Germany, Italy, Spain and the United Kingdom between 2020 and 2021 were analyzed. GE patient extracted Data includes information on demographics, CD symptoms, and treatment.

Patients in our analysis were diagnosed and treated for CD between ≥ 1 years and < 3 years prior to data collection and split into 2 groups (those that had switched treatment in the past 12 months (switchers), and those that had not switched in the past 12 months or had never switched (non-switchers)).

Treatment switch was defined as the initiation of a new treatment or discontinuation of a treatment. Inverse probability weighted regression adjustment was used to assess the impact of switching on clinical characteristics, adjusting for CD severity, most prevalent symptoms at diagnosis, and time since diagnosis.

Results: Data were from 207 GEs and 483 patients with CD receiving treatment at the point of data collection. Patients were mean age 34.9 years, had a mean BMI of 23.6, mean disease duration of 5.6 years and 55% were female. In total, 119 patients were identified as switchers and 364 were identified as non-switchers. When adjusting for covariates (weighting of covariates resulted in a standardized mean difference of $< 10\%$, indicating a good balance), patients who switched were more likely to have moderate-severe CD ($p < 0.05$), and more likely to be currently experiencing a flare than non-switchers ($p < 0.05$) (Table). Switchers were also more likely to experience key disease symptoms than non-switchers ($p < 0.05$). Switchers were more likely to experience worsened severity of symptoms ($p < 0.05$), as well as worsened outcomes such as increased impairment in the ability to go to work and to conduct normal daily activities ($p < 0.05$), compared with non-switchers (Table).

Conclusion: We found significant associations between treatment switch and worsened clinical symptoms and functional impairment. This highlights the importance and significant unmet need for effective treatment early in the CD treatment journey.

	Switchers (n=119)	Non-switchers (n=364)	p value
<i>Current disease status</i>			
Physician subjective disease severity (0: mild, 1: moderate/severe)	0.42	0.18	< 0.05
Flaring status (0: not flaring, 1: flaring)	0.18	0.04	< 0.05
<i>Current symptoms (0: no symptom, 1: symptom experienced)</i>			
Abdominal pain	0.41	0.28	< 0.05
Non-bloody diarrhea	0.29	0.14	< 0.05
Night-time bowel movement urgency	0.08	0.02	< 0.05
Fatigue	0.34	0.24	< 0.05
<i>Mean symptom Severity (0: none, 5: extremely severe)</i>			
Overall symptom severity	2.03	1.49	< 0.05
Abdominal pain severity	1.82	1.27	< 0.05
Sleep disturbance severity	1.50	0.95	< 0.05
Fatigue severity	1.98	1.38	< 0.05
Impairment in ability to go to work	1.48	1.08	< 0.05
Impairment in ability to conduct normal daily activities	1.56	1.08	< 0.05

Table: Clinical characteristics and outcomes amongst treatment switching versus non-switching patients

Disclosure: Myrlene Sanon, Sumesh Kachroo, Timothy Hoops, and Dominik Naessens are employees of Johnson & Johnson and may hold stock or stock options in the company. Cynthia Willey reports being a consultant for Goldfinch Biotech Inc. and Otsuka Pharmaceutical, and a scientific advisor or member of the Journal of Clinical Therapeutics, Editorial Board. Jim Kershaw and Sophie Barlow are employees of Adelphi Real World, which is contracted as a consultant to Johnson & Johnson. Funding for this work was provided by Johnson & Johnson.

P0986

IMPACT OF SUBOPTIMAL RESPONSE ON CLINICAL AND HUMANISTIC BURDEN IN CROHN'S DISEASE

J. Kershaw¹, M. Sanon², S. Kachroo³, S. Barlow¹, T. Hoops², D. Naessens⁴, C. Willey⁵

¹Adelphi Real World, Cheshire, United Kingdom, ²Janssen Global Services, Horsham, United States, ³Janssen Scientific Affairs, Horsham, United States, ⁴Janssen Pharmaceutica NV, Beerse, Belgium, ⁵College of Pharmacy, University of Rhode Island, Department of Pharmacy Practice, Kingston, United States

Contact E-Mail Address: jim.kershaw@adelphigroup.com

Introduction: Current treatments for Crohn's Disease (CD) are associated with loss of treatment response, however studies assessing the burden of non-response in the real-world are scarce and the clinical and humanistic burden remains unknown.

Aims & Methods: We aimed to describe the burden of active disease on symptom severity, health-related quality of life (HRQoL) and work impairment in patients with CD. A retrospective analysis of physician-reported and patient-reported 2020-2021 data drawn from the Adelphi Real World Inflammatory Bowel Disease Specific Programme™ which is a real-world point-in-time survey of gastroenterologists (GEs) and their consulting patients with CD in the United States, France, Germany, Italy, Spain and the United Kingdom was conducted. Data included patient demographics, clinical status, treatments, and patient completed questionnaires including the EuroQoL 5-dimension 5-Level (EQ-5D-5L) and Work Productivity and Activity Impairment (WPAI). Patients were stratified into 3 groups by remission status: Remitters (RE): 'symptomatic remission, full mucosal healing', Partial Responders (PR): 'symptomatic remission, full mucosal healing not achieved or unknown', and 'full mucosal healing, symptoms remain', and Non-Remitters (NR): 'not in remission'.

Multivariate regression models adjusted for severity, symptoms, and age at diagnosis assessed impact of remission status on clinical and HRQoL outcomes.

	Remitters vs Partial Responders		Remitters vs Non-Remitters	
	Odds ratio	p value	Odds ratio	p value
<i>Symptom Severity (Scale: 0-5, where 0 = none, 5 = extremely severe) (Ordered Logistic Regressions)</i>				
Overall symptom severity (n=1786)	3.46	< 0.05	30.80	< 0.05
Abdominal pain severity (n=1783)	3.15	< 0.05	26.40	< 0.05
Sleep disturbance severity (n=1715)	2.28	< 0.05	10.02	< 0.05
Fatigue severity (n=1786)	2.59	< 0.05	15.90	< 0.05
<i>Treatment Patterns</i>				
Switched CD therapy in past 12 months (n=561) (logistic)	1.71	0.09	2.96	< 0.05
Number of treatment lines (n=1786) (linear)	Coefficient	P value	Coefficient	P value
	-0.01	0.92	0.21	< 0.05
<i>Patient-Reported Outcomes (Linear Regressions)</i>				
EQ-5D-5L	-0.03	< 0.05	-0.12	< 0.05
WPAI: % overall work impairment due to CD (n=326)	7.44	< 0.05	16.13	< 0.05

EQ-5D-5L: standardized instrument for measuring generic health status, completed by the patient at the time of consultation; a max. score of 1 = best health state; WPAI: measures patient's ability to perform regular activities; all measures: 0-100% (total impairment), higher percentage = worse impairment. Available for working patients only.

Table: Impact of suboptimal response on patient outcomes compared with remitters.

Results: 337 GE and 1,786 CD patients receiving treatment for ≥ 3 months were included (mean age 38.9 years, 53% female, mean BMI 24.0, mean disease duration 5.6 years). Patient group sizes were: RE (n=431), PR (n=949), NR (n=406).

Compared with RE the odds of having worsened symptom severity was higher amongst PR and NR, notably 26 to 30 times higher for NR patients for overall symptom severity and abdominal pain severity ($p < 0.05$) (table). NR was associated with receiving more treatment lines than RE, as well as having higher odds of switching CD therapies in the past 12 months ($p < 0.05$). PR and NR groups reported a decrease in HRQoL ($p < 0.05$) (table).

Conclusion: Not achieving or maintaining remission impacted symptom severity, treatment patterns, and patients' quality of life. Notably, non-remitters had up to 30 times higher odds of experiencing worsened symptom severity including fatigue, sleep disturbance, and abdominal pain thus impacting daily living. This highlights the importance and significant unmet need for effective treatment early in the CD treatment journey.

Disclosure: Jim Kershaw and Sophie Barlow are employees of Adelphi Real World, which is contracted as a consultant to Johnson & Johnson. Myrlene Sanon, Sumesh Kachroo, Timothy Hoops, and Dominik Naessens are employees of Johnson & Johnson and may hold stock or stock options in the company. Cynthia Willey reports being a consultant for Goldfinch Biotech Inc. and Otsuka Pharmaceutical, and a scientific advisor or member of the Journal of Clinical Therapeutics, Editorial Board. Funding for this work was provided by Johnson & Johnson.

P0987

IMPACT OF DISEASE FLARES ON RESOURCE USE, HEALTH-RELATED QUALITY OF LIFE AND PRODUCTIVITY IN PATIENTS WITH ULCERATIVE COLITIS IN EUROPE: AN ANALYSIS OF NATIONAL HEALTH AND WELLNESS SURVEY DATA

M. Sanon¹, S. Kachroo², C. Willey³, A. LaPrade⁴, N. Sternbach⁴, T. Hoops¹

¹Janssen Global Services, Horsham, United States, ²Janssen Scientific Affairs, Horsham, United States, ³College of Pharmacy, University of Rhode Island, Department of Pharmacy Practice, Kingston, United States, ⁴Cerner Enviza, Malvern, United States

Contact E-Mail Address: msanon@its.jnj.com

Introduction: Ulcerative colitis is a chronic inflammatory bowel disease that affects the colon and rectum. It requires lifelong treatment and often hospitalization and surgery. An important goal of treatment is managing and easing disease symptoms and increasing the length of clinical remission; however, despite the use of treatments, many treated patients continue to experience debilitating disease flares that can impact their daily life and wellbeing.

Aims & Methods: This study describes the burden of active ulcerative colitis flares on resource use, health-related quality of life (HRQoL), and work productivity in patients receiving ulcerative colitis treatment. The 2020 National Health and Wellness Survey in Germany, Spain, Italy, France, and the United Kingdom, which provides real-world information regarding disease characteristics, diagnosis, treatment, and patient-reported outcomes, was analyzed. Survey participants with diagnosed ulcerative colitis and on ulcerative colitis treatment were categorized by disease flare frequency as infrequent (0-2/year), intermediate (3-6/year), or frequent (> 1 /month to < 7 /week) based on response to the survey question, "How often did you experience disease flares as a result of your Crohn's disease or ulcerative colitis?" HRQoL was measured using the 5-dimension Euro-QoL questionnaire (EQ-5D), and work activity impairment using the Work Productivity and Activity Impairment questionnaire.

Results: A total of 62,319 respondents participated in the survey, of whom, 252 reported being diagnosed with ulcerative colitis and on treatment for ulcerative colitis. The average age of patients with frequent disease flares was lower than those with less frequent flares (infrequent, 53 years; intermediate, 48 years; frequent, 40 years).

Current smoking was most common in the group with the highest disease activity (infrequent, 18%; intermediate, 27%; frequent, 40%). In the past year, 19%, 31%, and 33% of patients with infrequent, intermediate, and frequent flares, respectively, had experienced depression.

The mean EQ-5D summary score decreased with increasing disease activity (infrequent, 0.75; intermediate, 0.73; frequent, 0.63), and mean EQ-5D VAS score was lower in patients with more active disease (infrequent, 65.5; intermediate, 60.0; frequent, 60.0), indicating poorer HRQoL. Absenteeism and presenteeism were highest in the group with frequent flares, and overall work impairment was reported by 32%, 38%, and 67% of respondents with infrequent, intermediate, and frequent flares, respectively. Additionally, within the past six months, a greater percentage of patients with frequent flares had emergency room visits or were hospitalized (50%, 53%) than patients with infrequent (22%, 16%) or intermediate flares (22%, 27%). Within the past 12 months, the proportion of patients for whom $> 25\%$ of flares had been treated with steroids was higher in patients with frequent (53%) or intermediate (51%) flares versus patients with infrequent flares (30%).

Conclusion: This analysis of real-world data demonstrates that patients with ulcerative colitis who were on a prescribed treatment for ulcerative colitis continue to experience disease flares, and those with more frequent flares experienced lower HRQoL, higher healthcare resource use, and lower work productivity. These results highlight the high disease burden in patients with ulcerative colitis and existing unmet needs with current treatment options for the disease.

Disclosure: Myrlene Sanon, Sumesh Kachroo, Timothy Hoops, and Dominik Naessens are employees of Johnson & Johnson and may hold stock or stock options in the company. Cynthia Willey reports being a consultant for Goldfinch Biotech Inc., Janssen Pharmaceutical Companies of Johnson & Johnson, and Otsuka Pharmaceutical, and a scientific advisor or member of the Journal of Clinical Therapeutics, Editorial Board. Anne LaPrade and Nikoleta Sternbach are employees of Cerner Enviza, which is contracted as a consultant to Johnson & Johnson. Funding for this work was provided by Johnson & Johnson.

P0988

IMPACT OF DISEASE FLARES ON RESOURCE USE, HEALTH-RELATED QUALITY OF LIFE AND PRODUCTIVITY IN PATIENTS WITH CROHN'S DISEASE IN EUROPE: AN ANALYSIS OF NATIONAL HEALTH AND WELLNESS SURVEY DATA

M. Sanon¹, S. Kachroo², C. Willey³, A. LaPrade⁴, N. Sternbach⁴, T. Hoops¹

¹Janssen Global Services, Horsham, United States, ²Janssen Scientific Affairs, Horsham, United States, ³College of Pharmacy, University of Rhode Island, Department of Pharmacy Practice, Kingston, United States, ⁴Cerner Enviza, Malvern, United States

Contact E-Mail Address: msanon@its.jnj.com

Introduction: Crohn's disease is a chronic inflammatory condition that affects the gastrointestinal tract. It is characterized by debilitating symptoms such as diarrhea, abdominal pain, rectal bleeding, and fatigue with disease progression leading to bowel damage and disability. Despite receiving treatment, many patients continue to experience disease flares, which can significantly affect patients' emotional wellbeing and capacity to perform daily activities.

Aims & Methods: This study describes the burden of active disease on resource use, health-related quality of life (HRQoL), and work productivity in patients with Crohn's disease receiving treatment. Data from the 2020 National Health and Wellness Survey in Germany, Spain, Italy, France, and the United Kingdom were analyzed. This survey provides real-world information regarding disease characteristics, diagnosis, treatment, and patient-reported outcomes.

Based on responses, survey participants with Crohn's disease and receiving Crohn's disease treatment were categorized by the frequency of Crohn's disease flares (per the survey question, "How often in the past year did you experience disease flares as a result of your Crohn's disease or ulcerative colitis?"): infrequent (0-2/year), intermediate (3-6/year), and frequent (>1/month to <7/week). HRQoL was assessed using the 5-dimension EuroQoL questionnaire (EQ-5D), and work activity impairment using the Work Productivity and Activity Impairment questionnaire.

Results: A total of 62,319 respondents participated in the survey, of whom, 226 reported being diagnosed with Crohn's disease and using a prescription medication to treat their condition. The mean age of patients with frequent flares was lower than those with less active Crohn's disease (infrequent, 48 years; intermediate, 42 years; frequent, 37 years).

Within the past 12 months, 25% and 24% of patients with infrequent or intermediate flares, respectively, had experienced depression, compared with 43% of those with frequent flares. Mean EQ-5D summary score decreased with increasing flare frequency (infrequent, 0.71; intermediate, 0.64; frequent, 0.59), and mean EQ-5D VAS score was lowest in patients with frequent flares (infrequent, 60.2; intermediate, 61.4; frequent, 50.1), indicating poorer HRQoL.

Absenteeism and presenteeism were highest in patients with frequent flares, and overall work impairment was reported by 44%, 51%, and 65% of patients with infrequent, intermediate, and frequent flares, respectively. In the past 6 months, a greater percentage of patients with frequent flares visited an emergency room or had been hospitalized (63%, 53%) than patients with infrequent (26%, 23%) or intermediate flares (41%, 30%).

The proportion of patients for whom >25% of flares had been treated with steroids in the past 12 months was higher in patients with intermediate (54%) or frequent (56%) flares versus patients with infrequent flares (32%).

Conclusion: This analysis of real-world data shows that in Europe, patients receiving treatment for Crohn's disease continued to experience disease flares, and those with frequent flares experienced poorer HRQoL, lower work productivity, and had higher healthcare resource use. The results demonstrated that the disease burden in patients with Crohn's disease is high, despite treatment, and highlights the importance for more effective treatment early in the CD treatment journey.

Disclosure: Myrlene Sanon, Sumesh Kachroo, Timothy Hoops, and Dominik Naessens are employees of Johnson & Johnson and may hold stock or stock options in the company. Cynthia Willey reports being a consultant for Goldfinch Biotech Inc., Janssen Pharmaceutical Companies of Johnson & Johnson, and Otsuka Pharmaceutical, and a scientific advisor or member of the Journal of Clinical Therapeutics, Editorial Board. Anne LaPrade and Nikolett Sternbach are employees of Cerner Enviza, which is contracted as a consultant to Johnson & Johnson. Funding for this work was provided by Johnson & Johnson.

P0989

PRE-ENDOSCOPY ANESTHESIOLOGY CLINIC EVALUATION DOES NOT REDUCE COMPLICATION RATES IN HIGH-RISK PATIENTS FOR SEDATION

T. Thurm^{1,2}, N. Zmora^{1,2}, R. Bruck^{1,2}, N. Bar^{1,2}, A. Philips^{1,2}, O. Shibolet^{1,2}, L. Deutsch (Mlynarsky)^{1,2}

¹Tel Aviv Sourasky Medical Center, Gastroenterology and Hepatology, Tel Aviv, Israel, ²Tel-Aviv University, Sackler School of Medicine, Tel Aviv, Israel

Contact E-Mail Address: nivz@tlvmc.gov.il

Introduction: Preoperative or pre-anesthesia evaluation is an established highly regulated practice in patients undergoing surgery [1-2], which has been shown to reduce complications, reoperations and mortality [3] and increase patient satisfaction [4]. However, the efficacy of employing a similar practice in patients undergoing endoscopic procedures, where the risk of acute severe complications induced by sedation is lower [5], has not been determined to date.

At our center, the pre-procedural evaluation strategy for ambulatory patients undergoing endoscopic evaluation included a gastroenterologist reviewing patients referral letters (an 'open access' approach) and assigning them to an anesthesiologist-supervised procedure in case of severe comorbidities (ASA score of III-b and above, class III (severe) morbid obesity (BMI>40), or Mallampati score of 3 and above), subjecting them to a potential high risk for sedation [6]. Since late 2016 there was a policy change, and all patients deemed as high-risk for sedation have been referred to a pre-endoscopy clinic evaluation carried out by an anesthesiologist.

Aims & Methods: We aimed at comparing endoscopy- and sedation-related complication rates between these two strategies. A retrospective review of an administrative database of all ambulatory upper and lower endoscopies performed at a single tertiary medical center between the years 2016-2017 was performed, as well as a review of the patients' records, including emergency room (ER) admissions, hospitalizations, imaging studies, operations and mortality 14 days following the procedures. Cases performed before policy change (BPC) were compared to cases performed after policy change (APC) with the primary endpoints of endoscopy- and sedation-related complications and death in the peri-procedural period.

Results: During the study period 18,240 ambulatory upper and lower endoscopic procedures were performed in 14,906 patients, 7,447 (49.96%) BPC and 7,459 (50.04%) APC, of which 580 were supervised by an anesthesiologist. The proportions of anesthesiologist-supervised procedures were comparable between the two time periods (BPC 295 vs APC 285, P=0.721), however APC there was a 25-fold increase in pre-endoscopy anesthesiology clinic assessments for high-risk patients for sedation compared to BPC (BPC 6 patients, 2.03% vs APC 146 patients, 51.22%, P<0.001). Nevertheless, no differences in post-procedural ER admissions, incidence of endoscopy- and sedation-related complications, number of imaging studies, hospitalizations, duration of hospitalizations and surgeries were observed between the two periods (p=0.065, p=0.065, p=0.109, p=0.445, p=0.366, p=0.314, respectively). Procedural-related mortality was also comparable between the periods.

Conclusion: Anesthesiology clinic evaluation of patients deemed a high-risk for sedation before endoscopic procedures does not conduce to decreased rates of procedure- and sedation-related complications. A selective, rather than a universal, referral of high-risk patients to a pre-endoscopy evaluation by anesthesiologist could increase the effectiveness of medical care and reduce the financial burden on health economies.

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P0990

ESTIMATING THE ENVIRONMENTAL IMPACT OF ENDOSCOPIC ACTIVITY AT A TERTIARY CENTER: A PILOT STUDY

T. Ribeiro¹, R. Morais¹, C. Monteiro¹, A. Carvalho¹, S. Barros¹, G. Macedo¹

¹Centro Hospitalar Universitário de São João, Gastroenterology, Porto, Portugal

Contact E-Mail Address: tiagofcribeiro@outlook.com

Introduction: Healthcare services are a major generator of waste, with significant environmental impact and potential harm for community health. The growing number of endoscopic procedures, frequently requiring the use of single-use disposable instruments, is responsible for the production of a large amount of waste. To this date, the reality of waste production at large European gastroenterology centers is not known.

Aims & Methods: This study aimed to estimate the amount of waste due to endoscopic practice at tertiary center in Portugal.

We calculated the mass (in Kg) of residues generated in the course of endoscopic practice during a period of 5 working days. We included residues produced at endoscopy suites, pre and postprocedure areas and during endoscope reprocessing. Residues were categorized as non-dangerous (group I - equivalent to urban residues and group II - non-hazardous hospital residues), of biologic risk (group III) and specific hazardous hospital residues (group IV). The production of residues which were separated for recycling/valorization (paper/card and plastic) was also quantified.

Results: During the analyzed period, 241 endoscopic procedures were performed. A total of 443.2 kg of waste (22.6 kg from groups I/II, 266.9 kg from group III e 3.9 kg from group IV) were produced. The endoscopy suite was responsible for 73.1% of the mass of residues, while pre/postprocedure areas and endoscope reprocessing were responsible for 13.0% and 13.9%, respectively. For each endoscopic procedure, 1.8 kg of waste was generated. Individual protection equipment accounted for 32.1 kg (7.3%) of waste. Of the total mass of waste only 17.8% (79 kg) were separated for recycling/valorization.

Conclusion: We performed a pioneer quantitative analysis of the waste production from a large-volume endoscopy service. These analyses are essential to accurately apprehend the reality of each center, which is a pivotal step to implement effective measures to improve resource utilization and more sustainable practices.

Disclosure: Nothing to disclose.

P0991

ASSESSMENT OF RESOURCE USE IN PATIENTS WITH HYPERMOBILE EHLERS DANLOS SYNDROME AND THEIR DIFFERENT FUNCTIONAL GI DISORDERS

S. Pandya¹, R. Topan¹, S. Williams², N. Zarate-Lopez³, Q. Aziz¹, A. Fikree¹

¹Wingate Institute of Neurogastroenterology, London, United Kingdom, ²Barts Health NHS Trust, London, United Kingdom,

³University College London Hospital, Gastrointestinal Physiology Unit, London, United Kingdom

Contact E-Mail Address: ha17323@qmul.ac.uk

Introduction: Hypermobile Ehlers Danlos Syndrome (hEDS), is a non-inflammatory connective tissue disorder characterised by joint hyper flexibility, skin hyperelasticity, and tissue fragility. Functional GI disorders (FGID) are reported in 98%, most commonly functional dyspepsia (FD) and irritable bowel syndrome (IBS) (1). Other comorbidities include chronic pain and fatigue, postural tachycardia syndrome, and anxiety. These patients, therefore, present to a variety of hospital settings. Patients with hEDS have poor quality of life, and high medication and healthcare use compared to the general population (1). Despite the increasing health burden in hEDS, no study has systematically explored healthcare utilisation in these patients or compared this in subgroups.

Aims & Methods: We aimed to evaluate the resource utilisation in hEDS patients diagnosed with FGID and compare this in those with IBS vs FD. We conducted a cross-sectional study from August '21 to January '22. hEDS patients from the charity organisation Ehlers-Danlos Support UK and tertiary Neurogastroenterology clinics completed questionnaires including the ROME IV questionnaire for FGID and the healthcare utilisation questionnaire, specifically developed to assess resource use.

Results: 660 subjects (median age 39 (range; 16-76), 95.8% female, 16.8% clinic) completed the questionnaires, of which 98.6% met the ROME-IV criteria for at least one FGID and 81.8% for at least 2 FGID. 62.9% had FD, 45.5% had IBS, and 32.1% had overlap FD and IBS.

81.7% had seen a healthcare professional in the last 6 months, most commonly GPs (60.9%) and physiotherapists (39.2%). Despite the high prevalence of GI symptoms, only 25.4% had seen a gastroenterologist. 18.6% presented to A&E. 10.4% were admitted to hospital - 31.9% stayed longer than 3 nights (range 1-118 inpatient days) and 30.4% had more than one admission over the last 6 months.

In terms of investigations in the entire cohort over the prior 6 months, imaging was performed in 43.0% - with the incidence of having an X-ray, CT, and MRI being 29.6%, 13.3%, and 20.4% respectively. 11.5% underwent endoscopy.

	IBS Only (N=90)	Functional Dyspepsia Only (N=197)	p value
% With gastroenterology input	17.8	34.0	0.004
% Attending A&E	12.2	23.9	0.02
% Admitted to hospital	2.2	16.2	0.0003
% With hospital stay >3 nights	0.0	6.1	0.2
% Imaging	41.1	39.1	0.7
% Endoscopic procedures	7.8	17.3	0.03
% On neuromodulators	46.7	52.3	0.4
% On opiates	46.7	40.1	0.3

Table 1: Comparison of healthcare use in IBS vs FD over the last 6 months.

The most common classes of prescribed medication were analgesics - simple analgesia (64.5%), neuromodulators (47.27%), and opiates (39.70%). PPI (52.1%), H1 antagonist (43.4%), and laxative use (37.4%) were also

notable. A high proportion paid for additional therapies e.g., 60.1% paid for their vitamin supplements, 31.4% paid for probiotics and 24.5% paid for acupuncture.

Compared to hEDS patients with IBS, those with FD were more likely to have gastroenterology input, attend A&E, be admitted, and have endoscopies. There was no difference in medication use (e.g., opiates) in the 2 groups (Table 1).

Conclusion: This large study of over 600 hEDS patients confirms high health resource utilisation in this cohort. Almost all patients had a FGID, with FD and IBS being the most common. Patients with FD had higher healthcare utilisation than those with IBS. These findings will have an impact on how services should be commissioned for this very co-morbid group of patients.

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P0992

APPLICATION OF MACHINE LEARNING ALGORITHM BASED ON MULTI-FEATURE FITTING IN THE DIAGNOSIS OF WHITISH NEOPLASTIC GASTRIC LESIONS UNDER WHITE LIGHT GASTROSCOPY

X. Zeng¹, Z. Dong¹, D. Gong¹, L. Yang², P. Jin², H. Yu¹

¹Renmin Hospital of Wuhan University, Department of Gastroenterology, Wuhan, China, ²PLA Army General Hospital, Department of Gastroenterology, Beijing, China

Contact E-Mail Address: 1018725972@qq.com

Introduction: Esophagogastroduodenoscopy (EGD) is the pivotal procedure in the diagnosis of upper gastrointestinal lesions, which helps to find gastric lesions, locate and qualitatively judge them, and further guide the formulation of treatment plans. Gastric cancer is one of the most lethal malignancies in the world and has become one of the most important causes of cancer death worldwide. Asymptomatic patients can detect early gastric cancer with aggressive gastroscopy screening.

Early detection of gastric cancer can provide opportunities for minimally invasive endoscopic treatment, such as endoscopic submucosal dissection (ESD). However, some gastric cancers appear as pale, depigmented lesions on endoscopy, such as signet ring cell carcinoma, and the typical appearance on routine endoscopy is pale, flat lesions that are easily overlooked even by experienced endoscopists.

Therefore, accurate diagnose of whitish gastric neoplastic lesions is crucial to improve prognosis, improve patient quality of life, and reduce patient disease burden. In recent years, great progress has been made in the application of artificial intelligence technology in the field of digestive endoscopy.

This abstract aims to develop machine-learning based multi-feature fitting algorithm to diagnose whitish neoplastic gastric lesions under white light endoscopy and enhance interpretability. Compare the diagnostic performance of the multi-feature fitting algorithm with the sole deep learning algorithm.

Aims & Methods: To develop machine-learning based multi-feature fitting algorithm to diagnose whitish neoplastic gastric lesions under white light endoscopy and enhance interpretability. Compare the diagnostic performance of the algorithms with the sole deep learning algorithm.

Retrospectively collected 210 non-neoplastic images from Renmin Hospital of Wuhan University, the Seventh Medical Center of PLA General Hospital, and Nanjing Drum Tower Hospital from November 2012 to December

2020, of which 170 were used as training set, the remaining 40 images were used as test set; 207 neoplastic images were collected, of which 165 pictures are used as training set, and the remaining 42 images are used as test set. The general shape of the lesion, whether the boundary is clear or not, whether the surface shape is regular, the background mucosa, and the location of the lesion are selected as key features.

The key features of each image was labeled by expert endoscopists. Multiple machine learning models were applied for training and testing. Use deep learning framework to train binary classification model to distinguish whether the lesion was neoplastic or not.

Results: In the test set, the accuracy, sensitivity and specificity of the sole deep learning algorithm were 81.96%, 71.43% and 92.5%, respectively. The accuracy, sensitivity, and specificity of KNN(K-Nearest Neighbor algorithm) were 86.9%, 90.7% and 82.93%, respectively; the accuracy, sensitivity and specificity of SVM(support vector machine) algorithm were 84.52-85.71%, 88.37-90.70% and 78.05-82.93% respectively.

Conclusion: Multi-feature fitting machine learning performed better than the sole deep learning algorithm for diagnosing whitish neoplastic gastric lesions under white light endoscopy.

Disclosure: Nothing to disclose.

P0993

DIAGNOSTIC ACCURACY OF 3D-BASED AI TECHNOLOGY TO IDENTIFY THE STATUS OF THE PREDICTED RESECTION IN MARGINS IN PATIENTS WITH LOCALLY ADVANCED AND RECURRENT RECTAL CANCER

G. Pellino^{1,2}, S. Jerí Mc Farlane³, A. Garcia-Granero³, J. Sancho Muriel⁴, V. Primo Romaguera⁴, B. Flor Lorente⁴, M. Gamundi Cuesta³, F.X. Gonzalez Argente³

¹Università degli Studi della Campania Luigi Vanvitelli, General and Colorectal Surgery, Aversa (CE), Italy, ²Vall d'Hebron University Hospital, Colorectal Surgery, Barcelona, Spain,

³Hospital Universitario Son Espases, Palma de Mallorca, Spain,

⁴Hospital Universitario y Politécnico La Fe, Valencia, Spain

Contact E-Mail Address: gipe1984@gmail.com

Introduction: R0 or tumour-free surgical margins resection represents the strongest prognosticator of survival in locally advanced primary (LAPRC) and locally recurrent rectal cancer (LRRC). Magnetic resonance imaging (MRI) is the technique of choice to assess the infiltration of surrounding structures, currently representing the ideal tool for preoperative planning. In LAPRC, MRI negative predictive value of infiltration is reported to be 94%, however, a 54% positive predictive value has been estimated. In addition, diagnostic accuracy of MRI might not exceed 60% in LRRC.

Aims & Methods: The aim of this study was to assess the usefulness of a three-dimensional image processing and reconstruction (3D-IPR) model to achieve R0 resections and to compare the diagnostic accuracy between MRI and 3D-IPR regarding the infiltration of surrounding structures in LAPRC and LRRC.

This is a prospective study performed at two referral centres for rectal cancer between January 2020 and January 2022. 3D-IPR was applied to MRI of patients with LAPRC or LRRC, before surgery. The MRI findings were compared with those of 3D-IPR, focusing on predicted surgical margins. The standard of reference was definitive pathology of the specimen.

Results: Twelve patients were evaluated (7 LAPRC and 5 LRRC). A complete agreement between MRI and 3D-IPR was observed in 16% of cases. One patient received anterior resection of the rectum, 4 en bloc rectal resection extended to surrounding structures, and 7 pelvic exenteration; 75% of specimens were classified as R0. The diagnostic accuracy was 33% for MRI and 91% for 3D-IPR.

Conclusion: The 3D-IPR method can be useful to improve diagnostic accuracy of MRI scans in assessing the relationship with surrounding structures in patients with LAPRC and LRRC.

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P0994

IT TAKES A VILLAGE: ENGINEERING AND BEHAVIORAL RESEARCH TOWARD THE DEVELOPMENT OF A DIGITAL OUTCOME MEASURE FOR CONSTIPATION MANAGEMENT THAT PATIENTS AND DOCTORS WANT TO USE

V.V. Lee^{1,2}, A.T.L. Truong^{1,2,3}, W. Thone¹, X.Z. Low¹, N. Le^{1,3}, S. Vijayakumar^{1,2}, N.Y. Lau¹, C.E. Chua⁴, K.T.H. Siah^{4,5}, M. Motani^{1,2,6,7}, D. Ho^{1,2,3,8,9}, A. Blasiak^{1,2,3,8}

¹N.1 Institute for Health, National University of Singapore, Singapore, Singapore, ²Institute for Digital Medicine (WisDM), Yong Loo Lin School of Medicine, National University of Singapore, Singapore, Singapore, ³National University of Singapore, Department of Biomedical Engineering, Singapore, Singapore, ⁴Yong Loo Lin School of Medicine, National University of Singapore, Department of Medicine, Singapore, Singapore, ⁵National University Hospital, Division of Gastroenterology and Hepatology, Department of Medicine, Singapore, Singapore, ⁶National University of Singapore, Department of Electrical and Computer Engineering, Singapore, Singapore, ⁷Institute of Data Science, National University of Singapore, Singapore, Singapore, ⁸Yong Loo Lin School of Medicine, National University of Singapore, Department of Pharmacology, Singapore, Singapore, ⁹Bio-Echo Asia Centre for Reproductive Longevity and Equality, Yong Loo Lin School of Medicine, National University of Singapore, Singapore, Singapore

Contact E-Mail Address: vvien.lee@nus.edu.sg

Introduction: Digital health solutions have been taking healthcare by storm, with a plethora of activity tracking tools emerging for self-monitoring and behavior adjustments toward health goals. While digital medicine has undergone an unprecedented boost during the COVID-19 pandemic, it is imperative that medical innovation in the digital health space is developed with a thorough understanding of the deployment context and

through a co-creation process with all the stakeholders to ensure a sustainable result for patient outcomes and healthcare system integration.¹ With this principle, the current study placed importance on integrating clinical relevance and understanding of patients through concurrent streams of technical and behavioral research when developing a new digital health tool.

Aims & Methods: We aimed to develop an artificial intelligence (AI)-based stool type classifier and bowel movement counter for constipation management tailored to Asian patients. In the *technical* stream, an image classifier that analyses stool consistency was developed using classical machine learning and deep neural network models on a clinician-annotated image dataset. The models were trained using 1541 images of potato-based stool models and 1322 web-scraped images of real stools, classified into Bristol Stool Form Scale (BSFS). The performance of the models were validated using 330 real stool images.

In the *behavioral* stream, 15 participants with chronic constipation (age range = 28-79 years, 10 females) were interviewed to further understand patients' attitudes and perception towards constipation-related digital health solutions. Additionally, we surveyed 153 Singapore doctors on their understanding of constipation and its treatment.

Results: In gold standard classification, the clinical team showed satisfactory agreements. The image classifier achieved 74.2% overall accuracy in classifying real stool images into three clinically relevant groups for the management of constipation – constipation (BSFS 1, 2), normal (BSFS 3, 4, 5), loose (BSFS 6, 7). When asked about stool classification and bowel movement frequency, participants expressed uncertainty about what is normal. The idea of using an AI-based stool classifier was perceived as potentially useful for personal tracking and relaying accurate information to their healthcare providers, however three participants voiced disinterest in taking pictures of their own stools.

Participants stated the importance of knowing when their stool is abnormal and receiving feedback from the digital tool regarding informative next steps and preventative warnings, which indicate the need for the image classifier to prioritize recall when balancing with precision.

The doctors' survey revealed knowledge deficit in constipation diagnosis and treatment, with 22.2% of doctors unable to describe the accurate stool scale and type for constipation. 83.0% of the doctors agreed that digital technology can potentially help close that gap.

Conclusion: Our AI-based stool image classifier and bowel movement counter is a promising digital health tool for supporting constipation monitoring.

Overall, both patient and doctor groups were receptive to digital health tools for constipation management, and provided clinical and behavioural insights to drive further development efforts and guide optimal digital tool design and implementation.

Future work can focus on patient segmentation, e.g. identification of patients with psychosomatic personas that will benefit the most from such solutions, and meaningful integration of the digital health solution into doctors' daily practice.²

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Disclosure: AB and DH are co-inventors or previously filed pending patents on artificial intelligence-based therapy development. DH is a shareholder of KYAN Therapeutics, which has licensed intellectual property pertaining to AI-based drug development.

P0995

CLINICAL VALIDATION OF DEEP LEARNING-BASED BOWEL PREPARATION ASSESSMENT SYSTEM: A SINGLE CENTER, PROSPECTIVE, TANDEM STUDY

L. Yao¹, H. Chen², H. Xiong², Q. Li², H. Yu³

¹Renmin Hospital of Wuhan University, Wuhan, China, ²The Eighth Affiliated Hospital, Sun Yat-Sen University, Shenzhen, China,

³Renmin Hospital of Wuhan University, Gastroenterology, Wuhan, China

Contact E-Mail Address: 292779656@qq.com

Introduction: Inadequate bowel preparation can have multiple negative impact on colonoscopy, including incomplete visualization of colorectal mucosa, higher miss rate of lesions (22–48%), more procedural difficulties, prolonged operation time, reduced interval time, and increased cost of colonoscopy. Patients with unqualified bowel preparation should receive early repeated colonoscopy to avoid the interval colorectal cancer. Manual bowel preparation assessment in clinical practice is easily affected by subjectivity and clinical experience. Therefore, we have developed a deep learning based bowel preparation assessment system. Such system has shown a strong correlation with the adenoma detection rate (ADR). However, the performance of the system in predicting missed adenomas due to poor bowel preparation remains to be explored.

Aims & Methods: This is a prospective, single center, tandem study. Patients who underwent screening colonoscopy in the Eighth Affiliated Hospital of Sun Yat-sen University from October 7, 2021 to March 4, 2022 were prospectively enrolled. The endoscopists and the system evaluated the bowel preparation independently during the colonoscopy withdrawal and the assessment results were blinded to each other. If the bowel preparation was judged as qualified by both of endoscopists and the system, the patient will receive a second colonoscopy immediately; if the bowel preparation was judged as unqualified by either of them, the patient will undergo colonoscopy again after re-cleaning the bowel. All polyps were biopsied with forceps once they were detected.

Results: As of March 4, 2020, a total of 105 patients were included, with an average age of 54.8 years. The overall polyp detection rate was 91.4% (96/105), and the adenoma detection rate was 55.2% (58/105). Among them, 37.1% (39/105) of patients was considered unqualified bowel preparation by doctors, and 42.9% (45/105) of patients was considered unqualified bowel preparation by artificial intelligence, with a consistent Kappa value of 0.518.

According to the endoscopists judgement, the adenoma missed rate (AMR) was 28.8% (19/66) in patients with qualified bowel preparation, and 43.6% (17/39) in patients who were unqualified. According to the deep learning system, the AMR in patients with qualified bowel preparation was 25% (15/60), and the AMR in patients who were unqualified was 46.7% (21/45). According to the endoscopists judgement, the missed detection rate of ≥ 5 mm adenomas in patients with qualified bowel preparation was 6.1% (4/66), and the missed detection rate of ≥ 5 mm adenomas in unqualified patients was 7.7% (3/39).

According to deep learning system, the missed detection rate of ≥ 5 mm adenomas in patients with qualified bowel preparation was 3.3% (2/60), and the missed detection rate of ≥ 5 mm adenomas in unqualified patients was 11.1% (5/45).

Conclusion: There is a significant difference in the AMR between qualified and unqualified patients with bowel preparation assessed by the deep learning system, and the performance is non-inferior to that of endoscopists. The system is expected to replace the existing manual assessment methods and provide automatic, accurate and objective bowel preparation assessment for the clinic.

Disclosure: Nothing to disclose.

P0996

PSYCHOLOGICAL INTERVENTIONS IMPROVE QUALITY OF LIFE IN PATIENTS WITH CANCER – A SYSTEMATIC REVIEW AND META-ANALYSIS OF RANDOMIZED CONTROLLED TRIALS

A.S. Bognár¹, S. Bunduc¹, B. Fogarasi¹, N. Vörhendi¹, D.S. Veres², K. Márta¹, P. Hegyi¹

¹Centre for Translational Medicine, Semmelweis University, Budapest, Hungary, ²Semmelweis University, Department of Biophysics and Radiation Biology, Budapest, Hungary

Contact E-Mail Address: bognar.sara@gmail.com

Introduction: Cancer is a leading cause of death worldwide carrying not only physical but emotional burden to the patients. Psychological symptoms are common among cancer patients and they can modulate the disease course and treatment adherence. During the treatment period patients' quality of life (QoL) may deteriorate.

Aims & Methods: This systematic review and meta-analyses investigated the effect of psychological interventions on the QoL and survival in cancer patients.

The systematic search was performed on PubMed, Cochrane and Embase from inception until 11 November 2021, without any restrictions. Eligible studies were RCTs investigating differences in QoL and survival in all type cancer patients undergoing psychological interventions besides standard of care (SOC) versus (vs.) SOC alone (experimental vs. control group).

The standardized mean differences (SMD) with 95% confidence intervals (95%CI) were calculated in the meta-analysis by the random effects model. I^2 -values and chi-squared tests indicated the statistical heterogeneity. The study protocol is registered on PROSPERO (CRD42021282327).

Results: Out of 10612 articles, we included 271 RCTs in the meta-analysis. Disease type and stage, intervention type and time of outcome assessment varied across the studies. We compared the differences in QoL measured at 12 weeks after the psychological intervention in the experimental vs. control group.

Our analysis showed a significant improvement in physical QoL in patients receiving group-based psychological interventions [SMD=0.29; CI=0.04 to 0.54; I^2 =95% (91%; 98%)]. A tendency was also observed in global QoL in the experimental group [SMD=0.37; CI=-1.75 to 2.49; I^2 =0% (0%; 90%)]. Individual psychological interventions as well increased the global QoL [SMD=0.35; CI=-0.07-0.78; I^2 =86% (78%; 91%)], physical QoL [SMD=0.33; CI=-0.03 to 0.69, I^2 =84% (73%; 91%)] and social functioning [SMD=0.22; CI=0.00 to 0.43; I^2 =63% (23%; 82%)] in the experimental group, respectively and significantly.

Conclusion: Our results revealed a medium to large effect of psychological interventions on both global and specific dimensions of QoL in all type cancer patients. Adding psychological interventions in SOC of cancer patients is justified. Further analysis of the interventions provider, environment, disease type and stage and other timepoints for outcome measurement, will substantiate more specific recommendations.

Disclosure: Nothing to disclose.

P0997

THE STATUS OF CLINICAL NUTRITION EDUCATION IN IRELAND: INTEGRATING CLINICAL NUTRITION EDUCATION INTO UNDERGRADUATE TRAINING. AN INITIATIVE OF THE IRISH SOCIETY OF CLINICAL NUTRITION AND METABOLISM

N. McGettigan¹, K. Allen¹, C. Dunne², K. Boland¹

¹Beaumont Hospital, Gastroenterology, Dublin, Ireland, ²St James Hospital, Gastroenterology, Dublin, Ireland

Contact E-Mail Address: neasamcgettigan@hotmail.com

Introduction: One-third of patients in Irish hospitals are at moderate-to-high risk of disease-related malnutrition with a recognised economic burden due to obesity and malnutrition. The Irish Society for Clinical Nutrition and Metabolism (IrSPEN) aim to increase integration of nutrition education into the postgraduate/undergraduate curricula in line with educational goals of ESPEN.

Aims & Methods: To survey practicing physicians on attitudes to clinical nutrition in the under- and postgraduate curriculum and unmet needs in clinical nutrition.

An anonymous online survey was distributed nationally among Irish doctors. A total 35 questions probing respondent demographics and facts to the ESPEN consensus on Nutrition Education in Medical Schools. Descriptive statistics and χ^2 testing was completed using Graphpad. $P < 0.05$ denoted statistical significance.

Results: Of 168 responses received, 41% ($n=58$) were male. Most worked in academic hospitals (93.4%, Table 1).

Demographic	N=168 (%)
Male	58 (34.7%)
Age:20-30 years	86 (51.5%)
31-40 years	59 (35.3%)
41-50 years	12 (7.2%)
>50 years	10 (6%)
Work Setting:Full time academic centre	146 (87.4%)
Part time academic centre	10 (6%)
Community Practice	11 (6.6%)
Grade:Intern	8 (4.8%)
Senior House Officer	42 (25%)
Registrar	81 (48.5%)
Consultant/Attending	36 (21.6%)
Speciality: Gastroenterology	43 (25.75%)
Surgery	12 (7%)
Respiratory	12 (7%)
Paediatrics	37 (22%)
Medicine for the Elderly	11 (6.6%)
Oncology	9 (5.4%)
General Practice	9 (5.6%)
Endocrinology	5 (3%)
Anaesthetics/Critical Care	4 (6.7%)
Cardiology	3 (1.8%)
Other	16 (12%)

Table 1. Respondents Demographics.

Fifty-eight (34.7%) were regularly involved in nutrition support but 24% ($n=40$) rarely/never. Despite 20% ($n=33$) of respondents regularly managing patients on parenteral nutrition (PN) and a fifth ($n=34$) regularly managing complications of obesity, confidence in assessment for artificial nutrition was low; 15.7% ($n=26$) for enteral nutrition and 8% ($n=13$) for PN. One-third ($n=54$) did not believe they had sufficient knowledge to manage complications of malnutrition feeding including refeeding syndrome, line sepsis or thrombosis. Trainees were less confident than attending staff in assessment of need for/management of artificial enteral feeding ($p=0.022$) and complications of PN ($p=0.01$). Over 70% of respondents reported they received <2 hours clinical nutrition education.

Furthermore, only 32% ($n=52$) received any formal training (lectures, tutorials, course modules) within postgraduate training (PGT), and these were more likely to be GI trainees ($p=0.01$). Ninety-two percent reported more focus/provision of education was required. A striking 99% felt additional focus on nutrition education in PGT was needed to educate patients and manage complications of malnutrition/obesity.

Conclusion: This survey elicits physician attitudes relating to nutrition education in the undergraduate and postgraduate curricula in Ireland. Practicing physicians identify the need to increase clinical nutrition education within the undergraduate and postgraduate curricula. Improved education and nutrition support teams have been shown to improve patient care, reduce complications and are cost effective in managing complications of malnutrition/artificial nutrition. IrSPEN are actively engaging with Irish medical schools and training bodies to address these deficits with multidisciplinary engagement from expert physicians and allied dietetic colleagues.

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P0998

COMPARATIVE ANALYSIS OF NUTRITIONAL BEHAVIOUR OF THE UKRAINIAN AND FOREIGN STUDENTS OF DANYLO HALYTSKY LVIV NATIONAL MEDICAL UNIVERSITY

C. Nasadyuk¹

¹Danylo Halytsky Lviv National Medical University, Biochemistry, Lviv, Ukraine

Contact E-Mail Address: nasadyukch@gmail.com

Introduction: Heart attack is the main cause of death globally, however over 70% of cardiovascular diseases is caused by modifiable risk factors, in particular tobacco, alcohol, diet, physical activity and sodium intake [1].

Aims & Methods: Aim of research was to evaluate nutritional habits of medical students from different countries. A modified Mediterranean Quality Diet Index Survey [2] (27 questions) was taken anonymously by 161 foreign students (FS) from India, Egypt, Zambia, Ecuador, Ghana, Greece, Lebanon, Morocco, Poland and 54 Ukrainian students (US), aged 18-25, on a voluntary basis. Number of answers for every question was expressed in %. Sampling error without design effect at 95% confidence did not exceed 7.72% for values close to 50%.

Results: The analysis of the survey showed that sunflower oil was the major fat used both by US and FS (72% of FS vs 55.6% of US), 17.4% of FS used olive oil vs 31.5% of US). Only US reported to consume pig fat (3.7%). 81.4% of FS consume meat vs 100% of US. Only 9.9% of FS consume fish 2-3 times per week vs 37% of US. 32.9% of FS eat fresh fruit every day vs 27.8% of US. 56.5% of FS eat vegetables every day vs 37% of US. 6.2% of FS eat fast food every day vs 1.9% of US; 9.9% of FS never eat fast food vs 13% of US; 72.7% of FS are having fast food several times per month vs 70.4% of US. 46.6% of FS consume nuts 2-3 times per week vs 31.5% of US. Only 31.7% of FS have breakfast regularly vs 57.4% of US; 61.5% of FS have breakfast sometimes vs 38.9% of US and 6.8% of FS never have breakfast

vs 3.7% of US. 9.3% of FS have sweets several times per day vs 35.2% of US. Only 28.6% of FS always read the nutritional value of food they buy vs 18.5% of US. 81.4% of FS never smoke vs 64.8% of US; 52.8% of FS never consume alcohol vs 14.8% of US. For 59.6% of FS the main daily drink is still water vs 75.9% of US. More than 90% of FS and US cook for themselves and about 70% answered that they liked to cook. 95% of FS are interested in healthy diet vs 70.4% of US.

Conclusion: The survey revealed some disturbing facts about eating habits of medical students (sweets abuse, low consumption of fish, nuts, fruits and vegetables). Questioned FS appeared to smoke less, rarer consume alcohol, eat more fruits and vegetables, however US more frequently consume olive oil, fish and prefer still water as a main daily drink but eat more sweets. During the professional training of medical students more attention should be paid to the issues of healthy eating.

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P0999 WITHDRAWN

P1000

THE RELATIONSHIP BETWEEN DIET, THE GUT MICROBIOME AND HEALTH OUTCOMES: PERCEPTIONS OF CONSUMERS AND NUTRITION PROFESSIONALS

G. Williams¹, L. Tapsell¹, E. Beck¹

¹University of Wollongong, Nutrition and Dietetics, Wollongong, Australia

Contact E-Mail Address: georgina.williams@newcastle.edu.au

Introduction: The influence of diet on the gut microbiome and subsequent health effects is increasingly of interest across popular media and scientific literature yet an exact definition for 'gut health' remains elusive. Evidence-based dietary guidelines to improve overall health via gut-mediated mechanisms are also not available, largely due to the multifactorial and individualised nature of the microbiome, and heterogenous study designs.

Engaging consumers and nutrition professionals to explore what is required for practice change in this field, could direct future study design to improve translatability.

Aims & Methods: The aim of this qualitative study was to explore the perspectives of both consumers and nutrition professionals towards gut health. We aimed to complement the predominantly quantitative data in this field to improve evidence translation towards better clinical practice, and subsequently improved health outcomes.

We conducted online focus groups (adults; no formal medical or nutrition training) and interviews (adults; with formal dietetics qualifications), questioning the understanding of 'gut health' and its influences, associated health outcomes and perceptions of evidence-based recommendations in this field. Discussions were transcribed verbatim and inductive thematic analysis was completed in duplicate.

Results: Fourteen focus groups (n=38, 15 males, 23 females) and 14 interviews (2 males, 12 females) were conducted. Consumers considered 'gut health' important for 'overall wellbeing' despite the role of the microbi-

ome being poorly understood. Consumers were more likely to report fermented foods or probiotic supplements as beneficial to 'gut health' before food groups recommended by national dietary guidelines. A barrier to dietary changes to promote gut health was the lack of transparent and practical guidelines as well as the perception that dietary change was required only for curative, rather than preventative, health measures.

Nutrition professionals reported an understanding of the significance of diet in influencing both gastrointestinal function and the microbiome. A balanced whole food-based diet, as recommended by current dietary guidelines, was generally considered ideal for gut optimisation. Despite this, dietitians reported higher levels of confidence in managing specific, diagnosed gastrointestinal conditions and symptoms rather than 'gut microbiome' related health outcomes. Reasons for this included uncertainty around current literature and a lack of evidence-based guidelines or tangible outcome measures in this area of dietetics practice and the multifaceted and highly individualised nature of 'gut health'.

Participating nutrition professionals mentioned the importance of multidisciplinary and personalised management of 'gut health', which included assessment and management of environmental, social and psychological influences.

Conclusion: While current research does not infer that dietary choices for 'gut health' differ to general dietary guidelines, opportunistic framing of these recommendations as good for 'gut health' may motivate improved adherence at a population level given the current interest in this term.

Food-based research that involves nutrition professionals, is needed to inform nutrition education for consumers on the potential role of the gut microbiome in preventative health care. Practical food-based recommendations can be used to support gut-related behavioural change as well as assist nutrition professionals to promote dietary choices consistent with current dietary guidelines.

Disclosure: Nothing to disclose.

P1001

PHENOMENON OF AN INCREASE OF THE BLOOD-BRAIN BARRIER PERMEABILITY IN RATS WITH STRESS-INDUCED METASTATIC COLON ADENOCARCINOMA

I. Agranovich¹, A. Khorovodov¹, A. Terskov¹, N. Navolokin^{2,1}, A. Shirokov^{1,3}, I. Fedosov¹, O. Semyachkina-Glushkovskaya¹

¹Saratov State University, Saratov, Russian Federation,

²Saratov State Medical University, Saratov, Russian Federation,

³Institute of Biochemistry and Physiology of Plants and Microorganisms, Russian Academy of Sciences, Saratov, Russian Federation

Contact E-Mail Address: ilana.agranovich@yandex.ru

Introduction: There is evidence that an increase in the permeability of the intestinal mucosa (IM) affect the permeability of blood-brain barrier (BBB) [1]. In our previous study, we discovered significant IM leakage in rats with stress-induced metastatic colon adenocarcinoma (SICA) associated with (1) a high expression of inducible nitric oxide (NO) synthase and beta2-adrenoreceptors; (2) a high production of NO and beta-arrestin 1 playing a crucial role in the regulation of IM permeability [2; 3].

Aims & Methods: Here, we aimed to answer the question, whether is interaction between the IM leaky and the BBB permeability in rats with SICA.

To answer to this question, we performed in rats SICA and in healthy rats:

1. The simultaneous study of the permeability of the mesenteric blood vessels (MeBVs) to FITC-Dextran 70 kDa and the mesenteric lymphatic vessels (MeLVs) to Evans blue (Eb) using *in vivo* multiphoton imaging with the further *ex vivo* confocal imaging of permeability of MeLVs and MeBVs using the specific markers of blood and lymphatic endothelium;

2. The analysis of the permeability of the blood brain barrier (BBB) to FITC-dextran (FITCD) 70 kDa using ex vivo multiphoton visualization and the quantitative analysis Eb in the brain tissues using spectrofluorimetric assay;
3. The study of the expression of tight junction (TJ) proteins, such as the Zonula 1 (ZO1), the Clandin-5 (CLDN), in the Junction Adhesion Molecule (JAM) in MeBVs/MeLVs and in the brain of healthy rats and rats with SICA using confocal assay.

N=10 in each group of all series of experiments.

To induce SICA, the rats underwent to a long term combination (during 9 months) of social stress (overpopulation) and daily diet including of toluidine (2 g/kg) in food and water with nitrites (2 g/l). The analysis of SICA presence was performed using in vivo photodynamic diagnosis with 5-aminolevulinic acid (20 mg/kg, per os) and ex vivo using histological method.

Results: Our results revealed that 83% of rats (25 of 30) demonstrated the SICA development with metastasis spreading in 64% of rats (16 of 25) in the liver (11 of 25) and in the lungs (5 of 25).

In all rats with SICA was observed the high permeability of MeLVs to Eb and MeBVs to FITC-Dextran that was accompanied by a decrease in the expression of CLND, ZO1 and JAM. There were not the leakage of tested tracers and the changes in the expression of TJs in MeLVs and MeBVs in healthy rats.

Interesting notice that only rats with SICA and metastatic spreading showed the high BBB permeability to FITCD and to Eb in the 13 areas of the brain vs. healthy rats, including the cortex, hippocampus, thalamus, cerebellum, pons and medulla. The high BBB leakage in rats with SICA was accompanied by decrease of the expression of CLND, ZO1 and JAM in the brain vs. healthy rats.

Conclusion: Our data clearly demonstrate the high permeability of MeBVs and MeLVs associated with the decreased expression of TJs in all rats with SICA. However, the leakage of BBB with the TJ integrity injuries were observed only in rats with SICA and metastasis spreading. Thus, there is a direct link between the high permeability of BBB and the spread of metastases in animals with SICA, associated with a decrease in the expression of TJ and an increase in vascular leakage throughout the body.

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Disclosure: Nothing to disclose.

P1002

COMPREHENSIVE LIFESTYLE-MODIFICATION IN PATIENTS WITH CROHN'S DISEASE - A RANDOMIZED CONTROLLED TRIAL

J. Langhorst^{1,2}, Ö. Öznur^{2,1}, C. Uecker^{2,1}, C. Schlee^{2,3}, R. Reissmann², N.S. Bauer^{2,1}

¹University Duisburg-Essen, Department of Integrative Medicine – Translational Gastroenterology, Bamberg, Germany, ²Klinikum am Bruderwald - Sozialstiftung Bamberg, Department of Internal and Integrative Medicine, Bamberg, Germany, ³University of Bamberg, Department of Sociology, Bamberg, Germany

Contact E-Mail Address: jost.langhorst@gmx.de

Introduction: Patients with Crohn's Disease suffer from impaired health-related quality of life (HrQOL). Environmental and lifestyle factors are well excepted factors modifying the course of disease in CD. There is a need for structured programs which address non-pharmacological treatment options in CD.

Aims & Methods: The aim of this study was to investigate the effect of a comprehensive mind-body lifestyle-modification day clinic program in patients with Crohn's disease.

N=35 patients in clinical remission with impaired QOL (IBDQ < 170) were randomly assigned to the intervention group (IG, n = 19) or control that received a single workshop of intense training in non-pharmacologic self-help strategies (CG, n=16). The intervention group participated in a 60-hour day clinic over 10 weeks (6h once a week - average attendance: 9.1 ± 1.1; Min.: 7) including mindfulness, stress management, exercise therapy, meditative movement therapies, mediterranean diet, self-help strategies and social support. Health related quality of life (IBDQ), disease activity (HBI), fecal inflammation marker lactoferrin, psychological symptoms (HADS), core self-efficacy (CSES) and perceived stress (PSS) were measured with standardized questionnaires at baseline (Week 0) and post intervention (week 12).

Results: Subjects were predominantly female (63%), 48.1 ± 12.3 years old with a mean time of disease of 20.5 ± 11.6 years and did not differ in sociodemographic characteristics and medication. Intention to treat analyses provided evidence for a significant improvement in quality of life (p=.021), psychological symptoms in general (p = .013), anxiety (p = .006) and core self-efficacy (p= .010) among participants in the IG compared to CG at the end of the intervention. No effect on disease activity, depression and perceived stress were observed.

Conclusion: A comprehensive mind-body lifestyle-modification day clinic program in patients with Crohn's disease based on non-pharmacologic therapy modules can improve health related quality of life, psychological symptoms and self-efficacy in patients with Crohn's disease.

Disclosure: Jost Langhorst

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The other co-authors: no conflicts of interest.

P1003

BRADYENTERIA SYNDROME AND COMORBIDITY

K.S. Shemerovskii¹, R.K. Kantemirova², P.V. Seliverstov³

¹Private Educational University of Higher Professional Education "St. Petersburg Medical and Social University", St. Petersburg, Russian Federation, ²Federal State Budgetary Research Institute named after G.A. Albrecht of the Ministry of Labor of Russia, St. Petersburg, Russian Federation, ³Military Medical Academy named after S.M. Kirov, St. Petersburg, Russian Federation

Contact E-Mail Address: constshem@yandex.ru

Introduction: Violation of the defecation rhythm regularity is a risk factor for colorectal cancer and cardiovascular mortality. However, the relationship between bradyenteria syndrome and comorbidity remains poorly understood.

Aims & Methods: The aim of this study was to prove the fact that bradyenteria is a risk factor for comorbidity.

334 people aged from 24 to 68 years were examined, 66% of women. Weekly monitoring of the circadian enteral rhythm was used to identify the frequency and acrophase of this rhythm in patients with a cardiologic profile. Euenteria corresponded to the daily defecation rhythm with a frequency of at least 7 times a week. Bradyenteria was detected by the frequency of defecation rhythm from 1-2 to 5-6 times a week. The risk of obesity was assessed by Body Mass Index. The risk of hypertension was compared for individuals with euenteria and bradyenteria. The level of anxiety and depression was determined by the hospital scale (HADS), the propensity to take laxatives was analyzed.

Results: In persons with euenteria, the morning bowel habit dominated, which was 3.5 times more common than evening defecation. In patients with bradyenteria, the absence of morning bowel habit prevailed, which was 3.2 times less common than evening defecation.

There were three main stages of bradyenteria. The first bradyenteria stage (light) was at a frequency of 5-6 times a week. The second bradyenteria stage (moderate) was at a frequency of 3-4 times a week. The third (severe) was at a frequency of 1-2 times a week.

It was shown that mild and moderate stages of bradyenteria occurred (in 61% and 30% of cases) almost 10 times more often than the severe stage (9% of cases). Violation of the circadian sleep-wake cycle increased the risk of bradyenteria by 1.7 times.

It was found that in patients with euenteria, the incidence of arterial hypertension was 12% but in people with bradyenteria – 34%. In patients with euenteria, the achievement of the target blood pressure level (in 77% of patients) was 4.8 times higher than in individuals with bradyenteria syndrome (in 16% of patients).

The risk of obesity in patients with euenteria was 7%, and in patients with bradyenteria – 24%. Bradyenteria syndrome increased the risk of obesity by 3.4 times. Clinically significant depression occurred in 12% of patients with stage I bradyenteria, in 17% of patients with stage II bradyenteria and in 43% of patients with stage III bradyenteria.

The propensity to take laxatives increased from the mild stage of bradyenteria (16% of patients) to the moderate stage (30%) and to the severe stage of bradyenteria (64%).

Conclusion: 1. The absence of a morning bowel habit increased the risk of bradyenteria by 3.2 times.

2. Mild and moderate stages of bradyenteria were almost 10 times more common than the severe one.

3. Bradyenteria syndrome increased the risk of arterial hypertension by 2.8 times.

4. Bradyenteria syndrome increased the risk of obesity by 3.4 times.

5. Depression was detected in 12%, 17% and 43% of patients with stage I, II and III of bradyenteria.

6. Laxatives were taken by 16%, 30% and 64% of patients with stage I, II and III of bradyenteria.

7. Bradyenteria syndrome is a predictor of comorbidity.

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Disclosure: Nothing to disclose.

P1004

EXPERIENCE IN ORGANIZING URGENT TRAINING FOR GI PROFESSIONALS ON EMERGENCY CARE FOR ABDOMINAL INJURIES DURING THE WAR IN UKRAINE

O. Popova¹

¹Military Medical Clinical Center of the Eastern Region, Elling Training Center, Surgery Department, Dnipro, Ukraine

Contact E-Mail Address: oksana.nikolaevna.popova@gmail.com

Introduction: The war with Russia, which began on February 24, 2022, posed new challenges to the health care system in Ukraine. A large number of doctors weren't ready to work effectively in such conditions. This trend was observed not only in civilian health facilities, but also among military medics who were called up to the medical service of the Armed Forces from the civilian level, but did not have sufficient experience.

The issue of triage and providing emergency care for abdominal injuries has become particularly acute, as it is one of the most common types of injuries, the clinical manifestations of which are often unclear and the consequences - fatal.

Aims & Methods: The Board of the ELLING training center, together with the heads of health care facilities, decided to organize an express course on emergency care. The main requirements for the course were short deadlines, the ability to study without leaving work and the maximum ability to quickly apply the acquired knowledge.

The training was conducted online, but only one health care facility was recruited to one group. This was done in order to enable colleagues to immediately discuss, agree and adapt to the conditions of a particular institution changes that will occur in daily activities, providing an opportunity to immediately implement the acquired skills in practice.

The training took place in blocks of 1.5-2 hours during non-working hours for all group members. The course was built on a three-step scheme.

The first stage was universal for all trainees and included triage and the use of emergency ultrasound, including E-FAST. The educational material was illustrating each of which a clinical case. The clinical case was first discussed with the trainees, and then as a conclusion - a training unit was provided, which allowed to improve the quality of perception of the material.

The next step was training in profile groups. For surgeons it was a mastery of the concept of damage control, for gastroenterologists - the peculiarities of endoscopic examination for abdominal trauma, which allowed to involve these specialists more widely to emergency care.

Usually for the second degree one clinical case was developed, on which all possible "mistakes" were made, which were then discussed with the trainees.

The third stage was a round table, which took place two weeks after the completion of basic training. It discussed the main difficulties faced by experts in practice.

Results: For 6 weeks of work we were able to conduct training for 217 doctors from different regions of Ukraine. According to the forms of feedback, 10 from 12 heads of health care facilities, whose staff was trained, rated it as extremely useful in their work, 2 - as useful, but with some difficulties in practical implementation.

Among the trainees, the course received an average score of 4.65 out of 5 for the relevance of the material provided and 4.87 out of 5 for compliance with the learning process.

Conclusion: In our opinion, more attention should be paid to training all physicians to work in conditions of mass admission of wounded, injured and sick and in conditions of danger and limited resources. It is desirable to do it preventively. In the training of all GI professionals, special attention should be paid to emergency ultrasound and high-quality mastering of the basics of endoscopy.

Step-by-step approach and analysis of specific clinical cases with integration into the work of a particular health care facility, taking into account its features, became the key to the success of this course and greatly facilitated the work of our doctors.

Disclosure: Nothing to disclose.

P1005

USE OF VIDEO GAMES AND ACQUISITION OF ENDOSCOPIC SKILLS. A STUDY FROM TERTIARY CARE HOSPITAL, PAKISTAN

F. Kayani¹, J. Khan²

¹Bolan Medical College, Gastroenterology, Quetta, Pakistan,

²Bolan Medical College, Medicine, Quetta, Pakistan

Contact E-Mail Address: farhana_kayani@hotmail.com

Introduction: Performance of Gastrointestinal endoscopy requires adequate hand-eye coordination. Video games are an effective way to judge one's hand-eye coordination, and practicing these games may improve one's skills.

Aims & Methods: Our goal was to see if there is a correlation between skill in video games and skill in endoscopy. Also, we hoped to demonstrate that practicing video games can improve one's endoscopic skills.

Fifteen Gastroenterology residents (nine male, six female) volunteered to participate. On day 1, the students performed three endoscopic tasks (banding, targeted biopsy and object transfer) and were assessed for time to complete the task, number of errors committed, and hand-eye coordination. The students were then randomized to control (group A) or, training' (i.e., video game practicing; group B) arms.

In group B, each resident played three commercially available video games for 30 min on an X-box (Microsoft, Seattle, WA) for four weeks. 4 weeks later, all residents repeated the endoscopic skills and were reassessed.

Results: Spearman correlation coefficients demonstrated a significant relation between many of the parameters, particularly time to complete each task and hand-eye coordination at the different games. The hand-eye coordination also improved in group B residents. There was a weaker association between video game performance and endoscopic errors committed. Group B subjects improved significantly over those in group A.

Conclusion: We conclude that Gastroenterology residents with ongoing video game experience have superior endoscopic skills for tasks in terms of time to completion, improved efficiency and fewer errors when compared to nongaming counterparts. however, a larger study with more practice time is required to prove games to be helpful.

Disclosure: Nothing to disclose.

P1006

TOWARDS A GREENER ENDOSCOPY ROOM: RECYCLING PLASTIC WASTE

D. de Jong¹, A. Volkers¹, E. de Ridder², G.R. D'Haens¹, P. Fockens¹, M. Duijvestein³

¹Amsterdam UMC, location AMC, University of Amsterdam, Gastroenterology and Hepatology, Amsterdam, Netherlands,

²MINT Zorgadvies, The Hague, Netherlands, ³Radboudumc, Gastroenterology and Hepatology, Nijmegen, Netherlands

Contact E-Mail Address: d.c.dejong@amsterdamumc.nl

Introduction: About 6-8% of the Dutch CO₂ emission is attributed to the healthcare sector and this includes the use of energy, travelling to the hospital or the processing of waste (1). Recently, the environmental impact of the gastrointestinal (GI) endoscopy unit is gaining attention as it is the second highest clinical procedure-related waste generating department (2, 3). Despite the huge amounts of (plastic) waste produced daily by the endoscopy department, the bulk is currently not recycled. However, sustainable waste management is relatively easy to implement in daily practice. Nevertheless, the majority is not recycled.

Aims & Methods: This project aims to investigate the net benefit of a plastic waste recycling program in a GI endoscopy unit in terms of recycling percentage, carbon footprint and associated costs.

In this single-centre study, the type and amount of waste that was produced during routine endoscopies was collected and examined during a baseline measurement. The waste was collected in different waste streams; paper/cardboard, glass, contaminated residual waste and non-contaminated residual waste. Sustainable waste management scenarios were examined and compared in terms of CO₂ footprint, recycling rate, and waste treatment costs by using the Healthcare Sustainability Mode and Effect Analysis (HSMEA). The endoscopy employees were given a waste recycling training (i.e. presentation, Q&A and posters). A mobile waste bin was installed in every endoscopy room to segregate the plastic waste. Finally, the waste of 'post-training' endoscopic procedures was collected, compared with the baseline procedure and tested for correct waste separation.

Results: In total, 14.6 kg of waste was collected during 15 procedures during the baseline measurement (0.97 kg per procedure) with a proportion of recyclable plastic waste of 9.6%. Waste processing costs increased from €1.60 (all residual waste) to €2.06 (+28%) with recycling of plastic. The post-training measurement was comparable with the baseline measurement. However, 15% of the plastic waste contained 'incorrectly separated' plastics, mainly consisting of empty syringes and tubes.

After counselling, it is expected that this proportion will drop to 0% as the incorrectly separated waste consists of only two product types. Recycling the plastic waste led to a reduction of the carbon footprint with approximately 3%. Per endoscopic procedure, this results in a reduction of 0.14 kg CO₂ emission. Over the year 2019, this would have led to a reduction of 1481 kg CO₂ emission in our centre, which corresponds to 6875 km drive in a non-electric car.

Waste type	Kilogram	Kilogram per procedure	Percentage	CO ₂ -reduction
Recycling (clean)	1,42	0,09	9,7	-3 %
plastics	1,40	0,09	9,6	-2,9 %
paper/cardboard	0,02	0,001	0,1	-0,1 %
Clean, but not suitable for recycling	0,75	0,05	5,1	
Residual waste (contaminated)	12,40	0,83	85,1	
Total	14,57	0,97	100	-3 %

Table.

Conclusion: Recycling plastic waste is a small, but easily implementable step towards a more sustainable practice in the endoscopy department. The demonstrated environmental benefit, but also the enthusiasm of the personnel, are compelling reasons to implement this at other endoscopy rooms as well.

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P1007

VIGATU - FIRST EXPERIENCES WITH THE VIRTUAL REALITY-BASED PERSONAL ENDOSCOPY TRAINER

D. Henniger¹, V. Riemer², M. Engelke³, J. Kreiser⁴, A. Meining¹, T. Ropinski⁴, T. Seufert², A. Hann¹

¹Universitätsklinik Wuerzburg, Interventional and Experimental Endoscopy (InExEn), Internal Medicine II, Wuerzburg, Germany,

²University of Ulm, Institute of Psychology and Education, Department Learning and Instruction, Ulm, Germany,

³Bildungszentrum Ruhr Endoskopiefachweiterbildung, Herne, Germany, ⁴University of Ulm, Institute of Media Informatics, Visual Computing, Ulm, Germany

Contact E-Mail Address: a.hann@posteo.de

Introduction: Colonoscopy for colorectal cancer screening is one of the most common endoscopic examinations. It is highly standardized by national and international guidelines. In contrast, endoscopic training is limited by time available during daily clinic routine, experience of the trainer, the available patient population of the clinic, and patient safety.

We developed a publicly funded virtual reality (VR) based simulator called ViGaTu to enable physician and non-physician professionals to acquire knowledge and skills to perform guideline-compliant screening colonoscopy.

Aims & Methods: The aim of this study was to evaluate the first version of ViGaTu by a hands-on-training in VR using specialist endoscopy staff. Learning objectives included device knowledge, preparation for the procedure, sedation and complications.

Nurses and physicians from different hospitals were asked to participate in the study. Testing was performed with a conventional VR headset (Oculus Quest 2). Time spent in VR was measured. Subsequently, standardized questioning of baseline characteristics, professional experience, achievement of the above mentioned learning objectives and feasibility was performed.

Results: 9 physicians (6 male, 3 female, most common age group 35-39 years) with 7-9 years of professional experience participated. Additionally, 26 nurses (9 male, 17 female, most common age group 40-44 years) with 10-12 years of professional experience participated. Participants had performed or assisted in over 500 endoscopies. Mean time spent in VR was 20 min (standard deviation +/- 3.7). The learning objectives device knowledge, monitoring, propofol sedation and use of Team-Time-Out checklist were rated well with 4 out of 5 points. 5 of 9 physicians and 13 out of 26 nurses noticed the high degree of realism and practical relevance, the

high degree of immersion, and the richness of the content as positive. 3 physicians and 8 nurses noticed deficiencies in control/navigation. Many participant wished for the ability to perform polypectomy or other interventions (e.g. irrigation).

Conclusion: This first version of ViGaTu is already accepted by endoscopy-experienced nurses and physicians and is evaluated as useful and feasible.

By additional integration of a digital curriculum and implementation of polypectomy and other interventions in the final version of the simulator, VR-based learning can become an integral part of endoscopic training and simplify the teaching of current guidelines.

Disclosure: Nothing to disclose.

P1008

GOOD FOR THE ENVIRONMENT AND THE POCKET – AN AUDIT OF WASTE GENERATION AND RECYCLING PRACTICES WITHIN AN IRISH ENDOSCOPY UNIT

N. O'Morain¹, E. Donohoe¹, C. Regan¹, E. Joy², R. Stack¹, J. Doherty¹, G. Horgan¹, H. Mulcahy¹, E. McDermott¹

¹St. Vincent's University Hospital, Centre for Colorectal Disease, Dublin, Ireland, ²University College Dublin, School of Medicine, Dublin, Ireland

Contact E-Mail Address: neilmoran@gmail.com

Introduction: Ireland has one of the highest greenhouse gas emissions per capita in the European Union, at 13.3 metric tons of CO₂ equivalent per person (1).

Healthcare accounts for 30% of all public sector greenhouse gas emissions. General waste accounts for almost 60% of all waste generated in Irish hospitals. It has been estimated that one third of this could be recycled. A large volume of recyclable waste is generated in Endoscopy, however sustainable practices are not currently championed.

Aims & Methods: This quality improvement project sought to determine the volume of recyclable waste generated within Endoscopy and whether use of green bins in Endoscopy would be a cost-effective strategy. Total waste generated by patient-related activity during one week was audited. Non-clinical and clinical waste was weighed and sorted.

The percentage of recyclable waste was documented and the net cost savings calculated. The net savings on an annualised basis was estimated. Reduction in carbon dioxide emissions (CO₂e) were calculated using the Waste Reduction Model (WARM) (2).

Results: In total, 70 non-clinical and 56 clinical waste bins were collected. The median weight for non-clinical waste bins was 20.1kg (IQR 19.7-21.7kg) and 40kg (IQR 28.8-39.0kg) for clinical bins. A median of 14.1kg (70.5%) of non-clinical waste and 3kg (7.5%) of clinical waste was recyclable. Disposal cost/tonne was calculated based on most recently available Health Service Executive (HSE) waste management estimates. Net savings of €337/week by sorting 60.1kg was generated, and a reduction in carbon footprint by 21.7kg CO₂e. This equates to a cost saving of €17,524 per year, and a reduction in CO₂e of 1,128.4kg.

Conclusion: This project highlighted the impact sustainable practices can have on reducing the inappropriate use of non-clinical and clinical waste bins in Endoscopy. A considerable volume of waste generated can be recycled with considerable cost savings, and a significant environmental impact.

Following this project, green recycling waste bins, monthly educational sessions as well as a 'Green Endoscopy' noticeboard have been introduced into the Endoscopy Department. We plan to audit the effect of this initiative and determine how accurate these estimated cost and environmental savings are in time to present at UEGW.

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1. Eurostat Greenhouse Gas Emissions 2017 <https://ec.europa.eu/eurostat/statistics>
2. United States Environmental Protection Agency <https://www.epa.gov/warm>

Disclosure: Nothing to disclose.

P1009

EFFECT OF TRADITIONAL CHINESE MEDICINE HOT IRONING THERAPY ON RECOVERY OF GASTROINTESTINAL FUNCTION IN PATIENTS AFTER GASTROINTESTINAL ANASTOMOSIS

T. Zhang¹

¹Zhengzhou University, Henan, China

Contact E-Mail Address: 344780762@qq.com

Introduction: To explore the effect of hot ironing of dried ginger and *Evdia rutaecarpa* on the recovery of gastrointestinal function after gastrointestinal anastomosis based on ERAS concept.

Aims & Methods: A total of 100 patients with gastric cancer who received gastrointestinal anastomosis were selected as the research object. They were randomly divided into the control group and the intervention group. Patients in the control group were given routine western intervention methods of accelerated rehabilitation surgery, while patients in the intervention group were given routine western intervention methods+dried ginger, *Evdia rutaecarpa* hot ironing at Shenque point in abdomen and Renmai Jiuwei point to Guanyuan point. Observe the following indexes of patients in the two groups:

1. Recovery time of gastrointestinal function, including postoperative exhaust time, postoperative defecation time, eating time and hospitalization time;
2. Subjective clinical scores of patients on the 1st day before operation, 1st day, 3rd day and 5th day after operation, including abdominal pain, abdominal distension and gastrointestinal symptoms.

Results: The first exhaust time, first defecation time, first feeding time and total hospitalization time in the intervention group were shorter than those in the control group, with statistical significance ($P < 0.05$). There were no significant differences in abdominal pain, abdominal distension and gastrointestinal symptom scores between 2 groups 1d before surgery and 1d after surgery ($P > 0.05$). The abdominal pain, abdominal distension and gastrointestinal symptom scores in the intervention group were lower than those in the control group on the 3rd and 5th day after surgery, with statistical significance ($P < 0.05$).

Conclusion: Based on ERAS concept, hot ironing of dried ginger and *Evdia rutaecarpa* at Shenque point and Renmai Jiuwei point to Guanyuan point can further promote the recovery of gastrointestinal function after operation and shorten the recovery time of gastrointestinal function.

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P1010

TRANSCRIPTIONALLY INACTIVE NRF2 INFLUENCE COLON MORPHOLOGY AND FUNCTION IN FEMALE MICE VIA MODULATION OF ESTROGEN LEVEL AND ESTROGEN RECEPTORS EXPRESSION

A. Piechota-Polanczyk¹, D. Klimczyk¹, M. Kopeć¹, A. Kopacz¹

¹Jagiellonian University, Department of Medical Biotechnology, Faculty of Biochemistry, Biophysics and Biotechnology, Kraków, Poland

Contact E-Mail Address: aleksandra.piechota-polanczyk@uj.edu.pl

Introduction: One of the determinants of homeostasis in the intestines is the proper function of Nrf2 (nuclear factor erythroid 2-related factor 2). It is a transcriptional factor that regulates many antioxidant and detoxification genes.

However, the Nrf2 gene polymorphism is related to ulcerative colitis, inflammatory bowel diseases (IBD) and its transcriptional deficiency may trigger IBD-like changes in the colon of older female mice without visible symptoms of bowel diseases.

Therefore, our objective is to address the sex-dependent impact of Nrf2 transcriptional deficiency on colon function and to delineate the possible mechanisms that govern intestinal homeostasis in these mice.

Aims & Methods: We used the 3- and 6-month old (m.o.) C57BL/6J mice with functional Nrf2 (wild-type (WT)), with transcriptionally inactive form of Nrf2 (transcriptional knockout (KO)) or lacking IL-10 (IL-10 KO), which spontaneously develop IBD. Mice were subjected to whole gastrointestinal transit, castor-oil induced diarrhea and colonic bead expulsion tests. Blood was collected for morphology and serum for IFN- γ , IL-1b, TNF- α and estradiol assay. The colon samples were stored for histological and immunofluorescent analysis of intestinal damage, myeloperoxidase (MPO) activity, glutathione assay, estrogen receptor (ER)- α , ER- β and, GPR30. Further, the effect of estrogen on GI tract functionality was verified in 3-month-old Nrf2 WT and Nrf2 KO female mice treated with estradiol for 28 days.

Finally, to confirm that estrogen receptors can influence colon contractility, organ bath assay on isolated colon tissue was performed. To inhibit Nrf2 transcriptional activity, 3 m.o. and 6 m.o. female mice were treated intraperitoneally with ML385 (30mg/kg/day), or DMSO for 7 days prior to tissue isolation and isolated colon samples were treated with selective ER- α or ER- β inhibitors.

Results: The results indicated that Nrf2 TA abrogation, alike IL-10 deficiency, in females trigger functional and microscopical phenotype, resembling IBD. Females had significantly changed GI function and younger Nrf2 tKO females had significantly higher WBC, GRA, and LYM blood counts, which were comparable to IL-10 KO mice. Histologically, in Nrf2 KO female mice, there was an enlargement of the lamina propria and depletion of goblet cells in all parts of the colon, as well as significant thickening of muscularis mucosae in the proximal colon.

Further results showed that lack of Nrf2 TA in young females does not lead to increased oxidative stress or fibrosis, however, it impacts the inflammation as only young Nrf2 KO females had significantly elevated colon MPO activity.

Importantly, Nrf2 TA influences estrogen level and estrogen receptor location. Nrf2 KO females have significantly reduced serum level of estradiol and altered expression of the ER- α and ER- β , especially in the proximal and middle colon.

Conversely, the expression of GPR30 was significantly reduced in the whole colon. Of note, estradiol treatment led to a notable improvement in colon motility in Nrf2 KO mice and raised the level of ER- α and GPR30 to a comparable level between genotypes.

Finally, organ bath assay on isolated colon tissue showed that stimulation of ER- β receptors, but not ER- α , significantly influences colon contractility in control but not in ML385-treated mice.

Conclusion: Summing up, our data suggest that Nrf2 transcriptional activity may modulate GI function and especially colon contractility by influencing estrogen and estrogen receptor signaling in females. (Supported by the Sonata 14 program of the National Science Centre 2018/31/D/NZ4/00077 to APP).

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P1011

HIGH PREVALENCE OF SIGNIFICANT GASTROINTESTINAL PATHOLOGIES AMONG PATIENTS REFERRED FROM PRISON TO GASTROENTEROLOGY

M.G. Shiha¹, A.R. Robertson¹

¹University Hospitals of Leicester, Department of Gastroenterology, Leicester, United Kingdom

Contact E-Mail Address: Shiha202@gmail.com

Introduction: Great Britain has the highest rates of imprisonment in western Europe. Although equal access to healthcare is a universal human right, many prisoners experience substantial health inequalities leading to an increased morbidity and mortality risk compared with the general population.

Aims & Methods: We aimed to examine the clinical outcomes of patients referred from prison to secondary care gastroenterology and endoscopy at a large university hospital between January 2020 and December 2021. Referrals, clinic records and endoscopy reports were retrospectively reviewed.

Results: A total of 47 patients (100% male, median age 46 years) were referred from prison to gastroenterology outpatient clinics (n=35, 74.4%) or directly to endoscopy (n=12, 25.5%). The most common indications for referrals were dysphagia (n=10, 21.2%), rectal bleeding (n=9, 19.1%), diarrhoea (n=7, 15.2%) and abdominal pain (n=6, 12.7%), follow-up for known inflammatory bowel disease (n= 6, 12.7%) and viral hepatitis (n=3, 6.3%). Twenty-seven (57.4%) patients underwent endoscopic evaluation including gastroscopy (n=16), flexible sigmoidoscopy (n=10), colonoscopy (n=4) and video capsule endoscopy (n=2). Clinically significant endoscopic findings included new diagnosis of colitis (n=5), colonic polyps (n=2), oe-

sophageal cancer (n=1), Barrett's oesophagus (n=1), gastrointestinal stromal tumour (n=1), bleeding haemorrhoids (n=1) and ileitis (n=1). Only five patients had normal endoscopy.

Conclusion: Patients referred from prison with gastrointestinal symptoms have a high prevalence of significant pathologies. One-in-four patients had inflammatory bowel disease, half of whom were newly diagnosed. We call for policies and actions to ensure equal access to secondary health-care for this group of incarcerated vulnerable young patients.

Disclosure: Nothing to disclose.

P1012

ESTROGEN REGULATES DUODENAL GLUCOSE ABSORPTION THROUGH THE EFFECT OF ESTROGEN RECEPTOR- α ON GLUCOSE TRANSPORTERS

W. Shan¹, J. Xu¹, R. Xie¹

¹Affiliated Hospital of Zunyi Medical University, Department of Gastroenterology, Zunyi, China

Contact E-Mail Address: shanweixi1994@126.com

Introduction: Obesity is closely related to abnormal glucose metabolism and absorption. Clinical studies have found that the obesity rate of middle-aged and elderly women, especially menopausal women, has increased significantly, but the specific regulation mechanism is not clear. It is known that menopausal women are accompanied by a significant decrease in estrogen, but whether this change in estrogen level can regulate the metabolism and absorption of glucose is rarely reported at home and abroad.

This study clarified estrogen through in vivo animal experiments and in vitro cell experiments. The effect of changes on the absorption of glucose in the duodenum and possible regulatory mechanisms.

Aims & Methods: C57 mice were selected to establish an ovariectomized surgery model, and the sham-operated group was used as a control to dynamically compare the body weight, venous blood glucose levels and observe the changes in body fat distribution of the two groups of mice. Immunohistochemistry was used to detect the expression of estrogen receptors (ER- α , ER- β) and sugar transporters (SGLT1 and GLUT2) in the duodenum of the two groups of mice.

The Ussing chamber experiment compares the short-circuit current changes caused by glucose absorption in the duodenum of ovariectomized mice. Western-blot detects the expression changes of the target gene protein, agonists and inhibitors verify the important role of the PKC signaling pathway, construct ER- α and ER- β shRNA lentiviruses to transfect SCBN cells, and observe the changes in the expression of SGLT1 and GLUT2.

Results: We first observed the correlation between estrogen and blood glucose in women, which found that blood glucose in healthy women during menstruation was significantly higher than that during ovulation. Similarly, in ovariectomized (OVX) mice, with serum estradiol level decreased and ER- α and ER- β in the duodenum reduced, the weight, abdominal fat and blood glucose increased significantly. However, interestingly, the expression of SGLT1 and GLUT2 and the glucose absorption in duodenal decreased significantly.

It was further confirmed that estrogen could significantly up-regulate the expression of SGLT1 and GLUT2 in SCBN cells, and this trend can be reversed after silencing ER- α , but it doesn't work after silencing ER- β , suggesting ER- α may be the key receptor of estrogen regulating glucose transporter. Mechanism study found that estrogen downstream can activate PKC pathway.

Overall, our findings indicate that estrogen promotes glucose absorption, estrogen and its receptor (ER- α) deficiency can inhibit the expression of SGLT1 and GLUT2 through PKC signaling pathway, thereby reducing the glucose absorption.

Conclusion: estrogen promotes glucose absorption, estrogen and its receptor (ER- α) deficiency can inhibit the expression of SGLT1 and GLUT2 through PKC signaling pathway, thereby reducing the glucose absorption.

Disclosure: Nothing to disclose.

P1013

THE IMPACT OF THE COVID-19 PANDEMIC ON PATIENTS WITH ULCERATIVE COLITIS: RESULTS FROM A GLOBAL UC PATIENT SURVEY

L. Peyrin-Biroulet¹, K. Ylänne², A. Sipes³, M. Segovia^{4,5}, S. Gardiner⁶, J.C. Cappelleri⁷, A. Mulvey⁸, R. Panaccione⁹

¹University of Lorraine, CHRU-Nanc, Inserm, NGERE, Department of Gastroenterology, Nancy, France, ²Sidekick Health, Kopavogur, Iceland, ³Patient Representative, Columbia, United States, ⁴Pfizer Inc, Collegeville, United States, ⁵Rutgers University, New Brunswick, United States, ⁶Pfizer Inc, New York, United States, ⁷Pfizer Inc, Groton, United States, ⁸The Harris Poll, Chicago, United States, ⁹Division of Gastroenterology and Hepatology, Department of Medicine, University of Calgary, Calgary, Canada

Contact E-Mail Address: peyrinbiroulet@gmail.com

Introduction: The COVID-19 pandemic presented challenges around disease management, lifestyle changes and provision of care for patients with ulcerative colitis (UC).

Aims & Methods: This UC Narrative global survey (United States, Canada, Japan, France and Finland) was conducted by The Harris Poll between 25 August and 13 December 2021, among 584 patients with UC (confirmed by endoscopy) aged ≥ 18 years who had attended a gastroenterologist or internist's office in the past 3 years, had not had a colectomy, and had ever taken prescription medication for UC. The survey aimed to understand how the COVID-19 pandemic impacted patients with UC and assessed overall disease management, telehealth use, healthcare experience and perceived quality of care, emotional well-being, reliance on alternative support systems and preferences for virtual/in-person interactions with doctors. Data were from patients who consented and completed the survey; analysed using descriptive statistics.

Results: Overall, 25% of patients experienced more UC flares during the pandemic than in 2019. Most patients taking prescription medication (88%) were very/somewhat satisfied with their current treatment plan but overall, 53% strongly/somewhat agreed that they were hesitant to change their treatment plan during the pandemic.

Factors that patients agreed helped to control UC symptoms included having fewer social outings (37%), working from home (29%) and having less busy schedules (28%).

Factors that patients agreed made controlling UC symptoms more difficult included having more anxiety/stress (43%), hesitancy to visit a hospital or office (34%) and being unable to get an appointment with their doctor (23%). Virtual appointments were more common during the pandemic than before and more patients relied on alternative support systems for management of UC (Table).

Overall, 79% were very/somewhat satisfied with their ability to access needed healthcare during the pandemic, and patients who used each appointment type were equally very satisfied/satisfied with the overall quality of care at in-person (81%) and virtual (81%) appointments. However, in-person appointments were preferred by 68% of patients when meeting a new doctor, 55% when experiencing a flare, 52% for regular check-ups and 21% for UC prescription refills.

Conclusion: During the pandemic, most patients with UC were satisfied with their current treatment plan and ability to access healthcare, and more patients relied on alternative support for management of UC, but many were negatively impacted by anxiety/stress.

	Prior to the pandemic	During the pandemic	Plan to do after the pandemic	Have never done or plan to do
Talked openly with their doctor about how their disease impacts their life	54%	54%	44%	17%
Set goals with their doctor for managing their disease	48%	46%	40%	25%
Communicated with a nurse at their doctor's office between appointments	45%	40%	34%	32%
Used an online patient portal to contact their doctor's office or see lab results	31%	47%	33%	32%
Used social media to connect with other patients or learn about ulcerative colitis	24%	39%	27%	46%
Used symptom tracking or disease management apps	23%	31%	29%	48%
Relied on information from patient advocacy groups	19%	27%	22%	54%
Relied on patient support groups	15%	22%	22%	59%
Had virtual appointments with their doctor	13%	55%	32%	31%

Table. Disease management before, during and after the COVID-19 pandemic: reliance on alternative support systems for management of ulcerative colitis.

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A. Mulvey is an employee of The Harris Poll, which was a paid contractor to Pfizer.

R. Panaccione has received consultancy and/or advisory board fees from AI4GI, AbbVie, Amgen, Arena Pharmaceuticals, Atlantic Healthcare, BioBalance, Boehringer Ingelheim, Bristol Myers Squibb, Celgene, Coronado Biosciences, Cosmo Technologies, Eagle, Eisai Medical Research, Elan, Eli Lilly, EnGene, Ferring Pharmaceuticals, Genentech/Roche, Gilead Sciences, Given Imaging, GlaxoSmithKline, Innomar, Janssen Pharmaceuticals, Lycera, Meda, Merck & Co., Merck Research Laboratories, Novo Nordisk, PDL Biopharma, Pfizer Inc, Prometheus Laboratories, Protagonist, Receptos, Robarts Clinical Trials, Sandoz, Sanofi Genzyme, Satisfai Health, Shire Pharmaceuticals, Sigmoid Pharma, Specialty Rx, Sublimity, Takeda and Theravance Biopharma.

P1014

ZONULIN CONCENTRATION IN PATIENTS WITH INFLAMMATORY BOWEL DISEASES WITH AND WITHOUT COVID-19 INFECTION

O. Knyazev^{1,2}, A. Kagramanova¹, D. Kulakov¹, A. Lishchinskaya¹, B. Nanaeva², R. Gudkova¹, A. Parfenov¹

¹Moscow Clinical Scientific Center named after A.S. Loginov, IBD, Moscow, Russian Federation, ²State Scientific Centre of Coloproctology named after A.N. Ryzhyh, IBD, Moscow, Russian Federation

Contact E-Mail Address: kagramanova@me.com

Introduction: Zonulin is a protein, reversibly increasing the permeability of the intestinal wall by changing the structure of tight junctions of the lateral surfaces of intestinal epithelial cells. Fecal zonulin is used for non-invasive assessment of increased intestinal permeability.

Normal values of zonulin in stool (≤ 110 ng/ml) indicate the absence of damage of the intestinal villous mucosal surface and normal density of intercellular contacts.

Aims & Methods: The aim of the study was to determine the level of fecal zonulin (FZ) in the feces of IBD patients with exacerbation of the disease and the presence of COVID-19 in the acute period and without COVID-19 to assess the degree of intestinal permeability.

Material and methods: 34 patients with IBD without COVID-19 (Me age — 32 years) and 19 patients with IBD with the presence of COVID-19 infection in the acute period (Me age — 44 years) were examined.

Untreated stool samples of patients were frozen and stored at a temperature of 80°C. FZ was measured by ELISA (IDK® Zonulin ELISA Kit, Immunodiagnostik AG, Germany) in ng/ml. Reference values: < 83.15 ng/ml - a variant of the norm, $83.15-110$ ng/ml - an elevated level, 110 ng/ml - a high level.

Results: In the stool samples of patients with IBD exacerbation without COVID-19 FZ was detected from 186.4 to 563.9 ng/ml (Me - 326), the average value was 333.4 ± 16.9 ng/ml. In the stool samples of patients with IBD exacerbation and COVID-19 infection, FZ was detected from 321.8 to 598.3 ng/ml (Me - 469.9), the average value was 464.9 ± 16.4 ng/ml ($p=0.000001$).

Conclusion: FZ concentration in the feces of IBD patients is significantly higher in IBD patients with the presence of COVID-19 infection in the acute period, which indicates a higher permeability of the intestinal wall.

Disclosure: Nothing to disclose.

P1015

DIFFERENCE BETWEEN COVID-19 ALPHA VARIANT, B.1.1.7, AND THE ORIGINAL VIRUS IN GASTROINTESTINAL SYMPTOMS AND MORTALITY, IS A NEGATIVE CORRELATION EXISTS?

Y. Niv¹

¹Ariel University, Medicine, Pardesia, Israel

Contact E-Mail Address: nivaron80@gmail.com

Introduction: Covid-19 disease was first diagnosed in Israel at the end of February 2020. Until the end of June 2021 842,536 confirmed cases and 6428 deaths were accumulated. In our multicenter, retrospective cohort study, we looked for gastrointestinal signs and symptoms in 2 periods (period I represents the 1st and 2nd waves and the original virus; period II represents the 3rd wave and the alpha variant), and correlated them with mortality.

Aims & Methods: Out of 22302 patients hospitalized in general medical centers we randomly selected 6329 admissions for the study. Of these, 3582 and 1106 were eligible for the study in the first period and in the second period, respectively.

Results: Gastrointestinal signs and symptoms, diarrhea, vomiting, abdominal pains and taste/smell loss, were more prevalent in the first period than in the second period (Table 1). Thirty-day mortality and in-hospital mortality were significantly higher in the 2nd period than in the 1st period, 25.20% versus 13.68%, and 21.17% versus 12.87%, respectively ($P<0.001$).

Parameter	Original virus (%)	Alpha variant (%)	RR
Age > 60 y	58.23	71.01	1.22
Gender men	55.06	57.89	1.05
Diarrhea	9.39	4.96	0.53
Vomiting	6.80	5.23	0.77
Abdominal pain	5.94	3.54	0.60
Taste/Smell loss	42.41	34.68	0.82
In Hospital Mortality	12.87	21.17	1.64
30-day Mortality	13.68	25.20	1.84

Table 1.

Conclusion: Mortality rates were 1.64 to 1.84 times higher on the 2nd period than in the 1st period and in negative correlation with gastrointestinal symptoms and signs.

Disclosure: Nothing to disclose.

P1016

FEATURES OF MICROBIOTA DISTURBANCES INTESTINE IN PATIENTS WHO UNDERWENT COVID-19

M. Adkhamova¹, S. Shamsiev², S. Kuranbaeva³

¹Tashkent Medical Academy, Department of Gastroenterology, Tashkent, Uzbekistan, ²Tashkent Medical Academy, GI Endoscopy, Tashkent, Uzbekistan, ³Tashkent Medical Academy, Department of Gastro Neurology, Tashkent, Uzbekistan

Contact E-Mail Address: adkhamova0511@mail.ru

Introduction: It is well known that COVID-19 affected not only the respiratory system but the general body system, including digestive system.

Aims & Methods: We aimed to study the intestinal microflora in patients who have had a coronavirus infection, caused by COVID-19.

We examined 42 patients aged 34 ± 7 years with the diarrheal syndrome (stools 7 ± 3 times a day) that developed after coronavirus infection. Viral pneumonia was detected in 26/42 patients, in connection with which courses of antibiotics were carried out. In 16/42, COVID-19 proceeded without the development of pneumonia. The microbiota was studied in stool cultures and bacterial growth in the lumen of the small intestine (SIBO) was determined by the hydrogen breath test. Feces were examined for Clostridium difficile toxins, as well as laboratory and instrumental examination was carried out.

Results: In all patients, stool cultures showed a decrease in obligate and growth of opportunistic microflora, in 12/42 - signs of SIBO. 31/42 were found to have C. difficile toxins, among which 26/42 received courses of antibiotics, and 5 had no antibiotic therapy during the last year. Colonofibroscopy revealed erosive hemorrhagic colitis in 31/42 patients.

In blood tests, 40/42 had lymphopenia. Clostridial infection was treated, followed by a combined probiotic course. 11 patients with intestinal dysbacteriosis in the absence of C. difficile received probiotic monotherapy. As a result of therapy, all patients had regular stools up to 1–2 times a day, and there were no C. difficile toxins on re-examination.

After a monthly course of the multi-strain probiotic, the composition of the fecal microbiota was restored and was not determined by SIBO. Colonofibroscopy showed no signs of inflammation, and lymphocyte counts returned to normal.

Conclusion: In all patients who underwent coronavirus infection, a violation of the fecal microbiota was revealed, with *C. difficile* activation in 73%. 28% of patients developed SIBO. Lymphopenia was found in 95% of patients with intestinal dysbacteriosis. Coronavirus infection COVID-19 leads to changes in the intestinal microbiota, which creates conditions for the growth of clostridial infection against the background of a decrease in the tension of the immune system.

Disclosure: Nothing to disclose.

P1017

BNT162B2 MRNA COVID-19 VACCINE SAFETY IN INFLAMMATORY BOWEL DISEASE PATIENTS ON BIOLOGIC THERAPY: A MONOCENTRIC REAL-WORLD STUDY

R. Pellegrino¹, G. Pellino², L. Selvaggi², F. Selvaggi², R. D'Onofrio¹, N. de Gennaro¹, A. Federico¹, M. Romano¹, A.G. Gravina¹

¹University of Campania Luigi Vanvitelli, Department of Precision Medicine, Naples, Italy, ²University of Campania Luigi Vanvitelli, Department of Advanced Medical and Surgical Sciences, Naples, Italy

Contact E-Mail Address: raffaele.pellegrino@unicampania.it

Introduction: During COVID-19 pandemic, vaccines were developed with the intention of providing a primary preventive intervention. Patients with Inflammatory Bowel Disease (IBD) were excluded from most of trials that led to the approval of anti-COVID-19 vaccines and are therefore worthy of real-life studies providing information on the safety of these vaccines in this clinical setting and especially for specific subgroups such as patients on biologic therapy this also in consideration of a certain degree of reluctance of IBD patients to get vaccinated.

Aims & Methods: A prospective observational real-life study was performed for estimating local and systemic adverse events (AEs) incidence related to BNT162b2 vaccine administration in IBD patients in therapy with biological drug. We also wanted to evaluate whether there was a vaccine-induced change in IBD activity or an AEs increase depending on the disease activity as well as whether there were subgroups more exposed to AEs or predictors of systemic AEs. Questionnaires regarding the occurrence of AEs were administered after each of the three doses of vaccine as well as gastroenterologic visits were performed before the first, second, third dose, and after the third dose for Partial Mayo Score (PMS) and Harvey-Bradshaw Index (HBI) evaluation.

Results: 80 patients were initially enrolled (43.75% with Crohn's Disease and 56.25% with Ulcerative Colitis, median age 47.5) and evaluated at the first-second doses and 74 patients at the third dose. Local AEs rate was 37.5%, 58.75%, 28.37% at the first, second, and third dose of vaccine, respectively. In contrast, the systemic AEs rate was 52.2%, 48.75%, 43.24%. There were no differences in the occurrence of local and systemic AEs between patients with Crohn's Disease and Ulcerative Colitis patients ($p > 0.05$). Non-hypertensive and non-diabetic ($p < 0.05$) patients experienced significantly fewer local AEs at first and second doses. Vaccination did not affect disease activity and no statistically significant difference in PMS and HBI was observed between the three doses. Comorbidities and concomitant therapies were not discriminating in the occurrence of AEs ($p > 0.05$). Clinic-demographic predictor variables for AEs were not identified and PMS and HBI were not found to be predictors of systemic AEs. No serious AEs were observed.

Conclusion: BNT162b2 vaccine showed a good clinical safety profile in our setting of IBD patients on biologic therapy in the absence of severe AEs and changes in baseline disease activity.

Disclosure: Nothing to disclose.

P1018

IMMUNOGENICITY AGAINST SARS-COV-2 VARIANTS AFTER THIRD DOSE OF MRNA COVID-19 VACCINE IN PATIENTS WITH IBD FROM PUERTO RICO

P. López-Marte¹, A. Soto¹, E. Rodríguez-Martinó², E.J. Ortiz³, M. Ferré-Lebrón³, S. Torres-Jorge¹, J. Santana-Bagur⁴, C.A. Sario¹, E.A. Torres^{1,2}

¹University of Puerto Rico - School of Medicine, Gastroenterology Research, San Juan, Puerto Rico, ²University of Puerto Rico - School of Medicine, Gastroenterology, San Juan, Puerto Rico, ³University of Puerto Rico - School of Medicine, Microbiology, San Juan, Puerto Rico, ⁴University of Puerto Rico - School of Medicine, Medicine- Infectious Diseases, San Juan, Puerto Rico

Contact E-Mail Address: paola.lopez.marte@gmail.com

Introduction: Management of inflammatory bowel disease (IBD) often relies on biological and immunomodulatory agents for remission through immunosuppression, raising concerns regarding the SARS-CoV-2 vaccine's effectiveness and safety. Recent evidence suggests that these patients can adequately neutralize the virus after two doses of the mRNA-COVID-19 vaccine. Nonetheless, the rapidly appearing variants have hindered the characterization of the vaccine's capacity.

We report the humoral response of patients with IBD without and with biologic and/or immunomodulatory therapy against seven SARS-CoV-2 variants 60 days after the third vaccine dose of COVID-19.

Aims & Methods: Subjects ≥ 21 years of age with Crohn's disease (CD) and ulcerative colitis (UC) with and without biological and/or immunomodulatory therapy were recruited. Blood samples were collected after 60 ± 7 days after receiving the third dose of mRNA COVID-19 vaccine [BNT162b2 (Pfizer-BioNTech) or mRNA-1273 (Moderna)]. Neutralizing capability using SARS-CoV-2 surrogate virus neutralization test (sVNT%) was measured against seven variants of SARS-CoV-2 virus: Alpha, Beta, Gamma, Epsilon, Kappa, Delta, and Omicron. A result of $\geq 30\%$ was positive for effective viral inhibition. Results were stratified by the mechanism of action of those subjects receiving therapy and compared with a healthy control group. The study is approved by the MSC IRB.

Results: 54 subjects with IBD unexposed and exposed to biological and/or immunomodulatory after 60 ± 7 days of third vaccine dose and 12 healthy controls after 60 ± 10 days of third vaccine dose are reported. For subjects with IBD, 81% (44/54) had a diagnosis of CD, 61% were males (33/54), and the mean age was 42. The majority of the subjects were receiving anti-TNF therapy (29/54), and one was on a concomitant corticosteroid. All subjects with IBD developed detectable antibodies.

Twenty-four subjects with IBD did not develop effective neutralizing capability against the Omicron variant. 70% (17/24) of those subjects were receiving anti-TNF therapy (10= adalimumab, 7= infliximab), two of them (2/17) had a history of COVID-19 infection, and one subject (1/17) did not develop neutralization against three other variants: Gamma, Epsilon and Kappa. All 12 healthy controls developed detectable antibodies and effective humoral responses against all seven variants of SARS-CoV-2.

Conclusion: Our study shows that humoral response after third vaccine dose from patients with IBD on anti-TNF therapy might not be protective against COVID-19 variants, particularly against Omicron. These patients might benefit from an additional vaccine dose, thus prospective and larger studies are needed to ensure optimal immunity for patients with IBD.

Disclosure: Nothing to disclose.

P1019

PATIENTS WITH LOW ALT LEVELS ARE AT INCREASED RISK FOR SEVERE COVID-19

D. Genzel¹, L.H. Katz¹, R. Safadi², J.M. Jacobs³, A. Shafrir^{1,4}

¹Hadassah Medical Center, Faculty of Medicine, Hebrew University of Jerusalem, Department of Gastroenterology, Jerusalem, Israel, ²Hadassah Medical Center, Faculty of Medicine, Hebrew University of Jerusalem, Liver Institute, Jerusalem, Israel, ³Hadassah Medical Center, Faculty of Medicine, Hebrew University of Jerusalem, Department of Geriatrics and Geriatric Rehabilitation, Jerusalem, Israel, ⁴Meuhedet Meuhedet Health Maintenance Organization, Jerusalem District, Tel Aviv, Israel

Contact E-Mail Address: ashershaf@gmail.com

Introduction: Alanine transaminase (ALT) levels are usually used as a sign of liver health. However, low ALT is associated with sarcopenia and frailty. The COVID-19 pandemic has caused immense morbidity and mortality, especially in older and frail patients. We evaluated the association of pre-infection low ALT and the risk for severe COVID-19.

Aims & Methods: We used data from Meuhedet Health Services, a national state-mandated HMO in Israel, serving more than 1.3 million patients from all over the country. Data regarding all subjects tested for SARS-CoV-2 from 1 March 2020 – to 31 December 2021 was collected. Clinical and laboratory data were collected, including ALT from the year prior to infection. Severe COVID-19 was defined as ≥ 10 hospitalization days, ICU admission, or death within 30 days of the infection. Patients with low ALT (ALT < 10 IU/l) were compared to patients with normal ALT (11–40 ALT/l). Patients younger than 18, with above-normal ALT levels and those without ALT in the year prior to COVID-19 infection, were excluded.

Results: During the study period, 58,961 adult patients with low or normal ALT levels were tested positive for SARS-CoV-2. 5,515 (10.32%) of the study population were in the low ALT group. The low ALT group was younger (40.53 ± 20.20 vs. 42.73 ± 17.28 , $p < 0.001$), less likely to be male (12.3% vs. 38.7%, $p < 0.001$), and had lower BMI (26.1 vs. 27.4 , $p < 0.001$).

There were more deaths in the low ALT group (2.4% vs. 0.6%, $p < 0.001$) and more lengthy hospitalizations (2.6% vs. 1% $p < 0.001$). ICU hospitalization were similar in both groups (0.5% vs. 0.4%, $p = 0.47$).

In a multivariate logistic regression controlling for age, sex, vaccination status, socioeconomic status, sector, hypertension, diabetes mellitus, and BMI, low ALT was associated with increased risk for 30-day mortality (OR 1.94, $p < 0.001$) and prolonged hospitalization (OR 1.93, $p < 0.001$).

Conclusion: Low ALT is associated with an increased risk for severe COVID-19 infection. This association may be due to frailty and sarcopenia, yet further studies are warranted to explore this association.

Disclosure: Nothing to disclose.

P1020

COMPARING PATIENT PROFILES OF COVID-19 VACCINATED AND UNVACCINATED CROHN'S DISEASE PATIENTS

P. Robinson¹, M. Thoo², C. Ng², D. Baldock¹, E. Baynton¹

¹Ipsos, London, United Kingdom, ²Ipsos, Kuala Lumpur, Malaysia

Contact E-Mail Address: elizabeth.baynton@ipsos.com

Introduction: The objective of this study is to investigate the defining characteristics of COVID-19 vaccinated and unvaccinated patients with moderate-to-severe Crohn's disease (CD) in the EU4+UK and highlight key differences between these two cohorts, as well as identifying driving factors for gastroenterologists to advise COVID vaccination.

Aims & Methods: A multi-centre online medical chart review study of patients with CD and UC was conducted between July – September 2021 among EU4+UK (UK, FR, DE, IT & ES) gastroenterologists practicing across hospital and private practices. Recruited from a large access panel, physicians were screened for duration of practice in their specialty and caseload. Respondents completed a three-part survey; doctor demographics, perceptual questionnaire, and patient record forms of their next 6 CD patients seen following receipt of the survey.

Results: In Q3 21, 203 EU4+UK gastroenterologists reported on 1106 CD patients. Rates of COVID-19 vaccination among this patient cohort were 86.1% vaccinated, 13.9% unvaccinated.

Reported vaccinated CD patients, when compared to the unvaccinated cohort, had a significantly higher average age (41 years vs 33 years, respectively; $p \leq 0.01$), a significantly higher physician stated rate of controlled disease (83% controlled vs 68%; $p \leq 0.01$), a significantly higher physician stated rate of remission (74% vs 61%; $p \leq 0.01$).

Reported vaccinated CD patients also had a significantly higher number of hospitalisations compared to unvaccinated patients (13.1 times vs 6.5 times; $p \leq 0.01$), as well as a significantly higher average number of surgeries compared to unvaccinated patients (1.3 surgeries vs 1.1; $p \leq 0.01$).

Reported unvaccinated CD patients were prescribed TNFi therapies at a significantly higher rate than those who are vaccinated (87.7% of overall market vs 78.3%; $p \leq 0.01$), while vaccinated patients experienced a significantly higher average time on their current therapy (17.1 months vs 13.2 months; $p \leq 0.05$).

Reported unvaccinated patients had a significantly higher average CRP score than vaccinated patients (14.8 vs 10.4; $p \leq 0.01$); a directionally higher average ESR score (22.5 vs 21.8); a directionally higher average CDAI score (155.4 s 146.0), and a significantly higher average daily frequency of diarrhoea (6.1 times per day vs 5.2; $p \leq 0.01$). First line reported patients have a directionally lower rate of vaccination than later line patients; patients on second and later lines of therapy constitute 25.4% of the vaccinated cohort vs 12.3% of the unvaccinated cohort.

'COVID-19 impact' was cited as a reason for choice of current biologic therapy directionally more frequently for reported unvaccinated patients than those who are vaccinated (5.5% vs 3%).

Conclusion: EU4+UK gastroenterologists sampled in this study appear to be more comfortable advising COVID-19 vaccinations to older patients, who are stable on their biologic therapy and are in remission, having a physician-defined controlled case of CD, and lower disease scores. COVID-19 impact may not have been top of mind for gastroenterologists; patient status played a more considerable role in defining a biologically treated CD patient's suitability for COVID vaccination.

These findings align with clinical guidelines in relation to COVID vaccinations for those with autoimmune disease or immunocompromised status, helping to protect this vulnerable cohort from more severe disease outcomes and increased rates of hospitalisation. Further investigation using comparator cohort is warranted.

Disclosure: Nothing to disclose.

P1021

THE SAFETY OF ENDOSCOPY UNITS DURING THE COVID-19 PANDEMIC

M.G. Gonçalves¹, A. Guimarães¹, T. Carvalho¹, P. Antunes¹,
S. da Silva Mendes¹, J.B. Soares¹, B. Arroja¹, A. Rebelo¹,
R. Gonçalves¹

¹Braga Hospital, Department of Gastroenterology, Braga, Portugal

Contact E-Mail Address: margaridagoncalves21@gmail.com

Introduction: The COVID-19 pandemic drastically changed the daily routine of all healthcare systems worldwide and endoscopy units were no exception. Endoscopic exams were considered to have a high risk of transmission, and therefore the safety of endoscopy units and the consequent need for pre-endoscopy SARS-CoV-2 screening were questioned early on.

Aims & Methods: The aim of our study was to assess the safety of endoscopy units during the COVID-19 pandemic, as well as the effectiveness/necessity for SARS-CoV-2 screening prior to endoscopies. This is a prospective and single-center study carried out in a Portuguese Tertiary Hospital. All patients who underwent endoscopic procedures between 1st September of 2020 and 28th February 2021 were included. The pre-endoscopy screening consisted of a specific questionnaire or a RT-PCR test for SARS-CoV-2 (nasal and oropharyngeal swab). Data were obtained through patient's clinical records and the Trace COVID platform.

Results: A total of 2166 patients were included. Patients had a mean age of 61.8 years and were predominantly male (56.2%, n=1218). Eighty-one (3.7%) patients had previous SARS-CoV-2 infection, with a median difference of 74 days (IQ 40,5:160,5) between infection and endoscopy. Most patients (70.2%, n=1521) underwent PCR screening for SARS-CoV-2 up to 72 hours before the procedure, with the remaining patients (29.8%, n=645) answering a questionnaire of symptoms and risk contacts up to 3 days before endoscopy. Of the patients who underwent RT-PCR screening for SARS-CoV-2, 21 (1.4%) tested positive, and all were asymptomatic at the time of the screening. The evaluation for SARS-CoV-2 infection up to 14 days after the endoscopic exams, identified 9 positive patients (0.42%) for SARS-CoV-2. The median difference in days between endoscopy and the diagnosis of infection was 10 days.

Conclusion: Pre-endoscopy screening with RT-PCR test for SARS-CoV-2 identified a very small number of patients with COVID-19 infection as well as patients with COVID-19 infection in the following 14 days. Therefore, the risk of infection in endoscopy units is negligible if screening of symptoms and risk contacts is applied and individual protective equipment is used.

Disclosure: Nothing to disclose.

P1022

AN ELUSIVE MANIFESTATION OF COVID-19: DYSPHAGIA DUE TO ESOPHAGO-GASTRIC JUNCTION DISORDERS

A. Manolakis¹, A. Trikola², D. Chougias³, A. Papaefthymiou³,
A. Koffas⁴, F. Fytisilis³, N. Viazis², G.J. Mantzaris², A.N. Kapsoritakis¹,
S. Potamianos¹

¹University of Thessaly School of Medicine and University Hospital of Larissa, Department of Gastroenterology, Larissa, Greece,

²Evangelismos General Hospital of Athens, Department of Gastroenterology, Athens, Greece, ³University Hospital of Larissa, Department of Gastroenterology, Larissa, Greece, ⁴Royal Free Hospital, Gastroenterology, London, United Kingdom

Contact E-Mail Address: manolakis@uth.gr

Introduction: Throughout the COVID-19 pandemic, several symptoms have been attributed to severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection. SARS-CoV-2-induced thrombosis, olfactory migration and autoimmunity have been implicated in the onset of neurologic

manifestations. Meanwhile, dysphagia emerged as a rather rare, neglected COVID-19-related symptom, initially linked to intubation. Its occurrence, however, in non-intubated patients as well shows that the pathogenesis of post-COVID-19 dysphagia remains unclear.

Aims & Methods: To examine whether post-COVID-19 dysphagia results from esophageal motility disorder(s). Patients presenting with post-COVID-19 dysphagia between January 2021-March 2022, underwent esophagogastroduodenoscopy, esophagram, computed tomography and two esophageal high-resolution manometry (HRM) studies 4-8 months apart. HRM studies were performed using a system with a 15mmHg integrated relaxation pressure (IRP) threshold for the diagnosis of esophago-gastric junction (EGJ) disorders and the Chicago classification version 4.0. SARS-CoV-2 infection was documented through at least one positive reverse transcriptase polymerase chain reaction (RT-PCR) test.

Demographics, history of anti-SARS-CoV-2 vaccination, need for hospitalization, symptom profile and duration, Eckardt scores (ES), treatment modalities were also recorded. Informed consent was obtained along with approval from the Ethical Committees of the University Hospital of Larissa and Evangelismos General Hospital of Athens, Greece.

Results: Twelve patients (9 female; mean age±SD: 63±6years) were included, seven with new-onset dysphagia (median ES:7) and five with aggravation of pre-existing dysphagia (median ES:8 vs 3). Based on HRM, all patients with new-onset dysphagia had EGJ outflow obstruction (EGJ-oo) whereas those with pre-existing dysphagia exhibited type II Achalasia. No other major abnormalities were recorded.

A female predominance was evident in the EGJ-oo group (female:male ratio of 2.5:1). Median time (interquartile range-IQR) from positive RT-PCR until development of dysphagia was 20(6) days. Achalasia patients exhibited higher median IRP values compared to the EGJ-oo group: 22.5(1.7) vs 17.3(1.8) (supine position;P=0.006) and required pneumatic dilatation for resolution of symptoms. In patients with EGJ-oo, dysphagia resolved spontaneously over a median(IQR) of 4(3.5) months and upon second HRM no EGJ-oo was documented based on intrabolar pressurization pattern and IRP: 13.6(1) vs 17.3(1.8) (supine position;P=0.06).

No differences regarding vaccination status or symptomatic/asymptomatic infection were recorded. Only one patient was hospitalized and received corticosteroids while no patients received antiviral therapy. All patients had no signs of meningitis/encephalitis, Guillain-Barré syndrome or myopathy. In two patients with EGJ-oo who had anti-SARS-CoV-2 antibody testing at 3-4weeks and at 3.5-4months from RT-PCR positivity, improvement of dysphagia coincided with a marked 3-fold drop in anti-SARS-CoV-2 antibody titres.

Conclusion: Post-COVID-19 dysphagia may result from EGJ disorders either triggered or fueled by SARS-CoV-2 infection. New-onset dysphagia is associated with EGJ-oo and seems to decrease and resolve spontaneously over time.

This improvement seems to coincide with waning anti-SARS-CoV-2 immunity, indirectly suggesting an (auto)immune pathogenetic pathway. On the other hand, post-COVID-19 aggravation of dysphagia corresponds to type II Achalasia and requires intervention in order to resolve.

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Disclosure: Nothing to disclose.

P1023

INFLAMMATORY BOWEL DISEASES DURING THE SARS-COV2 PANDEMIC ERA: THE EFFECTS OF COVID-19 ON PSYCHOLOGICAL STATUS AND DISEASE ACTIVITY

M.G. Demarzo¹, L. Caserta¹, B. Clivio¹, M.c. Parodi¹

¹Gastroenterology Unit, San Martino Hospital, Department of Surgery, Genova, Italy

Contact E-Mail Address: mgiulia.demarzo@gmail.com

Introduction: Covid-19 pandemic is responsible for a dramatic increase in mental health problems in the general population. Some categories have been identified to be at higher risk of psychological distress, such as people with pre-existing mental diseases, people from a lower socioeconomic background and young adults. There is a close correlation between stress and gastrointestinal symptoms¹.

Studies have shown that negative experiences may influence the immune system and cause illness. Particularly, inflammatory bowel disease (IBD) is known to may be exacerbated by negative emotional experiences².

Aims & Methods: The aim of our study was to evaluate the health-related quality of life (HRQoL) and the perception of stress in IBD patients affected by Covid-19 compared to IBD subjects who never got Sars-CoV-19 infection.

We recruited 41 IBD patients affected by Covid-19 and 43 age- sex- and race matched IBD controls in clinical remission. All patients were asked to complete by mail both the Short IBD Questionnaire (SIBDQ) and the Perceived Stress Scale (PSS) between September and December 2021. The evaluation was completed by telephone interview. Disease activity was assessed by the Harvey-Bradshaw Index (HBI, remission defined by HBI<5) for Chron Disease (CD) patients and by partial Mayo score (PMS, remission defined by PMS<2) for Ulcerative Colitis (UC) patients.

The primary endpoint was to determine the influence of Covid-19 on HRQoL of IBD patients. Secondary outcome was to observe if Covid-19-induced stress can exacerbate IBD disease activity.

Results: All 43 (100%) IBD controls filled in both questionnaires whereas only 29 (71%) Covid-19 positive patients completed both forms. No patient included experienced severe disease. Median age was 47 [(25-82 years, Covid-19 positive patients), (23-84 years, IBD controls)] in both groups; approximately half of population was male (n=16, 55%; n= 22, 51% in Covid-19 positive and control patients, respectively).

Considering the type of disease, we noticed a slight preponderance of Ulcerative Colitis among both patients (n=19, 66%) and controls (n=27,63%). Covid-19 patients had higher self-perceived stress compared to controls ($p=0.03$).

No difference was observed in SIBDQ between the two groups ($p=0.2$). Contracting Covid-19 was associated to a higher stress level (RR 1.54, 95% CI 1.16-2.04) and to an increased risk of disease flare (RR 2.15, 95% CI 1.17-3.95). Nevertheless, the health-related quality of life is quite similar (RR 1.25, 95% CI 0.91-1.72) in both IBD Covid-19 patients and controls.

Conclusion: Covid-19 appears to significantly influence psychological status of IBD patients compared to controls and to be associated with clinical recurrence in our cohort. Surprisingly HRQoL seems to be unaffected by Covid-19. Longer follow-up and larger sample size are needed to confirm our results.

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Disclosure: Nothing to disclose.

P1024

PARAMETRIC IMAGING WITH CONTRAST-ENHANCED ULTRASOUND (CEUS): A NOVEL APPROACH TO ASSESS SMALL BOWEL MANIFESTATION IN SEVERE COVID-19 DISEASE

H. Tews¹, A. Kandulski², S. Schmid³, S. Schlosser¹, S. Schirner¹, F.-J. Putz⁴, L.-S. Cosma¹, K. Gülow¹, M. Müller-Schilling¹, E.-M. Jung⁵

¹University of Regensburg, Departement of Internal Medicine, Regensburg, Germany, ²University Hospital Regensburg, Department of Internal Medicine, Regensburg, Germany, ³University Hospital Regensburg, Internal Medicine I, Regensburg, Germany, ⁴University of Regensburg, Department of Nephrology, Regensburg, Germany, ⁵University of Regensburg, Department of Radiology, Regensburg, Germany

Contact E-Mail Address: Hauke.Tews@ukr.de

Introduction: In this study, we investigate the effects of SARS-CoV-2 infection on the small intestine using state-of-the-art ultrasound methods including parametric analysis. In terms of intestinal diagnosis, CEUS is of particular importance for diagnosis and follow-up of structural bowel disease.

In pathophysiology of severe COVID-19 disease, a combination of hyperperfusion in the context of a systemic cytokine storm and hypoperfusion in the context of microemboli is suggested to account for COVID-19 affection of the small intestine.

Aims & Methods: The aim of our work was to evaluate the increasing evidence of gastrointestinal tract involvement during SARS-CoV-2 infection using CEUS. An additional focus was to enhance understanding of the nature of small intestinal involvement based on image morphology and to gain insight into pathophysiology using parametric analysis. We studied thirteen patients with severe SARS-CoV-2 infection. Modern ultrasonography with elastography, CEUS and parametric analysis was performed.

CEUS examinations of critically ill patients and the performance of intra-operative CEUS are supported by the new guidelines of the "European Federation of Societies for Ultrasound in Medicine" (EFSUMB). Contrast-enhanced computed tomography with an arterial, portal venous, and venous phase served as the reference method.

Results: Thirteen patients (8 male/5 female) with a mean age of 54 years were included in the study. Eight patients suffered from obesity of varying degrees. 85% of the severely ill patients had not been vaccinated against SARS-CoV-2. Delta variant of SARS-CoV-2 was the dominant variant in the study cohort. Five patients required ECMO therapy. Using CEUS microbubbles entered the intestinal lumen in 7 patients.

Early contrast enhancement in the mesenteric vessels was seen in 4 patients and very early contrast enhancement in one patient. A combination of segmental early and delayed contrast enhancement in the small intestine was detected in 5 patients.

Conclusion: Intestinal barrier disruption resulting from SARS-CoV-2 infection is common. Parametric analysis of contrast-enhanced ultrasound (CEUS) allows assessment of perfusion and of barrier disruption in the small intestine. We assume that intestinal barrier disruption in severe COVID-19 disease is a combination of hyperemia in the setting of systemic infection and hypoxemia in the setting of microemboli in a subset of patients.

Disclosure: Nothing to disclose.

P1025

THE IMPACT OF COVID-19 ON GASTROENTEROLOGY DEPARTMENT

D.I. Negru-Vodă¹, A. Stemate¹, E. Guluta¹, T. Spataru¹, L. Negreanu²

¹Carol Davila University of Medicine and Pharmacy, Gastroenterology Department, Emergency University Hospital, Bucharest, Romania, ²Spitalul Universitar de Urgență București, Internal Medicine Gastroenterology, Bucharest, Romania

Contact E-Mail Address: delia-ionela.mihop@drd.umfcd.ro

Introduction: There have been more than two years since a small particle known as Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-COV2) came to our lives to completely change them and a lot of other functional rules. As a consequence, the extent of this pandemic led to a transformation of many hospital departments into places used to attend patients with Coronavirus Disease (COVID-19).

In this context, the usual activity of the Gastroenterology Department in the Emergency University Hospital of Bucharest has temporarily changed, becoming a COVID-19 Department, where we noticed an increased prevalence of liver injuries associated with this disease.

Aims & Methods: We conducted a retrospective observational study, aiming to evaluate clinical and paraclinical characteristics of patients with COVID-19 and to investigate the impact of liver injury on COVID-19 severity. There have been included all the patients admitted to the Gastroenterology Department with moderate to severe SARS-COV2 infection from the period of January 1, 2020 to November 30, 2021. They were followed up to the discharge, death or transfer to other hospitals.

We created and analyzed a database from electronic health records, including demographic data, associated pathologies, symptoms on admission, results of biologic and imaging studies performed in our department, the requirement of Intensive Care Unit (ICU) admission and mechanical ventilation, length of hospitalization and mortality.

Results: From 816 patients older than 18 years old and without previously known liver disease, 284 (34,80%) of them presented liver injury (defined as an abnormal value of alanine transaminase, aspartate transaminase, alkaline phosphatase, gamma-glutamyl transferase or total bilirubin more than 2 times over the upper limit of normal on admission). Hepatic impairment at diagnosis was associated with pre-existing metabolic syndrome, pulmonary afflictions or acute hepatitis B.

After excluding the transferred patients, we remarked that a higher proportion of subjects included in the liver injury group needed ICU admission comparing to the other group (44.84% versus 37.80%, $p < 0.05$).

Furthermore, the requirement of mechanical ventilation was more increased in the first group (44.84%) whereas in the second one only 38.24% of the patients needed a modality of mechanical ventilation ($p = 0.05$).

The results of logistic regression analysis after the adjustment for sex, age and presence of cardiovascular, lung, oncologic comorbidities and metabolic syndrome confirm that liver injury on admission is the secondly most important risk factor after the age, for the mortality.

There have not been observed significant statistical differences between hepatic impairment group and the group without it on: sex, vaccination status, digestive symptoms on admission, inflammatory syndrome, length of hospital stay or cycle threshold values.

Conclusion: The results of this study are consistent with the hypothesis that hepatic function impairment in patients with COVID-19 represents a negative prognostic factor concerning ICU admission, the requirement of mechanical ventilation and mortality.

Disclosure: Nothing to disclose.