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ABSTRACT

Abstract Code: NGS15540-87 | The many faces of Wnt: A regulator of proliferation, differentiation, and cell death in the enteric nervous system

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Objective: The proper function of the enteric nervous system (ENS) critically depends on cellular homeostasis and a stable histoarchitecture of neural and non-neural cells within the gut wall. However, the molecular mechanisms regulating this equilibrium are still enigmatic. Our work follows the hypothesis that Wnt-signaling is centrally involved in tuning proliferation, differentiation, and death of ENS cells.
Methods: We systematically evaluated the influence of Wnt agonists (Wnt3A, R-Spondin1) and antagonists (Dkk1) on isolated murine and patient-derived ENS progenitor cells using proliferation and cell death assays as well as gene expression analyses and immuno-profiling of established differentiation markers. Moreover, we employed immunohistochemistry and in-situ hybridization in full thickness murine and human resectates to map the expression of relevant components of the Wnt-signaling cascade in intact intestinal tissues.
Results: The Wnt agonists Wnt3A and R-Spondin1 exhibited strong and significant pro-proliferative and neurogenic effects on murine and human patient-derived ENS cells in culture. Moreover, after inducing neural differentiation, we found a significant regulation of at least 35 genes relating to Wnt pathway activity control that was paralleled by a marked decrease in the proliferative capacity of cultured ENS cells. Intriguingly, the Wnt-pathway antagonist Dkk1 also increased the proliferation in ENS cells. However, this was followed by a high rate of cell death indicating that these cellular programs are controlled by Wnt-signaling intertwined into a complex and highly ramified regulatory network. Additionally, the localization of Wnt-signaling components we detected in enteric neurons and glial cells, both in mice and human resectates underlines the significance of our results for the in vivo situation.
Conclusions: Wnt-signaling plays a central role in the regulatory network responsible for maintaining the cellular homeostasis and cytoarchitecture of the ENS. By transferring our results from rodent models to patient-derived in vitro systems, we were able to show that Wnt-signaling took root deep in mammalian evolution making our findings directly useful for the understanding of basic patho-mechanisms of enteric neuropathies in development and aging.

Abstract Code: NGS15526-91 | Prevalence and risk factors of gastroesophageal reflux disease in Bulgaria: An internet-based survey

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Objective: Gastroesophageal reflux disease (GERD) involves classic symptoms of heartburn and/or regurgitation. It is a highly prevalent disease with significant economic impact and reduction in patient health-related quality of life. The global pooled prevalence of GERD is approximately 14.00% and varies significantly according to the region and country. More population-based studies are needed, especially in geographical regions lacking epidemiological data on the prevalence of GERD, such as Eastern Europe, particularly Bulgaria.
Methods: This cross-sectional, population-based study aimed to evaluate the prevalence of GERD in Bulgaria, and to assess the risk factors associated with this disorder. An internet-based health survey was sent to Bulgarian adults. Individuals were invited to complete an online questionnaire on general and GI health. The aim of the study was not explicitly stated. No personal identification data was collected (fully anonymized). The survey collected data on socio-demographic and behavioral characteristics, validated questions to assess GERD, diagnostic questions based on Rome IV criteria to assess irritable bowel syndrome (IBS) and functional dyspepsia (FD), and questions about antisecretory drugs usage.
Results: Data was collected from 1896 individuals (mean age = 35.5 years, SD = 11.7, 73.1% females). The prevalence of GERD in the study population was 26.2%, of which 8.45% had PPI-refractory GERD. Age ($P = 0.02$), BMI ($P < 0.001$), marital status ($P = 0.03$), occupation ($P < 0.001$), sexual problems ($P < 0.001$), FD ($P < 0.001$), and IBS ($P < 0.001$) were significantly associated with GERD prevalence. Patients with FD ($P < 0.001$; OR 5.38), patients with IBS ($P = 0.03$; OR 1.07), and with higher BMI ($P < 0.001$, OR 1.05) were at an increased risk of having GERD.
Conclusions: The first data on IBS prevalence in the adult population in Bulgaria has been reported. Disorders of gut-brain interaction have a significant impact on the prevalence of GERD. GERD prevalence shows differing associations, suggesting differences in pathophysiological processes.

Abstract Code: NGS15594-96 | Elevated cytokine response in reflux hypersensitivity

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Reflux Hypersensitivity (RH) is a new term that characterized by non-pathologic acid exposure and normal upper-GI endoscopy with a positive relationship between reflux episodes detected with ambulatory pH monitoring and typical symptoms. The best knowledge of the pathogenesis is related with the acid-sensitive receptors on afferent nerves within the acidic microenvironment in the esophageal epithelia. However, the data about the mechanisms underlying mucosal-inflammation is still limited. Therefore, we aim to determine the managing cytokines effect on "micro-inflammation" in those patients.

13 patients and 20 healthy-controls (HC) underwent Solid-State esophageal high-resolution manometry, 24-h impedance-pH monitoring and upper GI endoscopy. 3 esophageal biopsies of each subject were taken and cytokine panel was evaluated with Multiplex-ELISA. The statistical analysis for the independent variables were made with the Independent Sample T-Test for normally distribution and the Mann-Whitney U test for non-normal distribution. Principal Component Analysis (PCA) was applied to identify clusters.

The levels of CCL7,IL-4 and IL-6 were normally distributed and significantly increased compared to healthy controls ($P < 0.05$) (Table 1). IL-8,CXCL12,CCL23,GM-CSF and CCL21 did not show normal distribution and were significantly higher than controls ($P < 0.05$). Considering the high loading values CCL7,IL-6,CCL21 and CCL23 were on first component. The second component included IL-4 and IL-8. CXCL12 and GM-CSF were on the fourth component. Chemotaxis-related markers such as IL-6,IL-8,GM-CSF,CCL23 showed that neutrophils, macrophages, lymphocytes, monocytes and pro-inflammatory response are activated in patients. However, higher levels of CCL7 and IL-4 indicated the role of Th2 response and anti-inflammatory process. Additionally, the increasing levels of CCL21 and CXCL12 proved there is a homeostatic process ongoing to balance the response. The presence of high IL-4 also suggests that T cell transformation is more in the direction of Th2 cells in these patients and hypersensitivity reactions are at the forefront through the induction of IgE release from B-cells. The higher levels of these cytokines despite non-pathological acid exposure indicate the "micro-inflammation" via immune cells in RH group. The proinflammatory and anti-inflammatory process are active together within the epithelium. The homeostasis is maintained in the epithelium because there is not an acidic exposure and mucosal damage.

		Mean (pg/ml)	SD	Median	Variance
GMCSF	RH	35,1	44,7	**15,1***	**2001,8**
	HC	13	8,6	11,1	74
IL-4	RH	**3,0***	**2,1**	2,6	4,6
	HC	1,8	0,7	1,8	0,5
IL-6	RH	**2,4***	**1,4**	2	2
	HC	1,6	0,7	1,6	0,5
IL-8	RH	26,2	35,4	9,2	1252,4
	HC	7,5	16,9	3	286,6
CCL7	RH	**18,7***	**7**	15,2	48,7
	HC	13,5	6,4	12	41,5
CCL21	RH	96,1	95,1	**44,7***	**9042,6**
	HC	48,9	67,7	22,4	4588,6
CCL23	RH	17,9	24,4	**11,3***	**595,1**
	HC	7,8	4,9	7,7	24,1
CXCL12	RH	115,5	94,8	**84,1***	**8982,9**
	HC	40,4	20,2	33,8	408,6

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Abstract Code: NGS15510-84 | Differences in symptomatic and autonomic profiles in co-morbid irritable bowel syndrome and hypermobile Ehlers-Danlos Syndrome vs. irritable bowel syndrome alone

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Objectives: Studies have demonstrated a high prevalence of Functional Gastrointestinal Disorders (FGID), particularly irritable bowel syndrome (IBS) in patients with Hypermobile Ehlers-Danlos Syndrome (hEDS) and hypermobility spectrum disorders (HSD). We aimed to identify if those with overlap IBS and hEDS/HSD form a distinct phenotypic profile compared to IBS alone.

Methods: Case-Control study of females with overlap IBS and hEDS/HSD and IBS alone. Overlap group consisted of females with an established diagnosis of hEDS/HSD referred to Neurogastroenterology clinics. Patients underwent telephone interviews assessing for IBS using ROME IV criteria. Those meeting the criteria were included ($n = 60$). IBS alone group consisted of females with an established diagnosis of IBS previously seen by a hospital gastroenterologist. Patients underwent a video call to assess for presence of IBS using ROME IV and exclusion of hEDS/HSD using Beighton scoring system (≤3) and 5-point joint hypermobility questionnaire (<1) ($n = 50$). Both groups were issued with the following questionnaires: Irritable Bowel Syndrome Symptom Severity, Gastrointestinal Symptom Rating Scale, Visceral Sensitivity Index Score (reverse

scored), Patient Health Questionnaire Adjusted, Hospital Anxiety and Depression Scale, Quantitative measure of autonomic symptoms, and Health related Quality of Life. Continuous variables were summarised by mean and standard deviation and analysed using an unpaired t-test; significance set at $P < 0.05$.

Results: Patients with overlap IBS/hEDS had an increased IBS symptom severity (341.78 vs. 279.86; $P < 0.0001$), increased non-GI related somatization scores (15.97 vs. 8.6; $P = <0.0001$), higher prevalence of autonomic symptoms in all domains (41.37 vs. 26.14; $P = <0.0001$), and worse quality of life (47.08 vs. 65.86; $P = <0.0001$) than those with IBS alone. Patients with IBS alone had increased visceral sensitivity index scores than those with overlap IBS/hEDS (54.4 vs. 45.02; $P = 0.002$).

Conclusions: These results suggest that the overlap hEDS/IBS cohort may be a distinct phenotype governed by marked autonomic symptoms, increased prevalance of chronic pain and a lower visceral sensitivity index. These patients are more complex and have more multicomorbidity than those with IBS alone and may benefit from multidisciplinary treatment managing autonomic aspects as well as GI issues.

Abstract Code: NGS15372-90 | Sleep quality and insomnia are associated with a lower quality of life in functional dyspepsia

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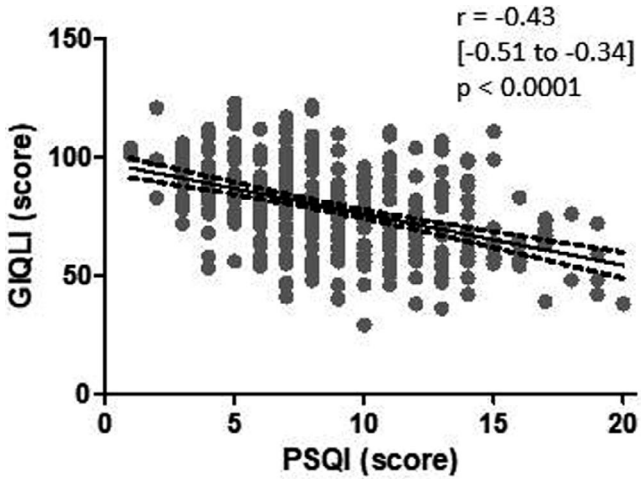
Background: Sleep disturbances are highly prevalent in patients with functional dyspepsia (FD) and are associated with worse symptoms severity, anxiety, depression, and productivity at work in this disease.

Objectives: Our aims were to assess the relationship between subjective sleep and quality of life (QoL) and to identify factors associated with poor sleep quality in FD.

Methods: 1,220 patients referred to our motility clinic between December 2017 and June 2019 were assessed using self-administered questionnaires: the TSS for the severity of symptoms, a 5-point Likert scale for heartburn, the GIQLI for GI-related QoL, the HADS for psychological distress, the PSQI for sleep quality and the ISI for insomnia. FD and its overlap with irritable bowel syndrome (IBS) were defined according to the Rome IV criteria.

Results: Among the total cohort, 355 patients with FD were identified (76.6% of women, mean age of 46.9 ± 15.7 years). Overlap with IBS was present in 44.8% of the patients. 81.4% had poor quality sleep; patients belonging to this subgroup were older, had a more altered QoL, a greater severity of their digestive symptoms and higher anxiety and depression scores. Sleep quality and QoL were correlated ($r = -0.43$ [95% CI: -0.51 to -0.34], $P < 0.0001$; see Figure 1). Independent factors predicting poor sleep quality were depression levels (OR: 1.40) and the severity of dyspeptic symptoms (OR: 1.28). Insomnia was found in 60.6% of the patients, with similar results.

Conclusions: We found a high prevalence of sleep disorders in patients suffering from functional dyspepsia. The presence of sleep disturbances was associated with altered QoL, higher severity of symptoms and higher psychological distress in this disease. Sleep quality and insomnia levels were correlated with GI-specific QoL.



Abstract Code: NGS15491-92 | Irritable bowel syndrome (IBS) and comorbid conditions: Relevance for symptoms and quality of life?

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Objective: Psychological distress, fibromyalgia and chronic fatigue are common in patients with IBS. A better understanding of the potential impact of this overlap on the overall severity of symptoms and quality of life in IBS is warranted. We aimed to use existing, large

European cohorts of IBS patients to retrospectively determine the effect of the comorbidities mentioned above on gastrointestinal (GI) symptom severity and quality of life (QoL).

Methods: IBS patients were recruited from five European centers, four cohorts from secondary/tertiary care (Barcelona, Gothenburg, Heidelberg, Maastricht) and one from primary care (Leuven). Validated cut-off levels from questionnaires or a doctor's diagnosis, were used to assess presence of psychological distress and somatic comorbidities. GI symptom severity was assessed using IBS-SSS or GSRS and QoL was measured with disease-specific IBS-QoL questionnaires (Hahn or Patrick & Drossman), or SF-36. The cumulative effect of mental and physical comorbidities on GI symptom severity and QoL was determined with linear contrast analysis, using standardized scores for GI symptom severity or QoL.

Results: 2403 patients with IBS were included in the analysis, 73.6% females. The prevalence of somatic and mental comorbidities in the different cohorts were common and is presented in Figure 1. Patients with comorbid conditions tended to be younger and more commonly females and patients with anxiety and/or depression or somatic comorbidities reported more severe GI symptoms and lower QoL than patients without these comorbidities. A gradual increase in GI symptom severity and a gradual decrease in QoL with increasing number of psychological and somatic comorbidities were seen in all cohorts combined, using groups of 0, 1, 2, and 3-4 comorbidities (GI symptom severity: - partial $\eta^2 = 0.10$, $P < 0.0001$; QoL: partial $\eta^2 = 0.30$; $P < 0.0001$).

Conclusions: By using large European IBS cohorts, we demonstrated that psychological distress, fibromyalgia or widespread bodily pain, and chronic fatigue are common among patients with IBS and increase overall GI symptom severity and decrease QoL. This should be taken into consideration when managing IBS patients in clinical practice.

Table: Baseline characteristics of IBS patients and prevalence of co-morbidities.

	Barcelona	Gothenburg	Heidelberg	Leuven	Maastricht
N	165	955	294	470	501
Female f/m (%)	112/53 (68%/32%)	719/236 (75%/25%)	211/83 (72%/28%)	348/113 (75%/25%)	367/134 (73%/27%)
Age median (range)	35 (18-64)	35 (18-76)	38 (17-78)	39 (18-83)	45 (17-79)
Anxiety, %	42%*	43%#	42%#	24%#	38%#
Depression n (%)	17%*	23%#	45%#	24%#	21%#
Fibromyalgia / widespread bodily pain n (%)	3%*	36%#	8%#	8%#	18%#
Chronic fatigue syndrome / severe fatigue n (%)	1%*	30%#	51%#	47%#	33%#
GI symptom severity £					
Psychological distress	P=0.11	P<0.001	P<0.001	P<0.001	P<0.001
Fibromyalgia/ Widespread pain	P=0.18	P<0.001	P=0.19	P<0.001	P<0.001
Chronic/ Severe fatigue	n/a	P<0.001	P<0.001	P<0.001	P<0.001
Quality of life £					
Psychological distress	n/a	P<0.001	P<0.001	P<0.001	P<0.001
Fibromyalgia/ Widespread pain	n/a	P<0.001	P<0.001	P<0.001	P<0.001
Chronic/ Severe fatigue	n/a	P<0.001	P<0.001	P<0.001	P<0.001

* Defined based on doctors' diagnosis
# Defined based on proxy measure from questionnaires
£ compared in patients with vs without comorbidities.

Abstract Code: NGS15496-97 | **In silico-based synergy assessment of the standardized herbal combination STW 5-II in functional dyspepsia**

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Background: Functional dyspepsia (FD) is a complex and heterogeneous disorder with multiple pathophysiological mechanisms. Therefore, the understanding of the precise molecular mechanisms of FD is challenging. STW 5-II, a combination of six plants (*Iberis amara L*, *Mentha piperita L*, *Matricaria chamomilla L*, *Glycyrrhiza glabra L*, *Carum carvi L*, *Melissa officinalis L*), is indicated for the treatment of FD and IBS symptoms in Germany.

Objective: In the present study we performed an *in silico* analysis to predict the potential FD target genes for the major native compounds in STW 5-II (n = 21). Validation of targets by Gene expression (GE) analyses (deep sequencing) and RT-PCR were undertaken in colon cells treated with either STW 5-II combination or each single herb.

Methods: Four databases were screened to identify the gene targets involved in FD pathogenesis. Compound-target networks for FD were constructed to elucidate relationships between STW 5-II's native compounds and FD targets. NCM460 cells were treated for 24 h with either STW 5-II combination, individual herbs, or omeprazole. RNA was isolated and gene expression (GE) analyses (1) and RT-PCR were performed.

Results: 96 genes have been identified as potential targets for FD. AKT1, NOS3, HSP90AA, TRPV and SMADs have been identified *in silico* as the most common targets for the different native compounds in STW 5-II. Their involvement was supported by GE-data (AKT1: 9.1f ($P < 0.01$), HSP90AA: 11.3f ($P < 0.01$), TRPV3: 3.1f ($P < 0.001$), SMAD3: 5.1f ($P < 0.01$). RT-PCR results further confirm the regulation of AKT1, NOS3 and SMAD2 by STW 5-II. Gene ontology and reactome pathway analyses of the GE-data indicate, among others, significant upregulations of cell motility (GO:2000145), epithelium development (GO:0060429), and the lipid metabolism (R-HSA-556833) by STW 5-II, whereas ATP regulated metabolic processes (GO:004634) were downregulated. The individual herbs in STW 5-II contributed differentially to its overall activity justifying the differential role of the six herbs in targeting different pathways in FD pathogenesis.

Conclusions: *In silico* and *in vitro* studies confirmed that STW 5-II is a multi-target herbal formula acting on relevant targets of FD. *In silico* tools validated by in *vitro* studies are useful to elucidate the complex molecular mechanisms of FD.

[1] Torre, D., Lachmann, A., and Ma'ayan, A. 2018

Abstract Code: NGS15524-89 | Distinctive plasticity of enteric glial cells in the jejunal mucosa of diarrhoea-prone Irritable Bowel Syndrome patients with and without bile acid diarrhoea

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Objective: To characterize the intestinal glial phenotype and potential association with clinical severity in bile acid diarrhoea (BAD) and diarrhoea-predominant Irritable Bowel Syndrome (IBS-D).

Methods: Mucosal jejunal biopsies were obtained from healthy volunteers (HV; n = 13) and age-matched diarrhoea-IBS meeting Rome III criteria (IBS-D; n = 21); bile acid malabsorption was assessed in IBS-D by SeHCAT rendering two subgroups of patients: IBS-D-SeHCAT+ (n = 9) and IBS-D-SeHCAT- (n = 12). IBS symptom severity score (IBS-SSS), life stress background (Holmes) and depressive (Beck's) symptoms were assessed. Gene expression in the jejunal mucosa of specific enteric glial cell (EGC) markers (S100 calcium-binding protein B(*S100β*), transcription factor SOX-10(*SOX10*)), neurotrophic markers (glial derived neurotrophic factor (*GDNF*), brain derived neurotrophic factor (*BDNF*)), and tight junction proteins (Zonula occludens-1(*ZO-1*), Occludin(*OCLN*) and Claudin 2(*CLDN2*) was evaluated by quantitative RT-PCR.

Results: No differences in clinical characteristics were found between IBS-D subgroups. Gene expression analysis showed significantly reduced expression of *SOX10* (IBS-D:0.81 ± 0.06; HV:1.06 ± 0.09; fold change (FC); $P = 0.016$), and the related neurotrophic factor *GDNF* (IBS-D:0.61 ± 0.05; HV:1.06 ± 0.01; FC; $P < 0.001$) in IBS-D compared to HV, without differences in *S100β* and *BDNF*. The epithelial integrity markers analysis showed higher expression of *CLDN2* in IBS-D compared to HV (IBS-D:1.36(0.98-2.54); HV:0.83(0.71-1.40); FC; $P = 0.069$), and no differences for other tight junction proteins. When stratifying by SeHCAT testing, the multiple comparison analysis between all groups was significant for glial markers and *CLDN2* (Figure 1). The greater differences in gene expression of glial markers were between IBS-D-SeHCAT- subgroup compared to HV, a down-regulation in all of them (*SOX10* $P = 0.035$; *S100β* $P = 0.105$; *GDNF* $P < 0.001$). However, the expression of barrier markers exhibited a significant increase of *CLDN2* expression only in the IBS-D-SeHCAT+ subgroup ($P = 0.043$), without differences in *ZO-1* and *OCLN*. The association between clinical symptoms and biological markers showed a negative correlation between *SOX10* and IBS-SSS ($r_s = -0.42$; $P = 0.015$) and abdominal bloating ($r_s = -0.57$; $P < 0.001$). Similarly, *GDNF* expression exhibited a negative correlation with IBS-SSS ($r_s = -0.42$; $P = 0.003$), abdominal bloating ($r_s = -0.43$; $P = 0.013$), as well as with the Beck's Inventory ($r_s = -0.42$; $P = 0.015$).

Conclusions: The jejunal mucosa of IBS-D patients without BAD exhibits distinct pattern of molecular markers expressed by EGCs compared to healthy control. ECGs related mechanisms might be involved in the pathophysiology and symptoms generation of IBS-D.

Figure 1. Multiple comparison of gene expression in jejunal mucosa in HV, IBS-D-SeHCAT+, IBS-D-SeHCAT-.

	HV	IBS- D-SeHCAT+	IBS- D-SeHCAT+ vs HV *P* value	IBS-D-SeHCAT-	IBS-D-SeHCAT- vs HV *P* value	*ANOVA P value*
SOX10 mRNA FC	1.14 (0.86-1.29)	0.92 (0.69-0.98)	0.379	**0.74 (0.51-0.98)**	**0.035 ***	**0.037 ***
S100β mRNA FC	0.94 (0.88-1.09)	1.02 (0.92-1.12)	> 0.999	0.85(0.65-0.92)	0.105	**0.038 ***
GDNF mRNA FC	1.04 (0.76-1.42	0.73 (0.60-0.77)	0.091	**0.49 (0.39-0.70)**	**<0.001 *****	**0.001 ****
CLDN2 mRNA FC	0.83 (0.71-1.40)	**2.17 (1.06-2.86)**	**0.043 ***	1.14 (0.93-1.51)	> 0.999	**0.048 ***

Abstract Code: NGS15581-92 | Long-term clinical efficacy and GERD rate of per-oral endoscopic myotomy (POEM) in the treatment of esophageal motility disorders: A systematic review and meta-analysis

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The long-term outcomes of per-oral endoscopic myotomy (POEM) in achalasia and other esophageal disorders are yet to be clarified. Recent data are scattered and may suffer from single-center bias. We performed a systematic review and meta-analysis of studies investigating long-term outcomes of POEM, with the aim to provide pooled data regarding clinical efficacy and safety (post-POEM reflux, AEs). We searched electronic databases (Medline/Pubmed, EMBASE, Scopus) for studies assessing outcomes after POEM, with a minimum median follow-up of 36 months. Pooled rates of clinical success and post-operative reflux were calculated. Sub-group analyses were performed based on manometry, orientation of myotomy, follow-up and disease duration, age and geography. To confirm the stability of our results, we performed the leave-one-out sensitivity analysis.

From 677 initial records, 11 studies satisfied the eligibility criteria. Studies were published between 2017 and 2021. All studies had retrospective design but one (prospective). Only one multicentric experience was included, with the majority being monocentric. Studies were based in USA (n = 6), in Mexico (n = 1) and in Asia (n = 4); only 1 European experience has been reported. A total of 2350 patients were included in the analysis, with a mean age of 50.13 +- 7.04 years (50.1% males). Median follow-up of all studies was 47.75 months. Manometric indication was achalasia in 95.4% (2241/2350), other non-achalasia motor disorders in 3.6% (89/2350). A total of 612 patients (26.7%) had received previous treatments, including 25 Heller myotomy. Pooled overall clinical success rate was 84.6% (I2 = 81.8%); at the sub-group analysis for achalasia indication the clinical success rate was 88.7 % (I2 = 69.1%). Pooled rate of overall post-POEM symptomatic reflux was 23.8% (I2 = 93.7%); in achalasia the rate was 18.2% (I2 = 95.4%). Pooled rate of severe AEs was 1.4% (I2 = 36.59%). Only 7 cases of post-POEM Barrett's esophagus have been found at a larger literature search.

According to our systematic review and meta-analysis, POEM for achalasia and non-achalasia motor disorders shows a satisfactory long-term efficacy, with an 84% success at a median follow-up of 47 months. Post-POEM clinical reflux seems to decrease over time, however long-term GERD objective monitoring is scarcely reported.

Abstract Code: NGS15576-96 | **Network modelling in chronic constipation**

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Background: Chronic constipation (CC) is a common condition affecting 14% of adults worldwide. Attributed to a complex – multifactorial – underpinning pathophysiology, CC remains both incompletely understood and difficult to treat. CC patients experience an array of interacting symptoms, with variable disease phenotypes, which at the moderate to severe end of the spectrum can worsen quality of life. By treating this complex heterogeneity in clinical features as a network, the underlying structure of symptom constellations may be revealed.

Objective: To characterise the network constellation of symptoms afflicting patients with CC.

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 with weighted undirected graphical networks, in effort to establish critical links between symptom and QOL domains, as well as derive eigenvector centrality (a measure of influence) of individual factors.

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 a Bayesian generative stochastic block model – an algorithm which permits common feature clustering - revealed the identification of six phenotypic symptom/QOL clusters. CC symptom phenotypes that were identified included the following: abdominal symptoms, rectal symptoms, dissatisfied, irritable, worried and a daily life disruptor (Figure 1).

Conclusions: In CC patients from a tertiary care setting there is significant interplay between clinical features which identify emotional factors such as stress, irritability, sadness and decreased self-confidence as significantly influential in the structure of the symptom landscape. Network modelling can reveal associations between symptoms and quality of life disruptors, permitting an improved understanding of this patient population. 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.

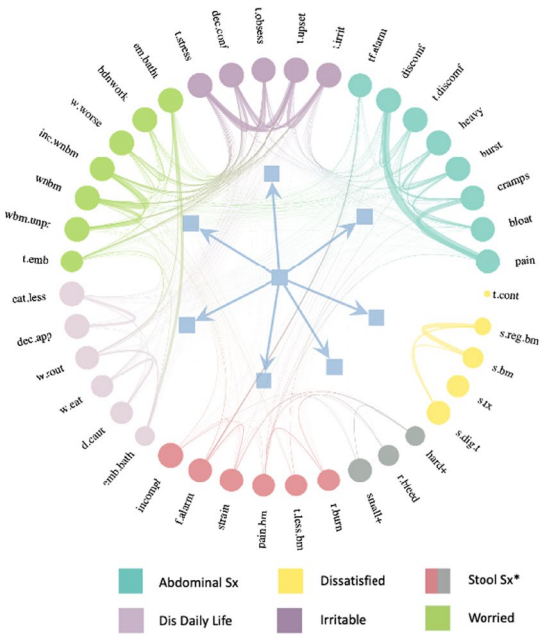

Figure 1: Stochastic block model illustrating the identification of six symptom/QOL domains in chronic constipation. *These spanned the following domains: abdominal symptom (teal), disrupted daily life [light purple], dissatisfied [yellow], irritable [dark purple], stool symptom [red and grey] and worried [green]*

Abbreviations: bdnwork: body not working; bloat: bloating; burst: bursting; cramps: stomach cramps; d.caut: diet caution; dec.app: decreased appetite; dec.comf: decreased confidence; dis: disrupted; discomf: discomfort; eat.less: eat less; em.batht: embarrassed of time in bathroom; emb.bath: embarrassed of going to bathroom; f.alarm: false alarm bowel movement; hard+: hard bowel movement; heavy: felt heavy; inc.wnbm: increased worry of no bowel movement; incompl: sensation of incomplete emptying; pain: pain in abdomen; pain.bm: painful bowel movement; r.bleed: bleeding after bowel movement; r.burn: burning after bowel movement; s.bm: satisfaction with bowel movement; s.dig.t: satisfaction with digestion time; s.reg.bm: satisfied with bowel movement regularity; s.tx: satisfaction with treatment; small+: small bowel movements; strain: straining during bowel movement; sx: symptoms; t.cont: time in control; t.discomf: time in discomfort; t.emb: time embarrassed; t.irrit: time irritable; t.less.bm: time with fewer less bowel movements than ideal; t.obsess: time obsessed; t.stress: time stressed; t.upset: time upset; tf.alarm: time with false alarm bowel movement; w.eat: worry about not choosing food; w.rout: worry about routine change; w.worse: worry condition will worsen; wbm.unpr: worry about unpredictable bowel movement; wnbm: worried about not having a bowel movement.

Abstract Code: NGS15538-94 | Gastrointestinal Permeability and Exercise intensity: Implications for anxiety and the gut-brain-axis

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Background/objective: The vital role of gastrointestinal barrier function and intestinal permeability is increasingly appreciated in health and disease. Shifts in intestinal barrier function might be able to impact the CNS via gut-brain axis signalling pathways. Evidence is accruing of an association between increased intestinal permeability and chronic low-grade inflammation and stress-related psychiatric disorders such asdepression. While exercise has beneficial effects in stress-related disorders, the mechanisms of action are currently unclear. It may transpire that the impact of exercise manifests as hormetic effects on gastrointestinal permeability and inflammation, by acting initially as an acute stressor that stimulates positive adaptation rather than deleterious consequences. This study assessed the impact of exercise training intensity (low, moderate, or high) on gastrointestinal permeability in sedentary healthy controls ($n = 35$), both acutely one hour post exercise and chronically over a 12-week duration following regular exercise training.

Methods: Assessments of fitness, mood, cognitive function and intestinal permeability were performed at baseline and on a monthly basis, throughout a 12-week exercise training programme (3-sessions/week). Intestinal permeability was assessed in plasma samples, pre-exercise and one-hour post-exercise, for each monthly visit using LPS-binding protein (LBP) and soluble cluster of differentiation 14 (sCD14) as biological markers.

Results: Preliminary analyses show regular exercise training to be associated with a significant increase in fitness ($P < 0.05$), measures of physical performance ($P < 0.001$), and a significant exercise intensity independent reduction in perceived anxiety ($P < 0.05$). Exercise had no benefits to on perceived stress levels, or depression, over the control group. Moreover, acutely, markers of intestinal permeability were unchanged one-hour post exercise. Chronically, a significant training effect ($P < 0.05$) on intestinal permeability, observed as a significant reduction in levels of both LBP and sCD14, was apparent for the moderate intensity exercise group.

Conclusions: Preliminary data shows that 12-weeks exercise training impacts on intestinal permeability, and reduced levels of perceived anxiety. Beyond being able to able the distinguish the therapeutic effects of exercise on mood, further research is needed to understand the downstream impact of exercise-induced alterations in gut barrier function for gastrointestinal physiology, inflammation, and gut-brain axis signalling, and the implications of chronic adaptation to exercise for health and disease.

Abstract Code: NGS15553-91 | Retention of small bowel video capsule endoscopy - Experience of an Irish Tertiary Referral Centre

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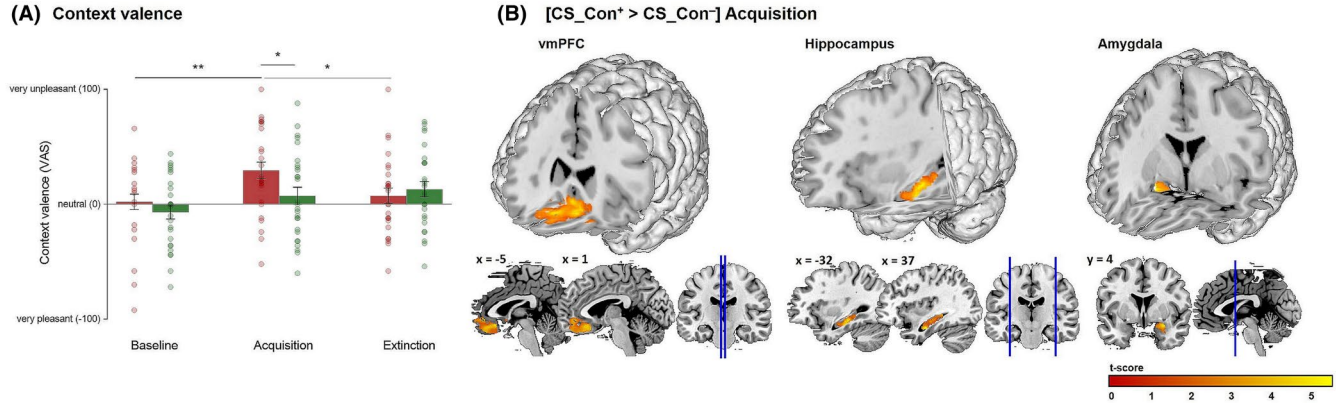
Introduction & Aim: Small bowel capsule retention is rare, approximately 2%, defined as visible retention on plain film of abdomen (PFA) after 14-days. Currently PFA is performed if the capsule is not seen to reach the large bowel during recording. Alternatively, for upper-gastrointestinal (UGI) capsule studies, risk of retention is determined if the capsule fails to reach the small bowel during recording. Given the similar physical specifications of the capsules (Medtronic) used, we hypothesize whether 14-day PFA is no longer required for small bowel capsules not observed in the large bowel.

Method: The use of patency capsule in our lab allows careful selection of small bowel capsule studies to minimise risk of retention. All PFAs performed over a 5-year period were reviewed to determine if careful selection and use of patency negates the need for capsule retention PFA screening.

Results: 688 small-bowel capsules were performed during the study period, 3% had prior patency capsule. 31 PFAs with a query of capsule retention were performed during the study period on 28 patients. This included 15 females, and the median age was 53.5 years. None of the films demonstrated evidence of capsule retention.

Conclusions: Our data suggest that 14-day PFA may no longer be required for capsules not seen to reach the large bowel. Advice regarding symptoms of capsule retention and precaution with magnetic resonance imaging, similar to current UGI capsule advice, may suffice. This may reduce the burden on radiology imaging slots and, in particular, eliminate unnecessary radiation exposure and rep



Abstract Code: NGS15474-93 | **When gut feelings teach the brain to fear pain: Context-dependent interoceptive pain-related learning and extinction in experimental visceral pain**

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Objective: Classical fear conditioning with experimental pain has provided important insights into the neural mechanisms underlying the acquisition and extinction of pain-related fear. However, patients' clinical reality is more complex, likely involving fear of multifaceted contexts rather than of isolated cues. Benign interoceptive sensations commonly experienced by patients suffering from disorders of the gut-brain axis may context-dependently become conditioned predictors of impending visceral pain. The relevance of contextual factors in shaping neural mechanisms underlying visceral pain-related fear learning, however, remains elusive. In a novel context-dependent interoceptive conditioning paradigm, we elucidated the putative role of the central fear network in the acquisition and extinction of pain-related fear induced by interoceptive cues and pain-predictive contexts.

Methods: In this fMRI study involving rectal distensions as a clinically-relevant model of visceroception, N = 27 healthy men and women underwent differential conditioning. During acquisition training, visceral sensations of low intensity as conditioned stimuli (CS) predicted visceral pain as unconditioned stimulus (US) in one context (Con^+), or safety from pain in another context (Con^-). During extinction training, interoceptive CS remained unpaired in both contexts, which were operationalized as images of different rooms presented in the MRI scanner.

Results: Successful contextual conditioning was supported by increased negative valence of Con^+ compared to Con^- after acquisition training, which resolved after extinction training (Figure 1A). Although interoceptive CS were perceived as comparatively pleasant, they induced significantly greater neural activation of the amygdala, ventromedial prefrontal cortex, and hippocampus when presented in Con^+ (Figure 1B), while contexts alone did not elicit differential responses. During extinction training, a shift from CS to context differentiation was observed, with enhanced responses in the amygdala, ventromedial, and ventrolateral prefrontal cortex to Con^+ relative to Con^-.

Conclusions: Context-dependent interoceptive conditioning can turn benign interoceptive cues into predictors of visceral pain that recruit key regions of the fear network. This first evidence expands knowledge about learning and memory mechanisms underlying interoceptive hypervigilance and maladaptive avoidance behavior, with implications for disorders of the gut-brain axis.

FIGURE 1. (A) Changes in context valence across experimental phases and (B) interoceptive CS-induced differential neural responses involving key regions of the central fear network

Abstract Code: NGS15502-85 | **The combined faecal short-chain fatty acids and microbiota profile predicts the response to a gluten-free diet in irritable bowel syndrome (IBS)**

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Objective: A gluten-free diet reduces symptoms in some patients with IBS through unclear mechanisms. We aimed to identify predictors of response to a gluten-free diet in IBS.

Methods: During this double-blinded, randomised, placebo-controlled cross-over study, IBS subjects (n = 20) followed two 14-days gluten-free diet periods with either placebo or gluten (14g/day) powder sprinkled over their meals, separated by a wash-out period (≥14 days). IBS symptoms (IBS-SSS) and stool form (BSF) were reported. We defined a *true responder* by a decrease in IBS-SSS ≥50 *only* after the gluten-free period, all others were *non-responders*. Faecal samples were collected both before and after the diet periods. Microbiota profiles were provided by a 16S-rRNA test (GA-map Dysbiosis Test), and quantification of short-chain fatty acids (SCFAs) by liquid-chromatography mass-spectrometry on extracted faecal supernatants. The combined microbiota and SCFAs data were analysed with principal component analysis (PCA) and multivariate factor orthogonal partial least squares discriminant analysis (OPLS-DA).

The goodness of fit and predictability of OPLS-DA are represented by the R^2 and Q^2 values, respectively. A model with $R^2 \geq 0.5$ and $Q^2 \geq 0.4$ is considered as a good discriminative and predictive model.

Results: IBS symptom severity improved after the gluten-free period (308 (272–353) vs. 258 (192–364), $P = 0.02$) with less reports of loose stool types (4.2 (3.7–4.8) vs. 3.8 (3.2–4.5), $P = 0.01$), but not after the gluten containing period (IBS-SSS: 318 (273–378) vs. 286 (238–348), $P = 0.06$; BSF: 3.9 (2.7–5.2) vs. 3.7 (3.3–4.8), $P = 0.81$). The PCA scatterplot (Figure 1A) indicated that *true responders* (n = 6) and *non-responders* (n = 14) could be separated based on their SCFAs and microbiota profiles. The OPLS-DA model from before the gluten-free period had a good fit ($R^2 = 0.57$) and good predictive ability ($Q^2 = 0.41$) to identify *true responders* and *non-responders* to a gluten-free diet intervention (Figure 1B), comprising the 20 most discriminative bacteria/SCFAs between *true responders* and *non-responders* (Figure 1C).

Conclusions: IBS symptoms are reduced by a gluten-free diet in a subset of IBS patients, and the response to diet can be predicted by the combined faecal SCFAs and microbiota profile. This highlights the importance of the gut microenvironment in IBS, where food components, microbiota, and metabolites interact.

Abstract Code: NGS15539-95 | Efficacy and timing of a blinded powder reintroduction in IBS patients on a low FODMAP diet

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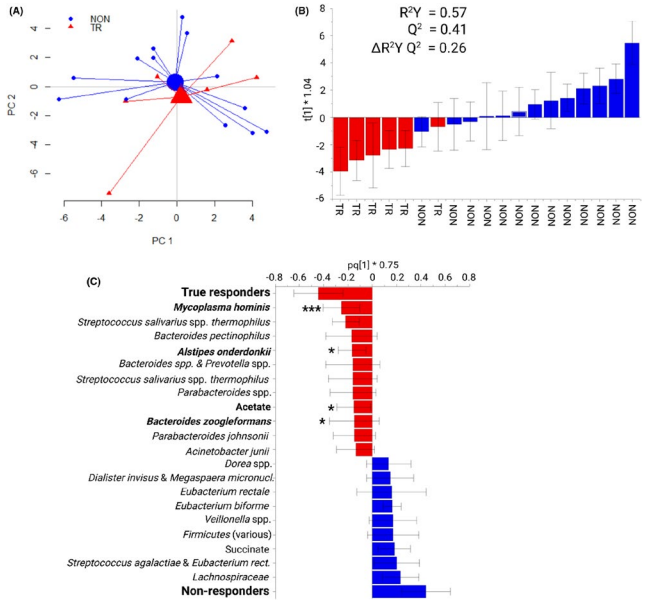
Objective: Several studies have established the efficacy of a low FODMAP diet for symptom control in patients with Irritable Bowel Syndrome (IBS). As the reintroduction phase is poorly structured, non-blinded and subjective, our aim was to develop a blinded reintroduction using FODMAP powders. In addition, we aimed to investigate the impact of the strict diet on quality of life, somatization, depression, and anxiety.

Methods: After baseline, tertiary care IBS patients followed a low FODMAP diet for 6 weeks. Responders to the strict diet, defined by a drop of ≥50 on Irritable Bowel Severity Symptom Severity Score (IBS-SSS), entered a reintroduction phase. Patients were challenged with 7 powders (fructans, fructose, GOS, lactose, mannitol, sorbitol, glucose) in a randomized blinded order. A rise in IBS-SSS (≥50) over the strict diet defined a trigger FODMAP. Changes in quality of life (IBS-QoL), somatization, depression (PHQ), and anxiety (VSI) were assessed. Patients filled out symptom diaries daily. Data were compared using paired Student's t-tests.

Results: Sixty IBS patients (34.9 ± 0.2years, 82% female, 24.9 ± 0.1kg/m^2) were recruited. IBS-SSS improved significantly after 2, 4, 6 weeks of strict diet compared to baseline (195 ± 14, 153 ± 14, 107 ± 13 vs. 306 ± 13, $P < 0.0001$, 88% response). Quality of life (19.9 ± 2.1 vs 32.3 ± 2.7, $P < 0.0001$), somatization (8.5 ± 0.5 vs. 12.4 ± 0.8, $P < 0.0001$), depression (4.4 ± 0.6 vs. 6.0 ± 0.3, $P = 0.001$), and anxiety (60.5 ± 2.4 vs. 51.7 ± 2.9, $P = 0.005$) improved significantly. Symptom recurrence was triggered in 84% of patients by an average of 2.1 ± 0.3 FODMAPs/patient. The most prevalent triggering FODMAPs were fructans and mannitol (52%), followed by GOS, lactose, sorbitol, fructose, and glucose (respectively 32%, 29%, 26%, 23% and 26%). Timing of symptom recurrence during intake of nutrients, showed a significant increase in abdominal pain already at day 1 for sorbitol (36 ± 9 vs 19 ± 6, $P = 0.01$), day 2 for fructans (32 ± 7 vs 16 ± 4, $P = 0.03$), mannitol (46 ± 10 vs 17 ± 4, $P = 0.003$), day 3 for lactose (32 ± 9 vs 18 ± 5, $P = 0.03$) and day 4 for GOS (39 ± 7 vs 20 ± 5, $P = 0.02$).

Conclusions: Significant benefit of the low FODMAP diet on symptom severity, somatization and depression is confirmed. A blinded reintroduction revealed a personalized pattern of symptom recurrence, with fructans and mannitol as the most prevalent triggers.



Significant symptom recurrence occurred already within the first 1 to 4 days of intake of trigger FODMAPs.

Abstract Code: NGS15464-92 | High amplitude propagated contractions with glycerin versus bisacodyl: A within subject comparison in children undergoing colonic manometry

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Introduction: The presence of high amplitude propagated contractions (HAPC) measured by colonic manometry (CM) reflect an intact

neuromuscular function of the colon. Bisacodyl and Glycerin are two colonic stimulants that induce colonic HAPC and are commonly used for the treatment of constipation. HAPC characteristics with each drug have not been compared before. We aim to compare the HAPC characteristics with Bisacodyl and Glycerin in constipated children undergoing CM.

Methods: This is a prospective multi-center cross-over study of children aged 2-18 years undergoing CM. We excluded patients with allergy to either drug, patients undergoing combined colonic and antroduodenal manometry as well as patients who had manometry catheter displacement. All patients received both Glycerin and Bisacodyl during CM. They were randomized to group A with Bisacodyl first and group B with Glycerin first, with 1.5 hours in between each dose. Categorical variables were described using percentages and compared by exact Chi-square test. The distributions of continuous variables were summarized using mean (sd), median (IQR), minimum and maximum and compared by Wilcoxon rank sum test.

Results: There were 21 patients recruited. Patients in protocol A (N = 11) had similar characteristics as patients in protocol B (N = 10) in all of the variables except age and BMI; patients in protocol B were older (mean = 7 vs 12 years of age for protocol A vs B respectively, $P = 0.013$) and had higher BMI z-scores (mean = -0.3 vs 0.6 in protocol A vs B respectively, $P = 0.012$). After adjusting for drug sequence for the carry-over effect and period effect, post-Bisacodyl HAPC cluster had a significantly longer duration (difference of 22 minutes, $P = 0.0015$) and a higher number of HAPC than the post-Glycerin (difference of 5 HAPC, $P = 0.0017$). Only one patient from protocol A had HAPC with Bisacodyl but not Glycerin.

Conclusions: Bisacodyl produces a higher number of HAPC with a longer duration of HAPC cluster compared to Glycerin. No significant differences were found in the onset of action, amplitude or distance of propagation.

Abstract Code: NGS15550-88 | Impact of ciprofloxacin exposure on small bowel excitatory and inhibitory neuromuscular pathways in young adult mice

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Objective: The European Medicines Agency (EMA) has recommended to restrict the use of fluoroquinolones for their disabling and potentially long-lasting adverse effects. The fluoroquinolone ciprofloxacin is a broad-spectrum antibiotic, widely used for treating gastrointestinal and abdominal infections with some potential adverse reactions, including neurotoxicity. Any change of microbial composition, elicited by antibiotics, could disrupt enteric nervous system (ENS) homeostasis, and lead to the onset of functional bowel disorders. This study aimed to assess the effect of ciprofloxacin on small intestinal neuromuscular response in young adult mice.

Methods: Male C57BL/6J mice (age = 8 ± 2 weeks; N = 52 mice) were orally gavaged with ciprofloxacin (50 mg/kg; CPX group) or with vehicle (tap water; CNTR group) for 14 days. In CPX and CNTR animals we evaluated: i) changes in motor response of isolated small intestinal segments, measured as changes in muscle tension following carbachol (0.001-100 μM), electric field stimulation (EFS, 0-40 Hz) or inhibition in non-adrenergic, non-cholinergic (NANC) conditions (EFS = 10 Hz, 1 μM atropine, 1 μM guanethidine), with or without 0.1 μM 1400W (inhibitor of inducible nitric oxide synthase, iNOS), or 100 μM L-NAME (pan-NOS inhibitor); ii) alterations in architecture and neurochemical coding of the myenteric plexus, analyzed by immunofluorescence distribution of HuC/D and nNOS neuronal markers, GFAP and S100β glial markers, and iNOS, alpha-synuclein and choline acetyltransferase (ChAT) in ileal longitudinal muscle-myenteric plexus preparations (LMMPs) or ileal frozen-sections.

Results: Ciprofloxacin treatment determined a marked decrease of cholinergic-mediated excitatory responses (-61% of carbachol Emax; -56% at 10 Hz-EFS; $P < 0.001$) and a significant reduction of ChAT immunoreactivity (-15%; $P < 0.05$). Ileal NANC-mediated relaxation, induced by both iNOS- and nNOS-derived NO, was also impaired and associated with a marked increase of iNOS immunoreactivity in LMMPs (+37%; $P < 0.01$). In the myenteric plexus of CPX mice, S100β and alpha-synuclein immunoreactivity significantly increased (+25% and +55%, respectively; $P < 0.01$), suggesting development of antibiotic treatment-induced enteric neuropathy.

Conclusions: Ciprofloxacin affects neuromuscular response, ENS architecture and neurochemical circuitry. Such changes are highly suggestive of a neurotoxic effect mediated by direct ciprofloxacin exposure and/or by indirect antibiotic-induced enteric dysbiosis, potentially contributing to foster functional bowel disorders later in life.

Abstract Code: NGS15373-91 | RNA sequencing of the oesophageal mucosa of patients with heartburn identifies dendritic cell population in functional heartburn

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Objective: The mechanisms underlying the most troublesome symptom of gastro-oesophageal reflux disease, heartburn, remain incompletely understood. The pathogenesis of heartburn in GORD is thus likely to involve the overlapping role of multiple mucosal factors including, 1) the integrity of the epithelial barrier, 2) expression of acid-sensitive receptors on nerve endings, and 3) mucosal inflammation. To identify gene markers associated with mucosal differences

between reflux phenotypes, we performed RNA sequencing in endoscopic biopsies of patients with heartburn.

Methods: RNA extracted from mucosal biopsies taken at endoscopy from 37 GORD patients phenotyped endoscopically and with objective reflux studies into EO (N = 10), NERD (N = 9), functional heartburn (FH) (N = 9), and Barrett's oesophagus (BO) (N = 9) and 7 healthy volunteers were sequenced using NEBNext Ultra II Directional RNA Kit and and NextSeq 500 High Output Kit. The corresponding patient samples were then stained with immunofluorescence with CD1a (Dako, M3571, 1:200) and CD3 (Dako, GA503, Ready-to-use) to confirm RNA-sequencing findings, and CD1a/CD3-positive cells were counted using FIJI.

Results: RNA sequencing analysis detected a higher Th2 cell presence in EO, FH and NERD compared to BO and healthy controls. Whilst presence of dendritic cells was detected in 4/7 healthy controls, EO and FH patients had higher levels of dendritic cell infiltration compared to BO and NERD patients. These findings were confirmed immunohistochemically, where CD1a-positive dendritic cell infiltration was significantly highest in the FH oesophageal mucosa ($P = 0.0108$), and dendritic cells were most frequently localised around the papillae. There was no significant difference in T-cell infiltration among GORD phenotypes.

Conclusions: Compared with oesophageal mucosa of controls and BO patients, the mucosa in patients with EO, FH and NERD had a significant increase in Th2 cell infiltration, suggesting the priming of the mucosa for a humoral or antibody-mediated immune response against extracellular toxins. Moreover, dendritic cell infiltrates predominantly in the FH oesophageal mucosa are likely to release paracrine factors which may heighten the sensitisation of nociceptive nerves and participate in oesophageal hypersensitivity in heartburn patients.

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Abstract Code: NGS15045-87 | Direct optogenetic stimulation of smooth muscle cells to control gastric contractility

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Objective: Antral peristalsis is required for sufficient gastric emptying. In gastroparesis, dysfunction of interstitial cells of Cajal (ICC) and enteric neurons leads to its failure and in return to burdening symptoms. Current treatment options, including gastric electrical stimulation, often are non-satisfying and fail to restore gastric emptying. In this work, we explore the feasibility of direct optogenetic stimulation of smooth muscle cells (SMC) via the light-gated non-selective cation channel Channelrhodopsin2 (ChR2) to control gastric motor function.

Methods: We used a transgenic mouse model expressing ChR2 linked to eYFP under the control of the chicken-β-actin promoter. Patch clamp experiments were conducted to quantify light-induced currents in isolated SMC. In antral smooth muscle strips, light-induced Ca^{2+} signals as well as isometric force were analyzed. Intraluminal pressure and in turn propulsion of gastric contents were quantified in intact stomachs upon light stimulation as well as pharmacological stimulation with 10 µM carbachol and global depolarization by 60mM K^{+}. Moreover, optogenetic stimulation was performed in a gastroparesis model induced by neuronal- and ICC-specific damage based on methylene blue photo-toxicity.

Results: In gastric tissue samples, membrane-bound eYFP signals were found in 36 ± 3% (n = 5) of SMC in which blue light (460 nm) induced inward currents typical for ChR2. These depolarizing currents led to contractions of antral smooth muscle strips with higher amplitudes than those triggered by supramaximal electrical field stimulation and comparable to those evoked by global depolarization, and induced light-triggered Ca^{2+} transients that spread from ChR2 positive SMC to neighboring negative SMC via gap junctions. In intact stomachs, panoramic illumination resulted in intragastric pressure increases, achieving 239 ± 46% (n = 6) in amplitude compared to the those induced by electrical field stimulation which induced gastric propulsion only in ChR2 expressing but not control wild type stomachs. While electric field stimulation responses were abolished within the gastroparesis model, light still efficiently generated pressure waves.

Conclusions: We herein demonstrate that direct optogenetic stimulation of SMC can be used to gain control over gastric contractility. In the future, restoration of motility in patients suffering from gastroparesis could be achieved by this novel approach.

Abstract Code: NGS15544-91 | IL-1-dependent enteric gliosis guides intestinal inflammation by modulating macrophage activation

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Background & Objectives: Enteric glial cells (EGC) modulate motility, maintain gut homeostasis, and contribute to neuroinflammatory mechanisms in intestinal diseases, including motility disorders. Interleukin (IL)-1 signaling plays a central role in intestinal inflammation activating various cell types, including EGCs. We investigated

the role of IL-1-triggered glia activation in intestinal neuroinflammation altering motility and macrophage activity.

Methods: We studied the impact of IL-1activated EGCs on disease progression in a mouse model of inflammation-induced motility disorder by applying various knock-out mouse lines deficient for critical components of the IL-1-signaling pathway such as Myd88, IL-1R1, IL-1α, and Il-1β. Histological and FACS analysis showed the impact on leukocyte infiltration, e.g., neutrophils and macrophages. Further RNA-sequencing glial-specific IL-1R1-deficient mice and primary EGC cultures treated with IL-1b provided a detailed view of functional differences following IL-1 activation. *In vitro* analyses of bone-marrow-derived macrophages treated to define the migration potential by transwell assays and the activation pattern by RNA-Sequencing after treating them with conditioned medium of EGCs.

Results: Glial-specific Myd88$^{-/-}$ and IL-1R1$^{-/-}$ mice are protected from inflammation-induced motility impairments and disease-typical leukocyte infiltration. RNA-Sequencing at early disease stages showed a distinct effect of glial IL-1-signaling-deficiency on gene clusters involved in macrophage activity and migration. Subsequent RNA-Sequencing in primary EGCs treated with IL-1β showed the upregulation of many factors involved in migration and macrophage differentiation supported the *in vivo* findings. Further *in vitro* studies proved the positive effect of EGCs on macrophage migration and the induction of their alternative inflammatory activation.

Conclusions: Glial IL-1 signaling modulates the development of motility impairments in intestinal inflammation by regulating macrophage activation and migration. IL-1 signaling blockage in EGCs is an effective treatment for inflammation-induced motility disorders and is a novel promising therapeutic approach.

Abstract Code: NGS15521-86 | Decoding early-life stress-induced comorbidities: Susceptibility to different domains of altered microbiota-gut-brain axis signaling

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Objective: Early life represents a critical neurodevelopmental window during which stressful insults can perturb the microbiota-gut-brain axis leading to the onset of visceral pain, often associated with depressive symptoms in adulthood. However, the biomolecular link between early life stress (ELS) and the increased susceptibility to visceral hypersensitivity and depression in adulthood is still unclear. Thus, we aimed to investigate the mechanistic basis for susceptibility or resilience to gut and brain dysfunction induced by ELS in a rat model of maternal separation (MS).

Methods: Male and female Sprague Dawley rat neonates were subjected to MS 3h/day (9 am-12 pm) for 11 days from postnatal day (PND) 2 to 12. In non-separated (NS, N = 30 rats[4 rat/litter]) and MS (N = 90 rats[4-5 rat/litter]) rat adult offspring (PND60) visceral sensitivity was assessed using colorectal distension (CRD). Forced swim test was performed to analyse depressive-like behavior. The behavioural data was standardized and combined to perform a two-step cluster analysis to identify natural groupings within the dataset. In female rats, cycle stage was monitored prior CRD. Changes in the gut microbiota composition (16S-rRNA sequencing) and metabolic profile will be assessed in stool collected from rat offspring before weaning.

Results: Female rats displayed significantly lower threshold and increased cumulative pain behaviors ($P < 0.01$) than males. Overall, MS rats showed a trend towards increased visceral hypersensitivity ($P = 0.1009$) compared to NS rats. Additionally, MS resulted in depressive-like behaviour in a sex-dependent manner ($P < 0.001$). The cluster analysis performed on the behavioural data revealed that MS rats could be stratified into four distinct behavioural phenotypes in response to ELS: resilient; depressive-like behaviour; visceral hypersensitivity; or a comorbid phenotype. Gut microbiota and metabolomics analyses are currently ongoing and will determine if the microbiota in early life reflects the different behavioral phenotypes induced by the MS.

Conclusions: Our study shows for the first time the presence of gut-brain behavioral phenotypes resilient or susceptible to ELS-induced visceral hypersensitivity and depression. Further analyses will determine whether the microbiome in early life predicts the individual phenotypes in adulthood, setting the base for developing precision microbiota-related protection strategies to prevent stress-induced disorders of the gut-brain axis interactions.

Abstract Code: NGS15495-96 | Integrated faecal microbiome-metabolome signatures reflect stress and serotonin metabolism in Irritable Bowel Syndrome

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Aims: To study the microbiome-gut-brain axis we aimed to identify profiles of fecal microbiota and metabolites associated with irritable bowel syndrome (IBS) and to specific phenotypes of IBS, and used metabolic reaction networks integrated with microbiota data to study the host-microbiome interaction.

Methods: Extensively phenotyped IBS patients (Rome III) and healthy controls (HC) were included in this cross-sectional analysis. Fecal metabolites were measured using proton-Nuclear-Magnetic-Resonance (^{1}H-NMR) spectroscopy. Gut microbiome was assessed by shot-gun-metagenomic-sequencing (MGS). Data were analyzed using Support-Vector-Machines for classification and regression, and kernel t-SNE to obtain unsupervised clustering of IBS for comparison with biological and clinical metadata.

Results: 314 subjects were included: 181 IBS, 133 HC. Fecal microbiome-metabolome profiles were associated to IBS and HC. These groups could be distinguished by metabolic phenotyping with an area-under-the-curve (AUC) of 79.5%, and by metagenomics data, with best AUC 77.3%, using microbial family taxonomic rank. This could substantially be improved by combining microbiota and metabolites; AUC 83.6% (Figure 1). There were no significant differences in predictive ability between three IBS subtypes based on predominant stool pattern when considering the microbiome-metabolome data. However, unsupervised clustering shows distinct subsets of IBS patients based on fecal microbiome and metabolome, associated to effects of psychological stress on gastrointestinal symptoms, onset of IBS after stressful events, levels of serotonin and its metabolite 5-hydroxyindoleacetate, medical history of previous abdominal surgery, dietary caloric intake and duration of IBS symptoms. Furthermore, metabolic reaction networks integrated with microbiota data provided insight in metabolic pathways.

Conclusions: Fecal microbiome-metabolome signatures for IBS were associated with altered serotonin metabolism and unfavorable stress response related to gastrointestinal symptoms. Host-microbiome interactions were reflected by pathways in metabolic reaction networks integrated with microbiota data. This supports the microbiota-gut-brain link in the pathogenesis of IBS.

Abstract Code: NGS15571-91 | **Contractility patterns and gastrointestinal movements monitored by a combined magnetic tracking and motility testing unit: A single case pilot study**

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Objective: Ingestible wireless capsules, including the 3D-transit electromagnetic capsule and the wireless motility capsule (WMC), describe gastrointestinal (GI) motility from changes in position or intraluminal pressure. This study aimed to combine information on contractile events in terms of position (assessed with the 3D-transit system) and change in pressure (assessed with the WMC) throughout the entire GI tract.

Methods: The 3D-transit capsule and the WMC were combined into a single-wireless unit system by tying the two ingestible capsules together. A single recording was performed in a healthy male. Three-dimensional space-time coordinates, pressure, and pH data were analyzed as the combined unit passed the GI tract. Major contraction patterns were defined according to pressure change over time. The contraction patterns were quantified for each GI segment and divided into four parts: stomach, small bowel, combined ascending, transverse and descending colon, and the rectosigmoid colon.

Results: The combined unit was well tolerated and passed the GI tract in 26 hours. Single contraction patterns with no significant progressive movement of the unit were most prevalent in the stomach and the rectosigmoid colon. Nine continuous contraction series were observed in the combined ascending, transverse and descending colon, where the two longest capsule movements moved the combined unit 24.4 cm and 51.7 cm along the 3D-trajectory of the colon (as measured with 3D-transit) with a motility index of 7.3 and 27.3 (as measured with the WMC), respectively. The motility indices (as measured with WMC) in combined ascending, transverse and descending colon were positively associated with capsule movements (as measured with 3D-Transit), both with a strong association to antegrade movements ($r = 0.7$, $P = 0.04$).

Conclusions: The combined system provides synchronous information about movements and gut contractions. These measurements can be used to extract more information from existing recordings and may enhance our understanding of GI motility in health and disease.

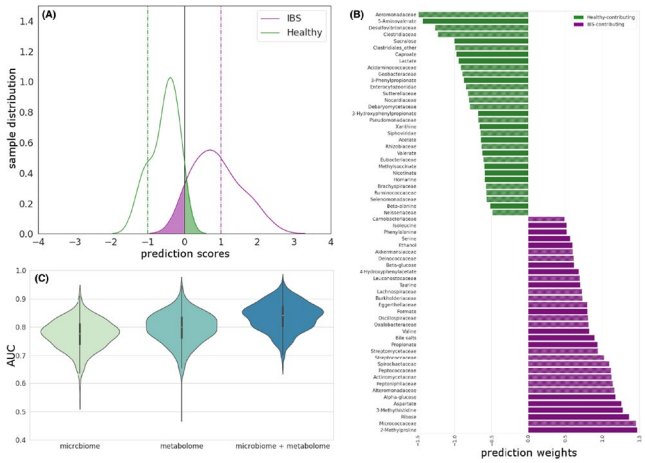

FIGURE 1. Examples of three-dimensional position (3D-transit) and pressure (wireless motility capsule) data. A) Capsule movement during continuous contraction (CC) series as shown in colors according to anatomical positions. B & C) Simultaneously pressure changes

during the movements of L1 (ileocecal junction) and L2 (descending colon).

Abstract Code: NGS15486-96 | Placebo response in pharmacological trials in patients with functional dyspepsia – A systematic review and meta-analysis

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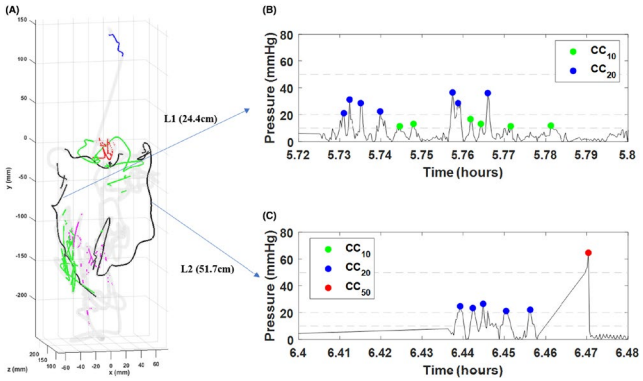
Objectives: Pharmacological trials in functional dyspepsia (FD) are associated with high placebo response rates. We aimed to identify the magnitude and the contributing factors to the placebo response.
Methods: We conducted a systematic review and meta-analysis including randomized controlled trials (RCTs) with a dichotomous outcome in adult patients with FD that compared an active pharmacotherapeutic treatment with placebo treatment. Our main outcome was identification of the magnitude of the pooled placebo response rate for the following endpoints: symptom responder, adequate relief responder, and combined endpoint responder (ie, the primary endpoint of each specific trial regarding treatment response). Several putative moderators were examined, including patient, disease, and trial characteristics.
Results: Of the 9829 publications identified, 25 RCTs were included in our analysis. The pooled placebo response rate was 33.4% (95% CI 26.9-40.6) using the symptom responder definition, 37.6% (32.1-43.5) using the adequate relief responder definition, and 35.6% (31.5-40.0) using the combined endpoint responder definition. A lower overall baseline symptom score was significantly associated with a higher placebo response rate. No other moderators were found to significantly impact the placebo response rate. Due to lack of data, no analyses could be performed according to individual FD subtypes or symptoms.
Conclusions: The pooled placebo response rate in pharmacological trials in FD is 33-38%. Future trials should consider applying an entry criterion based on minimal level of symptom severity in order to decrease the placebo response. We also suggest separate reporting of the core FD symptoms pending more concrete harmonization efforts in FD trials.



Abstract Code: NGS15542-89 | Symptoms and duodenal mucosal integrity of functional dyspepsia patients are improved by the low FODMAP diet

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Objective: The pathophysiology of FD remains poorly understood, but increased duodenal mucosal permeability and loss of tight junction molecule expression have been implicated. Adverse reaction to nutrients is an important candidate mechanism underlying these mucosal changes. Intragastric infusion of FODMAPs induced symptoms reminiscent of FD, with a rapid onset that precludes involvement of fermentation in the bowel. Our aim was to evaluate the effect of a low FODMAP diet on symptoms and mucosal permeability in FD.
Methods: Patients with predominant meal-related FD symptoms (PDS) followed the low FODMAP diet for 6 weeks. Throughout the study, patients filled out the Leuven PDS (LPDS) daily diary, scoring symptoms from 0 to 4 with a difference of 0.5 as clinically meaningful. In addition, patients filled out PAGI-SYM and PHQ. Before and after the diet, patients underwent an endoscopy with duodenal biopsies to evaluate mucosal integrity by transepithelial electrical resistance (TEER) and paracellular permeability for FITC dextran. In case of improvement, the strict diet was followed by a blinded reintroduction during which patients were challenged by 7 powders (fructans, fructose, GOS, lactose, mannitol, sorbitol, glucose). Results are compared by Student's t-test and Pearson correlations.
Results: Twenty-five FD patients (41 ± 2.9years, 81%female, 36%IBS overlap) completed the study. LPDS improved significantly after 2, 4, and 6 weeks of the strict diet (1.7 ± 0.1 vs 1.1 ± 0.2, 0.9 ± 0.1, 0.8 ± 0.2, $P < 0.0001$; 62% response), as well as individual scores for postprandial fullness, early satiation and bloating. In addition, PAGI-SYM (21.6 ± 2.7 vs. 40.3 ± 3.4, $P < 0.0001$), somatization (11.8 ± 1.1 vs. 13.5 ± 1.1, $P = 0.03$), and depression (5.7 ± 1.1 vs. 8.8 ± 1.3, $P = 0.0001$). Symptom improvement was associated with an increased TEER (23.9 ± 3 vs. 26.0 ± 2, $P = 0.045$) while flux was not significantly

altered (559 ± 75 vs 426 ± 41, $P = 0.14$). A large variety of FODMAPS were able to induce symptoms in a highly individualized pattern with on average 1.2 ± 0.5 FODMAPs/patient. Mannitol and GOS were the most prevalent triggering FODMAPs (29%), followed by fructans (21%), sorbitol (14%), fructose (14%), and lactose (12%).

Conclusions: A low FODMAP diet significantly improves PDS symptoms, as well as somatization and depression, associated with a restored duodenal mucosal integrity. Blinded reintroduction identifies a highly individual pattern of FODMAP triggers.

Abstract Code: NGS15575-95 | Transcutaneous vagal nerve stimulation as a potential treatment in functional gastrointestinal disorders: A meta-analysis of neuroimaging evidence

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

Objective: Using meta-analysis to identify the brain effects of active tVNS and sham stimulation in healthy participants.

Methods: 157 studies were identified from the Web of Science and PubMed databases, 4 of which were appropriate for statistical analysis, encompassing 60 participants (17 male, 27 female and 16 not provided). Using GingerALE meta-analysis of imaging data, activation likelihood estimation (ALE) at the cluster level was calculated. Studies were reviewed for concordance of brain activity in three domains: (1) tVNS vs. baseline; (2) sham stimulation vs. baseline; and (3) tVNS vs. sham stimulation.

Results: tVNS significantly increased activity in the insula, anterior cingulate, inferior and superior frontal gyri, caudate and putamen, with reduced activity in the hippocampi, occipital fusiform gyri, temporal pole and middle temporal gyri, when compared to null stimulation (Figure 1) (all $P < 0.005$). tVNS increased activity in the anterior cingulate gyrus, left thalamus, caudate and paracingulate gyrus and reduced activity in right thalamus, posterior cingulate cortex and temporal fusiform cortex, when compared to sham stimulation (all $P < 0.005$). Sham stimulation significantly increased activity in the insula and reduced activity in the posterior cingulate and paracingulate gyrus (all $P < 0.001$), when contrasted to null stimulation.

Conclusions: tVNS reproducibly activates brain areas implicated in the regulatory central autonomic network and deactivates pain processing nodes. Considering the centrality of dysautonomia to FGID pathophysiology, further therapeutic exploration of tVNS is warranted to determine if it can have therapeutic benefit in visceral pain. Brain activity differences between sham stimulation and null stimulation paradigms illustrate the importance of robust control stimulation procedures for future research.

Abstract Code: NGS15551-89 | Influence of sacral parasympathetic and thoracolumbar sympathetic nerve electrical stimulation on colonic motility in anesthetized Yucatan male pigs

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Background: The vagus (thoracolumbar and sacral) spinal nerves are the key autonomic nerves controlling colon motility. We recently showed that celiac branch of the vagus nerve electrical stimulation (ES) in pigs induces pancolonic motility response by involving, primarily, central network. The colon region-specific motility effects of spinal nerves ES is not well known.

Figure 1: Results of the activation likelihood estimation (ALE) analysis showing brain regions associated with (A) increased activity tVNS vs. null stimulation and (B) decreased activity tVNS vs. null stimulation.

Abbreviations: A, anterior; ALE, activated likelihood estimation; L, left; P, posterior; R, right.

Aim: Map the region specific colon motility response to thoracolumbar (T12-L1) and sacral (S1-S4) roots nerve stimulation (TNS and SNS) in an anesthetized porcine model, with or without anodal afferent (AB) or efferent (EB) block.

Method: In adult male Yucatan pigs (n = 8), a laminectomy was performed and unilateral (left root) SNS (S1-S4, 30 Hz, 0.3 ms, 0.5 mA, PT, 30 s ON/90 s OFF) was performed alone or concomitantly with AB or EB (40kHz, 0.1ms, 2mA), using cuff electrodes. In a separate study (n = 8), left root TNS (T12-L1, 10 Hz, 0.3 ms, 0.5 mA, continuous or 30Hz, 0.3 ms, 0.5 mA, PT, 30 s ON/90 s OFF) was done with needle electrode targeting afferent or both afferent/efferent fibers, without block. Proximal (pC), transverse (tC), distal (dC) colon and anal canal (AC) luminal manometric changes were monitored before, during and after stimulation. Area under the curve of contraction (AUC), luminal pressure heat-maps and frequency domain analysis of contractions were done.

Results: S2 ES induced a strong activation of motility in dC and AC during (mean change from baseline in %: 139.5 ± 67.1, $P < 0.05$ and 95.0 ± 59.3, respectively) and post stimulation. This activation was partially reduced by AB and EB in dC and only by EB in AC. S2 ES

also increased the power of whole contraction frequency spectrum in both dC and AC during stimulation (Figure 1). In contrast, S1, S3 or S4 ES had little effect on motility. TNS showed only moderate effect on motility of the different colonic regions and did not influence the contraction frequency spectrum.

Conclusions: In anesthetized male pigs, S2 ES induces a robust motility response in both distal colon and anal canal. It involves participation of central neural network for the distal colon, and efferent fibers in anal canal.

Abstract Code: NGS15606-90 | **Antroduodenal contractile function is diminished in type 1 diabetes with autonomic dysfunction: A novel analysis from wireless motility capsule pressure recordings**

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Objective: Antroduodenal hypomotility is a central component of diabetic gastroparesis syndrome and pylorospasm; however, detailed investigations are lacking. We hypothesized that impaired autonomic dysfunction contributes to dyscontractility. Thus, we aimed to differentiate contractility patterns of the antrum and duodenum in people with diabetes with (T1A) or without (T1N) autonomic neuropathy in comparison to healthy controls (HC) using wireless motility capsule (WMC) recorded pressure patterns.

Methods: Forty-four T1A, 43 T1N, and 19 HC underwent standardized WMC investigation. The antral and duodenal segments (10 min before and after passage across pylorus) were located, and antroduodenal transition time was noted. In each segment, the number of low (10-20 mmHg), medium (20-50 mmHg), or high (>50 mmHg) pressure peaks and motility index was obtained. Additionally, the motility index ratio between the antrum and duodenum segments was calculated.

Results: The antroduodenal transition time was prolonged in both T1A and T1N compared with HC (10.4 and 5.2 vs. 1.3 minutes, $P < 0.001$) and each other (10.4 vs. 5.2 minutes, $P = 0.004$). In the antrum, T1A had fewer high peaks than HC (1 vs. 3.5, $P = 0.02$), while no difference was seen to T1N. No difference was found for low peak, medium peak, and motility index. In the duodenum, T1A had fewer low and medium peaks (14 vs. 7, $P = 0.008$ and 6 vs. 3, $P = 0.01$) and a lower motility index than T1D and (7.7 vs. 8.6, $P = 0.008$) while no difference was seen for high peaks and in comparison to HC. The motility ratio was lower in T1N than both T1A (1.0 vs. 1.14, $P = 0.01$) and HC (1.0 vs. 1.12, $P = 0.02$)

Conclusions: The presence of autonomic dysfunction diminished antroduodenal contractility and prolonged transition time. Furthermore, the decreased numbers of antral high-pressure peaks, abnormal duodenal motility with lack of low/medium pressure peaks, and altered motility ratio indicate antroduodenal dyscoordination, and this could be considered as a therapeutically target in the future management of diabetic gastroparesis.

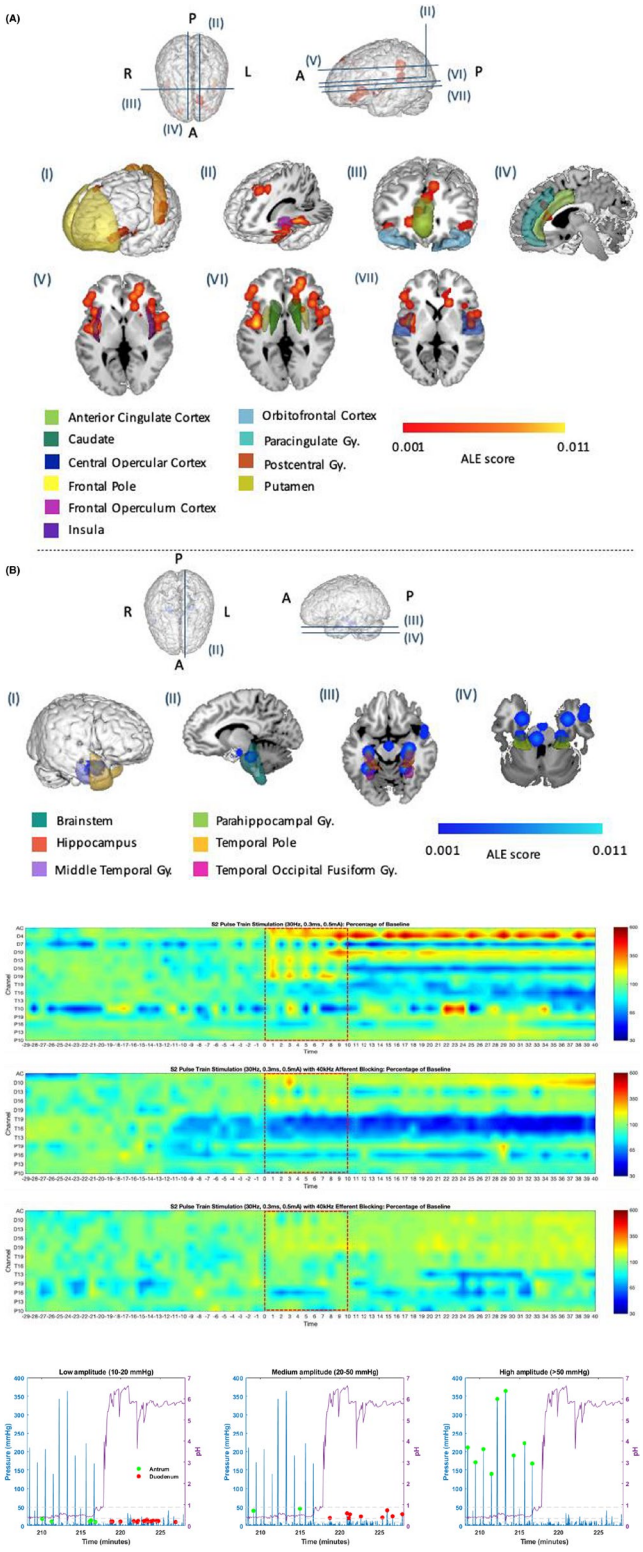

FIGURE 1. WMC trace 10 minutes before and after the pyloric passage with marked low (10-20 mmHg), medium (20-50 mmHg), and

high (>50 mmHg) pressure amplitudes in the antrum (green) and duodenum (red)

POSTERS

ANIMAL/MODEL MODELS OF MOTILITY AND VISCERAL PAIN DISORDERS

Abstract Code: NGS15384-93 – Poster of Distinction | Impact of prenatal stress on visceral hypersensitivity and gut microbiota in adulthood

C. Petitfils[1]; G. Payros[1]; S. Maurel[1]; A. Hueber[2]; G. Dietrich[1]; J. Motta[1]; M. Serino[1]; P. Le Faouder[2]; N. Cenac[1]

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Irritable bowel syndrome (IBS) is the most common intestinal disorder and is characterized by visceral pain and altered gut transit. The pathophysiology of IBS, which differs between patients, is mainly defined by an increased visceral sensitivity and gut microbiota dysbiosis. This syndrome leads to a reduced quality of life and is linked to anxiety and depression, making it a pathology of the microbiota-gut-brain axis. Prenatal stress (PS) has been identified as major risk factor for the onset of IBS symptoms and their severity. However, the causal link between prenatal stress and IBS has to be established. We hypothesized that PS induces a gut microbiota dysbiosis, and a change in bacterial metabolites, predisposing the adult offspring to visceral hypersensitivity and intestinal homeostasis disruption.

In mice, PS was induced by restriction stress with bright light for 30 minutes, three times a day between day 13 and 18 of gestation. In the adult offspring of both sexes, we evaluated visceral sensitivity to colorectal distention, paracellular permeability by 4kDa FITC-dextran gavages followed by fluorescence measurements in the plasma 4h later, mRNA expression of inflammatory genes in the colon by qRT-PCR and intestinal bioactive lipid concentration by mass spectrometry. The gut microbiota was assessed by MiSeq-based microbial for taxonomic analyses and by 16S RNA FISH staining to visualise its organization. Bacterial lipopeptides production was identified and quantified by mass spectrometry.

PS significantly increased visceral sensitivity to colorectal distensions. Paracellular permeability, gene expression and bioactive lipids concentration in the colon remained unaltered in PS offspring. The gut microbiota organization was modified with a bacterial infiltration in the sterile mucus layer and its composition altered in PS mice. The abundance of *Lactobacillus animalis* was decreased in PS mice and inversely correlated with visceral hypersensitivity. This bacterium produces two lipopeptides, C14asnGABA*OH* and C16PheGABA*OH*. Intracolonic administration of C14AsnGABA*OH* decreased PS-induced visceral hypersensitivity in mice.

Prenatal stress is sufficient to induce microbiota dysbiosis and visceral hypersensitivity in adulthood. This could represent a priming event for the development of functional disorders such as IBS. Bacterial lipopeptides containing GABA could represent a new therapeutic strategy to alleviate visceral hypersensitivity in IBS patients.

Abstract Code: NGS15519-93 – Poster of Distinction | Involvement of dopaminergic neurotransmission in small intestine motor dysfunction associated with bowel inflammation in Toll-like receptor 4-null mice

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Objective: Besides controlling host-defense, the innate immune Toll-like receptor 4 (TLR4) modulates repair processes and neuroimmune crosstalk. Changes in TLR4 expression or dopamine levels influence the onset and severity of inflammatory bowel diseases (IBD). Considering the potential involvement of dopamine and innate immunity in IBD pathogenesis, we aimed to assess enteric dopaminergic neurotransmission in absence of TLR4 signaling in a mouse model of dinitrobenzene sulfonic acid (DNBS)-induced colitis.

Methods: Male C57/Bl6 (WT) and TLR4$^{-/-}$ mice (9 ± 2 weeks old) were subjected to 2.5% DNBS-induced inflammation. Ileal disease activity was assessed by histological analysis. Changes in muscle tension were recorded following: i) non-cumulative addition of dopamine (0.1-300 µM); ii) 30 µM dopamine incubation with or without 10 µM SCH-23390 or sulpiride (D1 receptor or D2 receptor antagonist, respectively; iii) electric field stimulation (EFS, 4 Hz) in presence of 30 µM dopamine with SCH-23390 or sulpiride. Immunofluorescence distribution of the HuC/D neuronal or S100β glial markers were determined in longitudinal-muscle myenteric-plexus whole-mounts (LMMPs) preparations by confocal microscopy.

Results: DNBS-treated TLR4$^{-/-}$ mice showed a significant increase in dopamine-induced relaxation ($N = 5$, $P < 0.01$), which was significantly reduced in the presence of D1R antagonist ($P < 0.05$). After DNBS treatment, both WT and TLR4$^{-/-}$ mice showed a significant reduction of 4-Hz EFS-elicited contraction in the presence of dopamine ($N = 5$, $P < 0.001$), which was dependent on both D1R and D2R activity. These changes were associated to a marked reduction of HuC/D^{+} neuron number both in WT DNBS and TLR4 DNBS mice,

(−44% and −19%, respectively) as well as to a significant increase in S100β immunofluorescence in WT DNBS mice only.

Conclusions: In mouse small intestine, changes in dopaminergic neurotransmission after an experimentally-induced inflammation involve the participation of TLR4. These findings provide novel information on the neuroimmune interaction during IBD, highlighting the crosstalk between TLR4 and dopamine signaling on intestinal motor activity and neuroglial network.

Abstract Code: NGS15541-88 – Poster of Distinction | Muscularis macrophages express microglial genes and develop a DAM-like phenotype in aging

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Background: Muscularis macrophages (MMs), located in the gut muscularis, are critical to enteric nervous system (ENS) homeostasis and their perturbation is implicated in gastrointestinal motility disorders. We have shown that age-dependent MM alterations drive low-grade ENS inflammation, resulting in neuronal loss and gut dysmotility; however, the cause for these changes remains unclear. MMs function analogous to microglia, the resident macrophage population of the central nervous system, by providing neurotrophic support and clearing neuronal debris. In aging and neurodegeneration, microglia acquire a "disease" phenotype termed disease-associated microglia (DAM) that drives neuroinflammation.

Objective: We aimed to evaluate the immune composition of the muscularis externa, with emphasis on whether MMs share a genetic signature with microglia and if they acquire a DAM-like phenotype in aging.

Methods: Young, mid-aged, and old (3, 10, and 22-24 months) C57BL/6 mice were studied. Flow cytometry, single cell RNAseq (Figure 1A), and quantitative RT-PCR were performed on cells dissociated from the intestinal muscularis, lamina propria, and spinal cord.

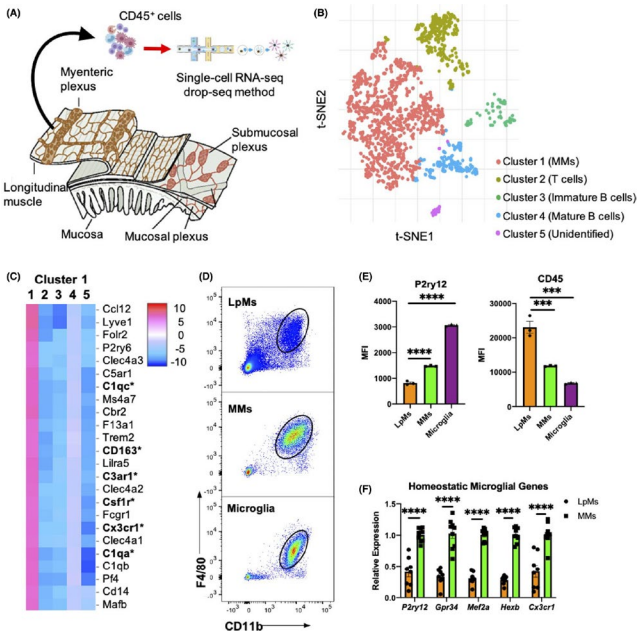
Results: Cluster analysis of scRNAseq data from CD45$^+$ cells of young and old mouse muscularis revealed five clusters, with four identified as MMs (cluster 1), T cells (cluster 2), immature B cells (cluster 3), and mature B cells (cluster 4) (Figure 1B). Cluster 1 (MMs) preferentially expressed microglial genes (Figure 1C). Macrophages (F4/80$^+$CD11b$^+$) from lamina propria (LpMs), muscularis (MMs) and spinal cord (microglia) (Figure 1D) confirmed that MMs share an expression profile with microglia including higher microglial purinergic receptor P2ry12 and lower CD45 compared to LpMs (Figure 1E). Expression of microglial homeostatic genes was higher in MMs versus LpMs (Figure 1F). On further analysis, the MM cluster segregated into two subclusters (1A and 1B). Subcluster 1B was relatively increased in old mice and enriched for DAM genes [*Lgals3*, *Bhlhe40*, *Spp1*, *Cd9*, *Itgax* (CD11c), *IL-1b*], while subcluster 1A was enriched for tissue protective/homeostatic microglial genes [*Mrc1*, *Stab1*, *Maf*, *Gas6*, *Gpr34*]. Flow cytometry of young, mid-aged and old mice confirmed an age-dependent increase in DAM markers including CD9, CLEC7A, CD11c and *Trem2*.

Conclusions: MMs exhibit a homeostatic signature analogous to that of microglia and acquire a DAM-like state in response to aging.

BRAIN GUT AXIS

Abstract Code: NGS15512-86 | Colonic distension distorts postprandial jejunal motility

L. G. Alcala-Gonzalez; D. Livovsky; F. Azpiroz; C. Malagelada



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Introduction: Abnormal motility patterns in the jejunum can be detected in patients with prominent colonic distension, and it is not clear whether these abnormalities reflect a primary jejunal dysfunction or are due to a reflex distortion.

Objective: To determine the effect of colonic distention on jejunal postprandial motility using high-resolution manometry.

Methods: Controlled, parallel, randomized study comparing the effect of colonic gas vs sham infusion in 14 age- and sex matched healthy subjects (19-44 years, 10 men). To induce a steady-state postprandial motor activity pattern, nutrients were continuously

infused in the proximal jejunum (2 Kcal/min) during the 2-h study period. Jejunal motility was measured by water-perfused high-resolution manometry (33 recording sites 1 cm apart; Mui Scientific, Mississauga, Canada). After 1 h postprandial recording (basal period), gas was infused during 7.5 min via a rectal tube (720 mL or sham infusion), and jejunal motility was recorded for 1 h.

Results: Jejunal postprandial motility during the basal period was characterized by two overlapping components: a) continuous segmental (non-propagated) activity (2.7 ± 0.4 contractions/min) and b) intermittent propagated (>10 cm) activity (3.9 ± 1.1 fronts of 2-5 clustered contractions/h). As compared to sham infusion, colonic gas distension: a) inhibited continuous segmental activity (by 17 ± 4%; P = 0.050 vs sham) and b) stimulated intermittent propagated activity (up to 9.0 ± 2.2 fronts/h; P = 0.02 vs sham).

Conclusions and Inference: Postprandial jejunal activity is modulated by long distance retrograde reflexes; colonic distension distorts the balance between segmental and propagated activity and may affect the normal response of the jejunum to food ingestion. Jejunal manometry in patients may be artifacted by colonic overload.

Abstract Code: NGS15466-94 | Comparing volatile organic compound profiling in breath and faecal samples to discriminate between patients with irritable bowel syndrome and healthy controls: A feasibility study

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Introduction: There is an unmet need for non-invasive, specific biomarkers to diagnose and evaluate patients with irritable bowel syndrome (IBS). Volatile organic compounds (VOCs), which are produced by the human metabolism, inflammation, and gut microbiota, and excreted in both faeces and breath, could serve as new biomarkers to this end.

Aim: To assess the feasibility of VOC profiling of faecal samples to distinguish IBS patients and healthy controls (HC) and to evaluate the agreement between faecal and breath samples.

Methods: In this feasibility study, breath, and faecal samples of 6 IBS-diarrhoea (IBS-D) patients and 6 HC were collected and analysed by multicapillary column/ion mobility spectrometry (MCC/IMS), as previously published (Van Malderen, 2020). Briefly, fresh faecal samples were snap frozen. After thawing, 0.5 grams of faeces was heated for 1 hour at 37 °C in a custom-made stainless-steel IMS-box. Headspace air and background samples were collected and analysed. The alveolar gradients of the VOCs were combined into models to discriminate IBS patients from HC, using lasso regression analysis and validated by leave-one-out-cross-validation. Principal component analysis was used to visually present IBS patients versus HC.

Results: IBS patients and controls had a mean (SD) age of respectively 45 (15.0) and 52 (15.6) years. The HC group included 2 males and 4 females; the IBS patients were all females. IBS patients were differentiated from HC using faecal samples with an accuracy, sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV) of 83%. In breath samples the differentiating accuracy was lower (75%) with a sensitivity of 83%, specificity of 67%, PPV of 71% and NPV 80%. Principal component analysis showed separate clusters of patients and HC.

Conclusions: We found a difference in VOC profiles between IBS-D patients and HC in both breath and faeces. Faecal samples showed a higher discriminating power than breath samples. However, considering the low sample size, overfitting is possible and further research in larger populations, taking other IBS subtypes and confounders (such as medication and diet) into account, is needed.

FIGURE 1. Principal component analysis faecal samples; 0 = healthy controls; 1 = IBS

Abstract Code: NGS15465-93 | Exhaled breath analysis for diagnosis and subtyping of patients with irritable bowel syndrome

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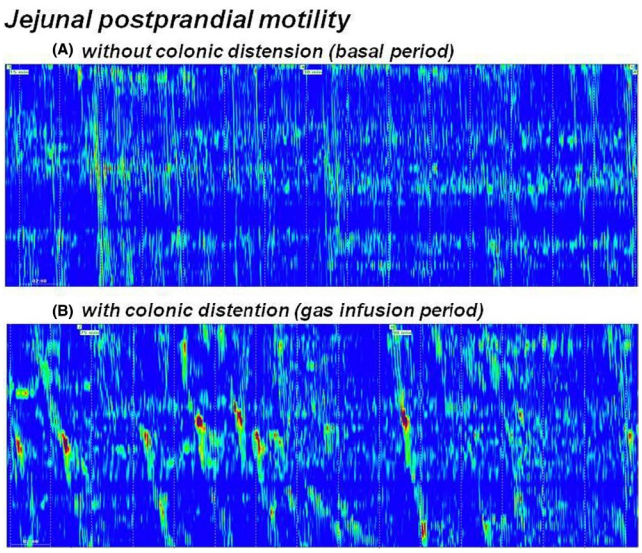


Introduction: Irritable bowel syndrome (IBS) is a chronic condition with an unmet need for non-invasive, specific biomarkers. Research on breath volatile organic compounds (VOCs), produced by the

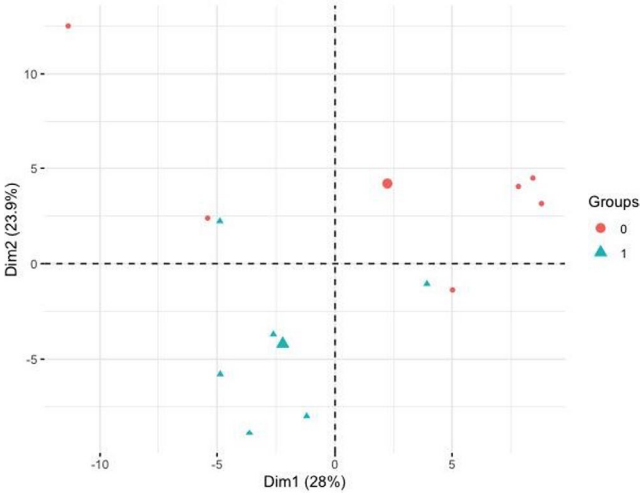
human metabolism, inflammation, and gut microbiota, is a new development in this area.

Aim: Internal validation of the discriminatory value of VOC breath profiling to differentiate IBS patients and healthy controls (HC) and to discriminate between IBS subtypes.

Methods: Breath and background samples of 62 IBS patients (28 diarrhoea, 14 constipation and 20 mixed) and 23 HC were collected and analysed by multicapillary column/ion mobility spectrometry (MCC/IMS). Preparation of sample collection (breath and background samples) has been previously described (Van Malderen, 2020). Using lasso regression analysis and leave-one-out cross-validation, IBS patients were discriminated from HC and the different IBS subtypes, based on the alveolar gradient of VOCs.

Results: Participants had a mean (SD) age of 35.2 (15.4) for HC, 38.6 (15.1) for IBS-D, 49.1 (17.4) for IBS-C and 38.1 (14.7) for IBS-M patients, and respectively 52%, 79%, 79%, and 90% were female. IBS patients (overall) were differentiated from HC, with a sensitivity of 66%, specificity of 70%, positive predictive value (PPV) of 85%, negative predictive value (NPV) of 43% and accuracy of 67% (Figure 1). When comparing the individual subtypes with HC the best differentiation was achieved for IBS-C compared to HC with 84% accuracy (64% sensitivity, 96% specificity, 90% PPV, 82% NPV). When comparing the individual subtypes to each other, accuracies ranged between 71% and 100% with the best discriminatory characteristics for IBS-D versus IBS-M.

Conclusions: Overall, the different breath VOC profiles of IBS patients and HC were confirmed in this cohort with an accuracy of 67%. Interestingly, the discrimination between HC and IBS subtypes resulted in distinct accuracies (range 56-84%), while the comparison between IBS subtypes achieved higher discriminatory values (71-100%) possibly related to their different pathophysiological processes. Further research considering confounders (medication, diet) and patient characteristics will enhance our understanding on the origin of VOCs and the potential use of VOCs in diagnosis and follow-up of IBS.



	IBS vs HC (62 vs 23)	IBS-D vs HC (28 vs 23)	IBS-C vs HC (14 vs 23)	IBS-M vs HC (20 vs 23)
Sens	66% (54%-77%)	57% (39%-74%)	64% (38%-86%)	35% (17%-57%)
Spec	70% (49%-86%)	74% (54%-89%)	96% (80%-100%)	74% (54%-89%)
PPV	85% (73%-93%)	73% (52%-88%)	90% (60%-100%)	54% (28%-79%)
NPV	43% (28%-59%)	59% (40%-75%)	82% (64%-93%)	57% (39%-73%)
Acc	**67%** (57%-76%)	**65%** (51%-77%)	**84%** (69%-93%)	**56%** (41%-70%)

	IBS-C vs IBS-D (14 vs 28)	IBS-C vs IBS-M (14 vs 20)	IBS-D vs IBS-M (28 vs 20)	IBS-D vs IBS-M+IBS-C (28 vs 34)
Sens	36% (15%-62%)	60% (38%-79%)	100% (86%-100%)	79% (61%-91%)
Spec	89% (74%-97%)	93% (70%-100%)	100% (90%-100%)	71% (54%-84%)
PPV	63% (28%-89%)	92% (68%-100%)	100% (86%-100%)	69% (51%-83%)
NPV	74% (57%-86%)	62% (40%-80%)	100% (90%-100%)	80% (63%-92%)
Acc	**71%** (57%-84%)	**74%** (57%-86%)	**100%** (94%-100%)	**74%** (62%-84%)

Abstract Code: NGS15481-91 | **GABA modulates jejunal myoelectric activity by nitrergic pathways: Experimental study**

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Objective: GABA (γ-aminobutyric acid) is an important inhibitory neurotransmitter in the central nervous system but has also been demonstrated in enteric neurons. The aim was to investigate the effect and mechanism of GABA on the jejunal myoelectric activity in rats.

Methods: 14 male Wistar rats were used. Previously three stainless steel electrodes were implanted into the muscular wall of the proximal jejunum. An infusion cannula for drug administration also was inserted into the jejunum. A 7-day recovery period was provided post-surgery. The recording of jejunal myoelectric activity was performed after the animals had fasted for 18 h with free access to water. Fasting gastrointestinal motility was recorded for 1 h before- and for 2 h after administration of the drugs. In the first session, GABA was administered into jejunum 70 mg kg–1. In the second session, nitroglycerin was administered into jejunum 0.8 mg kg^{-1}. In the third session, GABA was administered into jejunum 15 min after nitroglycerin. A visual analysis of electromyograms is performed, i.e. the calculation of time parameters of electrical activity that characterize the migrating myoelectric complex (MMC).

Results: The MMC, recorded in the proximal jejunum, was observed in all animals in baseline recordings. GABA induced irregular spiking activity (only MMC Phase II) during 32 (26; 34) min. Nitroglycerin abolished MMC Phase III in the jejunum; Phase I and Phase II were registered during 22 (14; 22) min. The administration of GABA after nitroglycerin caused MMC Phase II during 18 (17; 22) min; Phase III did not occur.

Conclusions: The results indicate that GABA modulates jejunal myoelectric activity by nitrergic pathways.

Abstract Code: NGS15492-93 | **Gut microbiota modulates acute stress-induced alterations in the gut metabolome**

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Objective: While there is strong evidence for interactions between the microbiota-gut-brain axis and host physiology in the context of chronic stress, little is known about the role of the microbiome in host response to acute stress. Determining the underlying mechanisms by which stress-induced metabolic microbiota outputs may provoke functional changes in the gut and brain is critical for developing future therapeutics to alleviate the adverse consequences of traumatic stress. Here, we aimed to identify microbial and host metabolites that are significantly altered following exposure to acute restraint stress.

Methods: Adult male C57Bl/6 conventional, germ-free and colonized germ-free mice underwent a 15-minute restraint stress exposure. Caecal contents and colonic mucosal scrapings were collected from naïve and stressed mice, either immediately or 45 minutes following stress. Caecal contents and colonic mucosal scrapings underwent untargeted metabolomics analysis.

Results: Stress exposure induced shifts in both conventional and colonized germ-free caecal contents, with reductions in short-chain fatty acid content and altered tryptophan metabolites. Indoleacetate and indolepropionate, tryptophan metabolites produced exclusively by the gut microbiota, were significantly altered with stress exposure in both caecal contents and colonic mucosal scrapings. Germ-free caecal contents also differed between stressed and naïve mice, but resulted in enrichment of distinct pathways, including valine, leucine and isoleucine biosynthesis. Stress exposure altered metabolites associated with tryptophan metabolism in colonic mucosal scrapings in both conventional and colonized germ-free mice.

Conclusions: Overall our results suggest that acute stress induces rapid changes in both microbial and host metabolism at the host-microbe interface. To our knowledge, this is the first time that a direct effect of acute stress on microbial metabolism has been demonstrated, with changes in indoleacetate and indolepropionate, tryptophan metabolites produced exclusively by gut microbes. In addition, acute restraint stress altered metabolite levels in both caecal contents and colonic mucosa in a microbiome-dependent manner. Several identified metabolites are microbial in origin known to alter gut-brain axis signalling pathways, and therefore may underlie at least some of the physiological changes in the gastrointestinal tract arising from host-microbe dialogue following acute stress exposures.

Abstract Code: NGS15543-90 | Is the gut microbiota involved in neurogenesis in patients with severe traumatic brain injury?

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Objective: There is growing recognition of the strong link between the gut microbiome and the brain. The existing literature suggests that the gut microbiota is involved in regulating the levels of biomarkers and neurotransmitters [1]. Thus, the aim of this study was to investigate role of gut microbiota in neurogenesis in patients with brain injury in a chronic critical illness (CCI).

Methods: A total of 27 chronical patients at the intensive care unit (ICU) after brain injury of various etiologies were included. Composition of the gut microbiota was analyzed using PCR kits (Colonoflor-16, AlphaLab; Russia). Biomarkers of neurogenesis such as brain-derived neurotrophic factor (BDNF), ciliary neurotrophic factor (CNTF) and glial acidic fibrillar protein (GFAP), and also neurotransmitters (dopamine, serotonin) were measured by enzyme linked immunosorbent assay method using reagent kits by Cloud Clone, USA.

Results: We obtained the potential evidence in favor connection of the intestinal microbiota with the processes of regeneration of nerve tissue (Figure 1). The strongest correlation was found in *Staphylococcus aureus* and *Lactobacillus spp.* with CNTF, as well as *Bacteroides thetaiotaomicron* with BDNF, GFAP, dopamine, serotonin ($P < 0.05$). The BDNF level in the patients was 5 times higher than the reference values. CNTF and GFAP were detected in patients, which are usually not found in healthy people.

Variables	GFAP	BDNF	CNTF	Dopamine	Serotonin
Lactobacillus spp.	ns	ns	0.67	ns	ns
Staphylococcus aureus	ns	ns	0.85	ns	ns
Bacteroides thetaiotaomicron	0.38	-- 0.52	ns	0.36	-- 0.48

FIGURE 1. The value of the correlation coefficient between serum biomarkers and some species of gut microbiota ($P < 0.05$).

Conclusions: Thus, the data support the potential involvement of gut microbiota in neuroregeneration processes.

References

[1] Silva YP, Bernardi A, Frozza RL. The Role of Short-Chain Fatty Acids From Gut Microbiota in Gut-Brain Communication. Front Endocrinol (Lausanne). 2020 Jan 31;11:25.

Abstract Code: NGS15471-90 | Oro-anal transit is associated with postprandial symptoms, breath hydrogen and methane in irritable bowel syndrome

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Objective: Abnormal oro-anal transit time (OATT) and rectal hypersensitivity are key pathophysiological factors in irritable bowel syndrome (IBS). The lactulose nutrient challenge test (LNCT) has been

developed as a physiologic test of visceral sensitivity and gut microbial fermentation in IBS. We aimed to investigate the associations between OATT, rectal sensitivity and postprandial symptoms in IBS during LNCT.

Methods: IBS subjects (n = 263) that completed the LNCT were included from two prospective studies. During the LNCT, eight postprandial symptoms were graded on 20-point Likert scales. Pre-prandial symptoms were assessed at baseline and postprandial symptoms were assessed every 15 minutes at 16 time points (15–240 min) after ingestion of a combined 25g lactulose nutrient drink (400 ml; 1.5 kcal/ml). Exhaled hydrogen and methane levels were also analysed. The subjects also underwent an OATT test with radiopaque markers and a rectal barostat test for assessment of rectal sensitivity. Linear mixed model analyses were used to assess the associations between OATT, rectal sensitivity, and the dependent variables (symptoms and exhaled hydrogen/methane). All analyses were controlled for comorbid FD, anxiety, depression, and somatization.

Results: At baseline, and to the same extent at the postprandial time points, a rapid OATT could predict more severe symptoms (gas, discomfort, nausea, rumbling, severe urgency), and higher hydrogen levels, and a slow OATT could predict higher methane levels (Table 1).

We found that the symptom patterns of nausea, severe urgency, and abdominal pain differed over time for different OATT (Table 1). The time-symptom curves reflected an earlier and later postprandial response in nausea and urgency for subjects with rapid and slow OATT, respectively. For abdominal pain, the analyses reflected an earlier postprandial increase for subjects with slow OATT. No significant main or interaction effects were found for rectal sensitivity.

Conclusions: Based on two prospective studies in IBS, oro-anal transit is not only associated with increased GI symptoms and gut microbial fermentation, but also specifically with postprandial symptom responses, highlighting its relevance in the pathophysiology of IBS.

TABLE 1. Mixed model analyses for OATT, assessing symptoms and breath analyses in irritable bowel syndrome

	Gas		Bloating		Abdominal discomfort		Abdominal distension		Nausea	
	F β±SE	P	F β±SE	P	F β±SE	P	F β±SE	P	F β±SE	P
Time	1.8	**0.023**	3.1	**<0.001**	1.5	0.078	2.1	**0.007**	3.7	**<0.001**
OATT	4.8 $-2e^{-2}\pm2e^{-2}$	**0.029**	0.1 $-6e^{-3}\pm2e^{-2}$	0.882	7.6 $-5e^{-2}\pm2e^{-2}$	**0.006**	0.1 $1e^{-2}\pm2e^{-2}$	0.724	4.8 $-6e^{-2}\pm2e^{-2}$	**0.029**
OATT by Time	0.9	0.577	0.7	0.843	1.0	0.426	0.5	0.964	1.8	**0.031**
	Abdominal rumbling		**Severe urgency**		**Abdominal pain**		**Hydrogen**		**Methane**	
	F β±SE	P	F β±SE	P	F β±SE	P	F β±SE	P	F β±SE	P
Time	2.6	**<0.001**	3.2	**<0.001**	1.2	0.234	17.1	**<0.001**	11.8	**<0.001**
OATT	20.9 $-8e^{-2}\pm2e^{-2}$	**<0.001**	23.4 $-8e^{-2}\pm3e^{-2}$	**<0.001**	0.1 $3e^{-2}\pm3e^{-2}$	0.765	14.2 $-2e^{-2}\pm2e^{-2}$	**<0.001**	13.0 $7e^{-2}\pm2e^{-2}$	**<0.001**
OATT by Time	1.2	0.244	1.7	**0.039**	1.8	**0.023**	0.9	0.591	0.8	0.731

F, test statistic for the respective independent variable of the mixed model; *β±SE*, beta coefficient, *i.e.* linear slope, and standard error for the main effect of the continuous variables (log-transformed).
Controlled for functional dyspepsia, anxiety depression and somatization. Significant effects are shown in bold. OATT, oroanal transit time.

Abstract Code: NGS15505-88 | The importance of endogenous opioid system in the process of aging of the gastrointestinal tract

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Introduction: Endogenous opioid system (EOS), composed of opioid receptors (OR: MOP, KOP, DOP) and peptides: β-endorphins, enkephalins and dynorphins is involved in the control of gastrointestinal (GI) motility and processes of secretion/absorption in the intestines. The alterations in the EOS may be the cause of the GI peristalsis impairment that occurs with age.

Aim: The aim of this project was to evaluate the involvement of EOS in the process of GI system aging.

Methods: In this study 24-, 44- and 64-weeks old Balb/C mice were used. The GI functions under physiological conditions were assessed in vitro (intestinal secretion) and in vivo (whole and upper GI transit, fecal pellet output). To investigate the involvement of EOS we tested the action of selective OR agonists on the colonic smooth muscles contractility and pellet excretion. The activity of myeloperoxidase and the concentration of glutathione were measured. The expression of the EOS components was assessed in the stomach, ileum and colon at protein and mRNA levels.

Results: The sensitivity of the colon to the forskolin/veratridine stimulation increased with age. The GI transit was prolonged and the number of fecal pellets excreted was decreased in the oldest group of mice when compared to younger. The colonic contractility was inhibited by OR agonists, but the response to the action of MOP and DOP, not KOP, agonists decreased with age. In vivo, the action of DOP agonist was reduced in 64 weeks old mice in comparison to younger animals. The activity of myeloperoxidase and the concentration of total glutathione increased with age. The expression of the genes encoding the EOS components decreased in the stomach and distal ileum with age. In the colon, the expression of the genes encoding MOP and DOP was higher in the oldest group. At a protein level the expression of DOP receptors and the concentration of β-endorphins in the colon increased with age.

Conclusions: The EOS maintains an important role in the process of aging of the GI tract and the alterations at molecular level in the EOS can be considered as involved in the pathogenesis of constipation in the elderly.

Abstract Code: NGS15017-86 | The intestinal brain regulation of pain and motility

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Introduction: The enteral nervous system or "intestinal brain" manipulates and/or depends on a large number of neurotransmitters, hormones from their systemic or local concentration. In addition, much depends on the combination of these biologically active

compounds (BAC). This is a self-regulating system and it protects itself from the flurry of BAC does not damage the complex multi-element system of regulatory and adaptation mechanisms.

Purpose: To determine the concentration and relationship between normal BAS in IBD and NSAIDs. Material and methods. A determination was made in 30 healthy and 68 patients with IBD. In 35 white rats in the extracts of the mucous of the colon ulcer and 30 animals were injected with NSAIDs. The concentrations of 5-HT, Ash, NO, Pg E2 and F2A were determined.

Results and discussion: Depending on the concentration of Ach and 5-HT, which in healthy individuals were the main physiological stimulants of motility. Patients with IBD significantly increased concentrations of 5-HT and NO. Motor skills were impaired due to the reduction of longitudinal and relaxation of the circular muscles of the intestine. Increased intensity of pain at rest and with bowel contractions. The introduction of NSAIDs caused the formation of ulcers and erosions of the mucous membrane of the small intestine and colon, increased the concentration of 5-HT and decreased prostaglandins, pain intensified.

Conclusions: The change in the concentration of the BAC disturbs the motility of the intestine. Increased serotonin causes hyperalgesia due to irritation of nociceptors. Increasing the Ach reduces the threshold of pain sensitivity.

ENDOSCOPY IN NEUROGASTROENTEROLOGICAL AND MOTILITY DISORDERS

Abstract Code: NGS15467-95 | Analysis of neurogastrointestinal and motility disorders from a national pediatric inpatient database: Exploring national demographic access and outcomes

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Objective: Characterize the incidence and demographic characteristics of patients with pediatric neurogastrointestinal motility (PNGM) conditions and the trends of inpatient motility tests using the Kids Inpatient Database (KID).

Methods: We queried the KID from 2003-2016 for US patients hospitalized (<18 years of age) for PNGM studies. Motility hospitalization rates per 1000 admissions were calculated and analyzed by year, hospital region, facility type and patient sociodemographic characteristics including: age, sex, race, insurance payer, and average median household income of county of residence.

Results: The estimated total number of inpatient encounters was 267, 318, 419, 580, 744 in years 2003, 2006, 2009, 2012, and 2016, respectively. Across all years other than 2016, the Midwest region had the highest hospitalization rate. Total hospital charges increased from $14,140 in 2003 to $33,021 in 2016. Patients were more likely to have a motility study in 2009 and 2012 compared to 2016. Patients with private or other insurance types were more likely to have a motility study compared to those who have governmental insurance [private: 1.29 (1.16, 1.44); Other insurance types: 1.77 (1.49, 2.09)]. Patients residing in lower income zip codes were less likely to receive a motility study than those in zip codes ≥75th income percentile [(0-25th percentile: 0.55 (0.48, 0.64) vs 51-75th percentile 0.77 (0.67, 0.87)].

Conclusions: Our study found that there are gender, income, insurance and regional differences in the rates of inpatient motility studies for pediatrics and an increased trend in hospital total charges for PNGM services. Future analysis should include analysis of services more commonly done in the ambulatory setting to understand combined procedure trends.

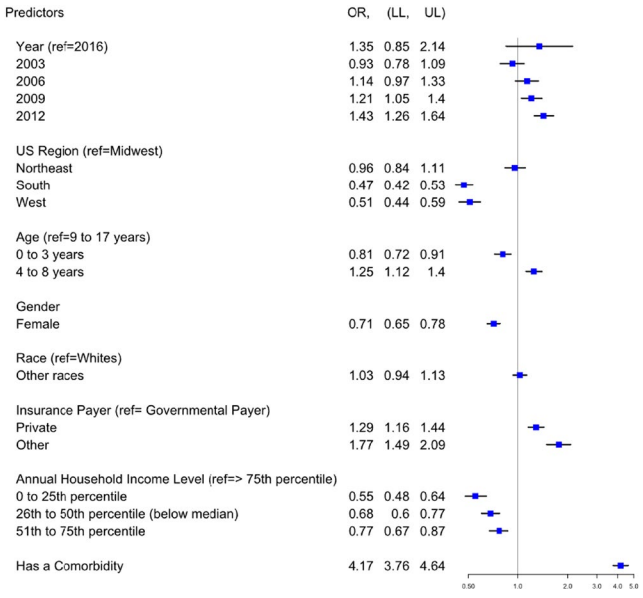

FIGURE 1 Predictors of Inpatient Pediatric Neurogastroenterology and Motility services.

FAECAL INCONTINENCE AND CONSTIPATION

Abstract Code: NGS15499-00 | Anal Sphincter Defect And Fecal Incontinence

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Introduction: Anal sphincter defects or injury can lead to fecal incontinence in conditions such as anorectal malformations and complications after surgery for Hirschsprung disease. TRUS (Transrectal Ultrasonography) is a less commonly utilized diagnostic tool for evaluating fecal incontinence in children. There is no published data in pediatrics on the relationship between the degree of anal sphincter defect and incontinence.

Case Presentation: 17 year-old male with history of autism spectrum disorder, presented with rectal prolapse, constipation, fecal incontinence and hematochezia. The rectal prolapse was 3-4 cm requiring reduction, associated with rectal bleeding and perineal discomfort despite having daily, soft stools. He has an alleged history of physical and sexual abuse with anal penetration by a previous caregiver. Work up including sweat chloride test was normal. Defecography showed weakness of the pelvic floor with rectal prolapse, pelvic floor descent and little to no change in the anorectal angle during straining. The prolapse was confined to the rectum. A contrast enema showed colon redundancy. Endoscopy was normal except for an inflammatory rectal polyp that was removed. Pelvic MRI showed a small defect in the external anal sphincter (EAS) at 8 o'clock (Figure 1A). Anorectal manometry (ARM) showed a low resting sphincter pressure (mean of 30 mmHg), with failed squeeze, normal RAIR with a dose response, and pelvic floor dyssynergia. 3-D images from ARM were concerning for more extensive sphincter defects (Figure 1B). TRUS (BK3000) showed more extensive defects in both the EAS (from 5-8 o'clock) and Internal Anal Sphincter (from 3-9 o'clock) (Figure 2). The hematochezia resolved post-polypectomy, however, rectal prolapse persisted requiring rectopexy. No surgical intervention to repair his anal sphincter defect. He is doing well 3 months after surgery without symptoms.

Discussion: TRUS is superior to MRI in characterizing anal sphincter defect and shows that continence is possible despite a significant defect in the anal sphincter. This reflects the compensatory mechanisms of the residual sphincter in the absence of other aggravating factors like rectal prolapse. We recommend, based on its accuracy, safety and cost, that TRUS be used more often for evaluation of fecal incontinence in children with suspected anorectal disorders.

Abstract Code: NGS15565-94 | Anorectal motility disorders in inflammatory bowel disease patients

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Background & Objective: Anorectal motility disorders are often responsible for the persistent, debilitating symptoms of IBD patients with quiescent disease. They are frequently misinterpreted as functional disorders, with the neglection of the motility post-inflammatory changes. The aim of the study was to identify and characterize the anorectal motility dysfunction in IBD patients admitted in a Tertiary Gastroenterology Centre in Bucharest, Romania.

Methods: We are conducting an ongoing prospective study initiated in August 2019, this being our first report of 15 evaluated patients. High resolution anorectal manometry was performed using the Sandhill Scientific high-resolution manometry system and the parameters were further analyzed using InSIGHT software. Patients' symptoms were recorded prior to the investigation using a standardized questionnaire. The manometric testing comprised measurements of anorectal pressure at rest, during squeeze, simulated evacuation, rectoanal inhibitory reflex (RAIR) and rectal sensory testing (first sensation, urgency and maximum discomfort).

Results: We included 8 patients with Ulcerative Colitis and 7 patients with Crohn's Disease, 10 females and 5 males, mean age 41 ± 10.79 years. 46.67% had active disease and only 26.67% had rectal active involvement. Symptoms were reported by 12 patients, urgency (50.00%), passive and active incontinence (91.67%), evacuation difficulties (16.67%), and intolerance of rectal therapies (25.00%) being the most frequent. Modified manometric parameters were found in 73.33% patients and were correlated with previous pelvic surgical interventions (P = 0.05); although, the latter doesn't seem to increase the risk of incontinence (P = 0.4) In 66.67% cases the manometric measurements correlated with the symptoms. Lower resting tone was registered in patients with passive incontinence (P = 0.001) and lower squeeze pressures (maximal, incremental and duration) were found in patients with active incontinence (P = 0.05). 25%.00 patients had rectal hyposensitivity and 53.33% presented anorectal dyskinesia.

Conclusions: A considerable proportion of patients proceed to suffer from persistent symptoms in the absence of active inflammation, with a major impact on their quality of life. Lack of awareness amongst clinicians may lead to unnecessary treatment escalation and under-utilisation of pelvic floor investigations.

Abstract Code: NGS15498-99 | Clinical and high-resolution anorectal manometry differences in women with and without fecal incontinence with third and fourth-degree obstetric tears

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Introduction: Severe perineal tears include third- and fourth-degree tears and may also be known as obstetric anal sphincter injuries (OASI). Third- and fourth-degree perineal tears even appropriately repaired, can cause serious long-term consequences for women including faecal incontinence and reduced quality of life.

Objectives: To determine clinical and high-resolution anorectal manometry (HRAM) differences between third and fourth degree OASI patients with and without fecal or flatus incontinence.

Material and Methods: Observational cross-sectional study. 166 patients were included. OASI were repaired in all the patients and HRAM with a solid-state catheter (Medtronic®) was performed 3 months after. Epidemiological, clinical and manometric data were obtained prospectively for all of them.

Results: Eighty-three (50%) of patients did not have any incontinence; 63 (38%) patients had FI and 20 (12%) only flatus incontinence. Epidemiological, clinical and HRAM results are expressed in the Figure 1. In the FI group the mean duration of the symptoms was 51 months (19.8-81.9), the mean Wexner score was 7.5 (6.5-8.6%) and 24 (38%) patients had a Wexner score ≥9. Thirty-nine (61.9%) patients had urge, 16 (25.4%) passive and 8 (12.7%) mixed FI. Twenty-six (41.3%) patients had daily episodes.

Conclusions: Although the third and fourth degree OASI were repaired in all the patients a significant number of them still had fecal and flatus incontinence after. Factors involved were older age, increased BMI, loose stools and increased bowel movements, lower anal canal pressures and rectal hypersensitivity. Pelvic floor prolapses were more frequent as well in patients with fecal and flatus incontinence.

	Fecal Incontinence (N=63)	Flatus Incontinence (N=20)	No Incontinence (N=83)	p-value
Epidemiological data				
Age (yr.)	43.5 (40.3-46.7)	33.9 (31.8-36.1)	33.7 (32.5-34.8)	< 0.001
BMI	26 (24.5-27.4)	23.1 (21.4-24.7)	24.5 (23.6-25.4)	0.077
Clinical data				
Nº vaginal deliveries (mean)	1.7 (1.5-1.9)	1.2 (1-1.3)	1.3 (1.1-1.4)	< 0.001
Type of tear Third-degree Grade 3a Grade 3b Grade 3c Fourth degree	 42 (66.7%) 13 (21.8%) 4 (6.3%) 2 (3.2%)	 13 (65%) 7 (35%) 0 0	 49 (59%) 27 (32.5%) 5 (6%) 2 (2.4%)	0.760
Pelvic floor prolapses (%) No Yes	 40 (63.5%) 23 (36.5%)	 12 (60%) 8 (40%)	 66 (71.1%) 17 (28.9%)	0.054
Bowel movements/week Normal >3 times/day < 3 times/week	 45 (71.4%) 11 (17.5%) 7 (11.1%)	 18 (90%) 1 (5%) 1 (5%)	 74 (89.2%) 1 (1.2%) 8 (9.6%)	0.023
Consistency of stools (Bristol; %) Normal (3-4) Diarrhea (5-6-7) Constipation (1-2)	 41 (65.1%) 17 (27%) 5 (7.9%)	 14 (70%) 3 (15%) 3 (15%)	 74 (89.2%) 2 (2.4%) 7 (8.4%)	0.004
Manometric data				
Mean anal resting pressure (atmospheric reference; mmHg)	69.5 (63-76)	74.3 (66.2-82.3)	82.5 (78.2-86.8)	0.001
Maximum anal resting pressure (atmospheric reference; mmHg)	78.9 (71.9-85.9)	84.5 (74.4-94.6)	91.1 (86-96.2)	0.022
Maximum squeeze pressure (atmospheric reference; mmHg)	114.5 (103.2-125.9)	137.2 (119-155.4)	151.9 (126.4-77.5)	0.001
Maximun incremental squeeze pressure (mmHg)	35.6 (26.9-44.3)	52.3 (35-70.3)	60.9 (35.6-86)	0.015
Long squeeze (duration; s)	16.8 (15.2-18.4)	15.8 (13-18.6)	16.6 (15.2-18.1)	0.640
Anal canal length (cm)	3 (2.9-3.2)	2.9 (2.6-3.1)	3.2 (3.1-3.3)	0.243
First sensation (mL)	15.9 (13.1-18.6)	15.5 (11.6-19.4)	12.6 (11.4-13.8)	0.071
Urge (mL)	76.4 (69.9-82.8)	77.5 (64-91)	96 (88.2-103.9)	0.003
Discomfort (mL)	102.3 (94.5-110.1)	103 (87.4-118.6)	123.8 (115.6-132.1)	0.002
Push manoeuvre (%) Normal Abnormal	 45 (71.4%) 18 (28.6%)	 15 (75%) 5 (25%)	 70 (84.3%) 13 (15.7%)	0.804

FIGURE 1. Epidemiological, clinical and HRAM data in the three groups

Abstract Code: NGS15473-92 | Constipation assessed by colic transit time: Segment study and transit type

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Introduction: Chronic constipation can have a negative impact on the patient's quality of life. The colic transit time calculated using radiopaque markers, is a non-invasive test, which may help in the study of constipation.

Objective: It was intended to study the type of constipation present in the adult and pediatric population, covered by our hospital.

Methods: A retrospective study was carried out, from 2018 to 2020, in our protocol each patient ingested a capsule with 10 markers per day, having performed an abdominal radiography on the seventh day. We evaluated the colic segment transit time and the total time.

Results: Adult patients (n = 11) were mainly 73% female (n = 8) with a median of 40 years old and presented changes in segmental transit in 63% (n = 7) with: terminal constipation (TC) in 27% (n = 3), TC and delay in the left colon in 18% (n = 2) and with delay in the right colon in 9% (n = 1) and left in 9% (n = 1). The type of transit was normal in 73% (n = 8) of the patients, of which 63% (n = 5) had segmental changes, and the remaining 3 patients had fast, moderately slow and slow colic transit respectively. Pediatric patients (n = 7) were female in 57% (n = 4) with a median of 9 years old and presented changes in segmental transit in 57% (n = 4) with: TC in 43% (n = 3) and delay in the left colon by 14% (n = 1). There was moderately slow transit in 57% (n = 4), normal transit in 29% (n = 2) and fast in 14% (n = 1) of patients.

Conclusions: Constipation affected all age groups, with female greater proportion in adulthood. In adults, despite the majority having a normal type of transit, segmental assessment may identify pathological changes. The pediatric population shows mostly changes both at the segmental level and in the type of colic transit. Segmental changes with TC were the most prevalent in both groups, raising the possibility of pelvic dysfunction.

Abstract Code: NGS15483-93 | Fecal incontinence: Effect of pelvic floor muscle training

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Background/Aim: To analyse the effect of a pelvic floor muscle training program, without facilitating techniques, in people with Fecal Incontinence.

Methods: Quasi-experimental study of a single group, of patients followed on Functional Anorectal Diseases Appointment, with Fecal Incontinence, referred to physiotherapy, carried out a pelvic floor muscle training program, of 12 sessions once a week. The primary outcome measures were: *Wexner scale*, *Fecal Incontinence Quality of Life (FIQL)* and Magnetic resonance defecography. They were measured at baseline and after intervention.

Results: 13 patients have been studied (12 women), with an mean age of 64.15 ± 11.25 (37-83). After intervention, significant differences were found: at Wexner index score at baseline 10.92 ± 2.98 and after intervention 5.46 ± 2.90 (P = 0.000); at *FIQL* in 4 dimensions (P < 0.05), with more effect dimension in Depression and in the Behavior; and in the measures of MR Defecography, in line M at rest (P = 0.012) and in rectocele during evacuation (P = 0.008).

Conclusions: The pelvic floor muscle training program, without the use of facilitating techniques, used in our study, showed significant improvements in the severity of symptoms (Wexner index), in the

Quality of Life (*FIQL*), and in some measures of the functional assessment of the pelvic floor, like the pelvic floor position at rest and decreased rectocele in evacuation.

Abstract Code: NGS15009-87 | High-resolution anorectal manometry results in patients with anal incontinence

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Introduction: Anal incontinence (AI) is a multifactorial functional pathology. Manometry anorectal is the gold standard for exploration of this disorder. The objective of this work is to describe the profile of anorectal high resolution manometry (MHR) in patients with AI.
Materials and methods: We have included the patients who consulted for AI and who had undergone a high-resolution anorectal manometry between 2019 and 2020. The parameters studied at the MHR were the resting pressure of the internal anal sphincter, the voluntary contraction, rectal sensitivity, inhibitory rectoanal reflex and abdominal and pelvic coordination.
Results: We included 21 patients. It was 12 men and 9 women. The median age was 55 ± 19.5 years. Clinical examination revealed hypotonic sphincter in 8 patients. Anomalies detected at the MHR were: resting anal hypotonia (n = 1; 4.7%), resting anal hypertonia (n = 13; 61.9%), contraction voluntary weak in amplitude (n = 8; 38%) and in duration (n = 8; 38%), abdominal and pelvic asynchrony (n = 3; 14.3%), rectal hyposensitivity (n = 1; 4.7%) and rectal hypersensitivity (n = 1; 4.7%).
Conclusions: MHR allows better understanding of the mechanisms involved in AI, providing thus a clearer etiological orientation. This would allow to apply a more targeted treatment in order to improve the burden of these patients.

Abstract Code: NGS15008-86 | High-resolution anorectal manometry results in patients with distal constipation

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Introduction: Distal constipation is a multifactorial functional pathology. High-resolution anorectal manometry was used to describe certain functional abnormalities associated with this pathology. The objective of this study is to describe the high-resolution manometric profile in patients with distal constipation.
Patients and methods: We have included the patients who consulted for distal constipation and who had benefited from a high-resolution anorectal manometry during 2020. The parameters studied at the high-resolution anorectal manometry were the resting pressure of the internal anal sphincter, voluntary contraction, rectal sensitivity, inhibitory recto-anal reflex and abdominal and pelvic coordination.
Results: Our work included 36 patients with distal constipation. The median age was 35.7 ± 18 years and the sex ratio M / F of 1. The duration of the distal constipation was 16 ± 3 years on average with extremes of 43 years and 1 year. The data from the proctological examination had showed normal anal margin examination in all patients, anal hypertonia on digital rectal examination in 6 patients (16.6%) and rectal prolapse in 4 patients (11.1%). The abnormalities detected at MHR were: abdominal and pelvic asynchrony (n = 8; 22.2%), including 11.1% (n = 4) anism type 1 and 11.1% (n = 4) anism type 3, functional megarectum (n = 5; 14%), rectal hyposensitivity (n = 7; 19.4%), Hirschprung (n = 5; 14%), anal hypertonia rest (n = 6; 16.6%) and ultra-lent waves (n = 5; 14%).
Conclusions: High-resolution anorectal manometry occupies an essential place in the exploration of distal constipation, however other morphological examinations should necessarily complete the high-resolution anorectal manometry data in case suspicion of a structural anomaly of the anal sphincter or pelvic static disorder.

Abstract Code: NGS15508-91 | Identification and characterization of novel candidate genes in familial Hirschsprung´s disease

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Objective: *Hirschsprung disease* (HSCR), is a rare congenital disorder characterized by aganglionosis due to functional impairment of enteric progenitor cells during embryonic development. Genetic and environmental factors are shaping the phenotype. So far, more than 25 genes have consistently been replicated. Although *RET* is the major disease gene, it accounts for only a fraction of cases. To further dissect HSCR genetics, we investigated an extended family including 18 individuals of three generations and two major branches with four HSCR patients.
Methods: The individual protein-coding genetic background was assessed by Whole Exome Sequencing (WES) and candidate variants were verified by Sanger sequencing as reported previously[1]. Validation of candidate genes was performed collecting data on expression, previous disease association, gene function, biological context and mutation prediction. To prioritize candidate gene relevance, a binary scoring system was developed based on validation criteria and verified by established HSCR risk gene variants. Considering the accumulation of genetic variants an individual risk score for each family member has been assessed as well.
Results: Filtering of the WES data for rare coding variants revealed *RET* in addition to various novel candidate genes in affected as well as some 'non-affected' relatives. To investigate common modifiers, four SNPs in *RET* and *SEMA3A* were assessed. SNP carriers

were found at higher risk for HSCR and one rare coding *RET* variant seemed not sufficient for the manifestation of HSCR. Applying our scoring system, the identified novel candidate genes *MARCH7* and *SLAIN2* displayed even higher scores than *RET*. Furthermore, all patients demonstrated a considerable higher risk score compared to their non-affected relatives. Of note, two of the parents scored similarly high and reported gastrointestinal complaints. This might be attributed to the genetic burden of gene variants assigned to be relevant in ENS development and function.

Summary and Conclusions: In summary, our results are in line with others, supporting the hypothesis that a certain threshold of gene variants needs to be crossed for the manifestation of the HSCR phenotype, indicating the genetic complexity of HSCR.

[1] Mederer, Schmitteckert, et al. Romero & Niesler. *PLOS Genetics* 2020 Nov 5. PMID: 33151932

FUNCTIONAL DYSPEPSIA, IBS, FUNCTIONAL DIARRHEA AND OTHER FUNCTIONAL DISORDERS

Abstract Code: NGS15497-98 – Poster of Distinction | A trial-based economic evaluation of peppermint oil for the treatment of Irritable Bowel Syndrome

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Background: Irritable Bowel Syndrome (IBS) is a prevalent, chronic gastrointestinal disorder that imposes a substantial socioeconomic burden. Peppermint oil is a frequently used treatment for IBS, but evidence about cost-effectiveness is lacking.

Objective: We aimed to assess cost-effectiveness of small-intestinal release peppermint oil versus placebo in IBS patients.

Methods: In a multicenter randomized placebo-controlled trial, cost-effectiveness was evaluated from a societal perspective. The incremental cost-effectiveness ratios (ICERs) were expressed as 1) incremental costs per Quality Adjusted Life Years (QALY), and 2) incremental costs per successfully treated patient, *i.e.* per abdominal pain responder (according to FDA definitions), both after an eight-week treatment period with placebo versus peppermint oil. Cost-utility and uncertainty were estimated using non-parametric bootstrapping. Sensitivity analyses were performed.

Results: The analysis comprised 126 patients (*N* = 64 placebo, *N* = 62 small-intestinal release peppermint oil). Peppermint oil was a dominant treatment compared to placebo in 46% of bootstrap replications. Peppermint oil was also more effective but at higher cost in 31% of replications. The net-benefit acceptability curve showed that peppermint oil has a 56% probability of being cost-effective at a conservative willingness-to-pay threshold of €10.000/QALY. Peppermint oil was also a dominant treatment per additional successfully treated patient according to FDA definitions, *i.e.* in 51% of replications. In this case, the acceptability curve showed an 89% probability of being cost-effective.

Conclusions: In patients with IBS, small-intestinal release peppermint oil appears to be a cost-effective treatment although there is uncertainty surrounding the ICER. When using abdominal pain responder as outcome measure for the ICER, peppermint oil has a high probability of being cost-effective. The use of peppermint oil, which is a low-cost treatment, can be justified by the modest QALY gains and slightly higher proportion of abdominal pain responders. More research and long-term data are necessary to confirm the cost-effectiveness of peppermint oil.

Abstract Code: NGS15535-91 – Poster of Distinction | Circulating serotonin in patients with irritable bowel syndrome. Before and after a 12-week strict low FODMAP diet intervention

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Background: Altered serotonin (5-HT) metabolism has been proposed to play a central role in the modulation of abdominal pain and motility disturbances in irritable bowel syndrome (IBS). Interestingly, the low FODMAP (fermentable oligosaccharides, disaccharides, monosaccharides and polyols) diet alleviates these complaints in a large proportion of IBS patients. However, the effect of a low FODMAP diet on circulating 5-HT metabolism in IBS patients remains to be elucidated

Aim: The aim of the study was to investigate alterations in fasting concentrations of 5-HT, 5-hydroxyindoleacetic acid (5-HIAA) and 5-HIAA/ 5-HT ratio in IBS patients before and after a 12-week strict low FODMAP diet.

Method: Fasting blood samples were collected from 41 IBS patients and 19 healthy controls (HC). Thirteen IBS-D/M patients were further enrolled in a 12-week dietitian-led strict low FODMAP diet intervention. 5-HT was quantified in platelet-poor plasma (PPP) using competitive ELISA, whereas 5-HIAA was quantified in serum through Liquid Chromatography with tandem mass spectrometry (LC- MS/MS). IBS symptom severity scale (IBS-SSS) and Bristol stool scale (BSS) were assessed to evaluate the effects on symptom severity and changes in stool consistency.

Results: IBS-C patients had lower 5-HT concentrations, whereas IBS-D and IBS-M patients had normal 5-HT concentrations, compared to HC. Thirteen eligible IBS patients completed the 12-week strict low FODMAP diet intervention. After the diet intervention, both 5-HIAA and 5-HIAA/ 5-HT ratio were significantly enhanced in IBS patients, compared to baseline. Interestingly, there was no differences in 5-HT levels. On average, IBS symptom severity decreased from moderate to mild after the diet intervention.

Conclusions: Our preliminary results show that altered 5-HT metabolism may be an important feature in IBS. We speculate that a 12-week strict low FODMAP diet may influence 5-HT metabolism, subsequently resulting in enhanced fasting serum 5-HIAA concentrations and an increased 5-HIAA/ 5-HT ratio, compared to baseline. Hence, low FODMAP-induced alterations in 5-HT metabolism may contribute to alleviation of IBS symptom severity.

FIGURE 1. Fasting platelet-poor plasma 5-HT (A) and serum 5-HIAA (B) concentrations before and after a 12-week strict low FODMAP diet intervention. * = statistically significant at $P < 0.05$ level. Abbreviations: 5-HT: serotonin; 5-HIAA: 5-hydroxyindoleacetic acid

Abstract Code: NGS15475-94 – Poster of Distinction | **Efficacy and safety of STW-5 II in an 8-week treatment of functional dyspepsia: a meta-analysis**

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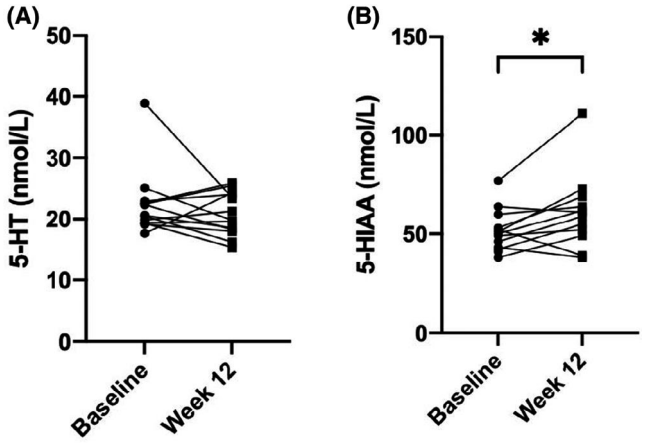
Objective: Treatment options for functional dyspepsia (FD) are scarce. For the commercially available herbal product STW5-II evidence from randomized, controlled clinical trials (RCTs) is available. This meta-analysis investigated the 8-week efficacy of STW 5-II regarding the improvement of FD symptoms (ROME-IV criteria) and the tolerability.

Methods: Two RCTs [1, 2] met inclusion criteria of 8-week treatment duration. Analysis set (AS) comprised patient data with at least one FD key symptom (fullness, early satiety, epigastric pain) of moderate severity at baseline. Meta-analyses (based on study specific ANCOVA results) were performed on improvement of the total sum symptom score (GIS [3]) and of single symptoms scores after 28 and 56 days.

Results: The AS comprised 326 patients (STW 5-II: 164, placebo: 162). Meta-analysis provided statistically significant results in favor of STW 5-II for the overall improvement of FD symptoms after 4 weeks (Mean difference (MD) 1.74; 95% CI 0.90; 2.58; $P < 0.001$) and 8 weeks (MD 2.07; 95% CI 1.09; 3.04; $P < 0.001$) treatment. The overall improvement of GIS sum score differed 1.63 after 4 weeks ($P = 0.0003$) and 1.91 after 8 weeks ($P = 0.0003$) treatment for STW5-II vs placebo. Key FD symptoms significantly ($P < 0.05$) improved in favor for STW5-II after 28 and 56 days: Fullness MD 0.28 (95% CI



0.10; 0.48; $P = 0.002$) and MD 0.29 (95% CI 0.09; 0.49; $P = 0.005$), Early satiety MD 0.25 (95% CI 0.06; 0.45; $P = 0.011$) and MD 0.26 (95% CI 0.05; 0.47; $P = 0.014$), Epigastric/ upper abdominal pain MD 0.26 (CI 0.10; 0.42; $P = 0.002$) and MD 0.3 (95% CI 0.10; 0.49; $P = 0.003$). No difference between STW5-II and placebo was seen for safety and tolerability.

Conclusions: STW 5-II improves both overall FD as well as key symptoms (ROME IV) after 4 and 8 weeks and is a considerable therapeutic option in this difficult to treat disorder.

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Abstract Code: NGS15511-85 – Poster of Distinction | **Improvement of functional dyspepsia symptoms by the six food elimination diet**

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Objective: The Rome IV criteria define functional dyspepsia (FD) by the presence of upper gastrointestinal symptoms in the absence

of readily identifiable organic abnormalities. FD is subdivided into postprandial distress syndrome (PDS), characterized by early satiation and postprandial fullness, and the epigastric pain syndrome characterized by epigastric pain or burning. Increased duodenal mucosal permeability and elevated mast cell and eosinophil counts have been reported in FD patients, associated with early satiation. Luminal food antigens are candidate triggers for these duodenal alterations. Our aim was to evaluate the effect of the six-food elimination diet (SFED) on symptoms, gastric sensorimotor function and duodenal alterations in PDS patients.

Methods: H. pylori negative PDS patients were recruited. The SFED was followed for an 8-week period. Patients filled out the Leuven Postprandial Distress Syndrome (LPDS) diary. Duodenal biopsies were obtained before and after the diet to evaluate mucosal permeability in Ussing chambers (trans-epithelial electrical resistance (TEER) and flux of a fluorescent-labelled dextran), and a gastric barostat study was performed. Changes in quality of life (QoL) were assessed by the Short Form Nepean Dyspepsia index. Data are reported as mean ± standard error of the mean. Results were considered significant if $P < 0.05$. A change in LPDS score of at least 0.7 was considered a clinically significant response.

Results: To date, 11 patients were recruited of whom 7 (6 females; 38 ± 6years; BMI 23.3 ± 1.3kg/m^2) finished the SFED. Combined LPDS score improved from 1.9 ± 0.7 to 1.2 ± 0.82 ($P = 0.0085$) with a responder rate of 71%. Baseline symptoms scores for early satiation, postprandial fulness and bloating were respectively 1.7 ± 1.1; 2.1 ± 0.6 and 1.9 ± 0.5, compared to respectively 1.0 ± 0.8 ($P = 0.006$); 1.3 ± 0.8 ($P = 0.018$); 1.2 ± 1.0 ($P = 0.049$) after 8 weeks. QoL did not significantly change (27.3 ± 12.1 vs. 25.0 ± 13.9; $P = 0.38$). Duodenal permeability including TEER (35.3 ± 12.4 vs. 34.6 ± 16.4 ohm.cm^2) and flux (6.7 ± 2.4 vs. 8.3 ± 3.7 pmol) was not significantly altered. Gastric accommodation was not significantly changed (229 ± 48mL vs. 145 ± 86mL, $P = 0.09$). Two patients with hypersensitivity to gastric distention at baseline normalized after the diet ($P = 0.45$).

Conclusions: This proof-of-concept study shows the potential for the SFED to improve symptoms in PDS patients, while QoL, gastric sensorimotor function and duodenal permeability are not significantly altered.

Abstract Code: NGS15507-90 – Poster of Distinction | **Origin of the gastrointestinal intraluminal pressure wave and its relationship with phasic contraction**

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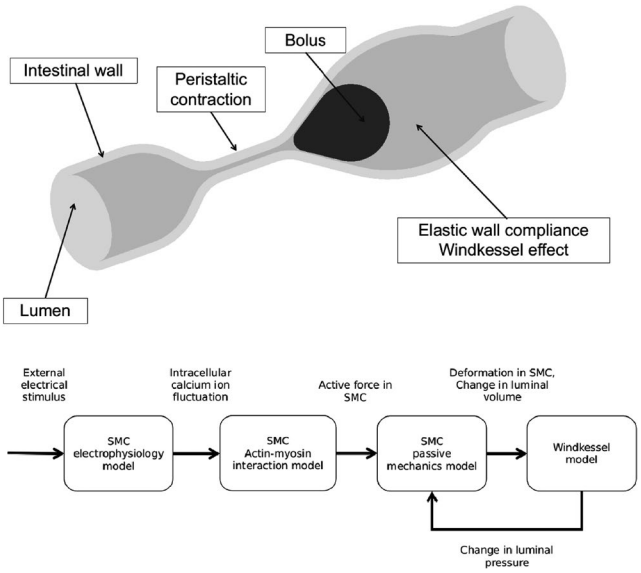
Objective: Gastrointestinal (GI) motility is a complex process that includes myoelectrical activity, GI tissue contraction, and transit. It is characterized by organized motor patterns and pressure waves inside the lumen resulting from phasic contraction of the wall. These pressure waves can identify patterns suggestive of myopathy, neuropathy, or obstruction. However, the relations of these pressure waves to the GI wall contraction are not well studied. Therefore, the objective of this study was to formulate a computational framework that can recreate the luminal pressure waves from the myoelectrical activities of the GI smooth muscle cells (SMC).

Methods: We used a multi-scale, multi-physics approach coupling biophysically-based SMC electrophysiology, excitation-contraction (EC), and finite nonlinear hyperelastic mechanics (HM) models with a two-element Windkessel model (WK). The SMC model described the dynamic characteristics of the ion channels of the cell membrane, whereas the EC model described the actin-myosin interactions that produced active force. The HM model transformed the active forces into mechanical deformation of the GI wall. Subsequently, the WK model computed the pressure inside the lumen arising because of the wall deformation. We used this coupled model to describe the transduction process from cellular electrical activity into the generation of intraluminal pressure waves of the GI tract (Figure 1).



Results: For simplicity, we assumed the intestine to be a circular cylinder. With applied external electrical pulses, the SMC model generated action potentials with peak and plateau potentials of -35mV and -40mV, respectively; whereas, the EC model produced active contractile waves of magnitude 3.5kPa. We observed a reduction of 80.64% in the luminal area, and the corresponding rise in the luminal pressure was 2.7kPa. The computed pressure waves were found to be comparable with the experiments.

Conclusions: Our coupled framework was able to establish a relationship between the change in myoelectrical activity and intraluminal pressure. We found that the pressure becomes maximum at the vicinity of the peak wall contraction that was consistent with experimental data. In the future, this modeling strategy will offer a multitude of opportunities to investigate GI motility in health and disease.

A model for the pressure wave generation in the intestine

Abstract Code: NGS15375-93 – Poster of Distinction | **Reporting of comorbidities and overlap syndromes in functional dyspepsia trials: a systematic review of RCTs over 15 years**

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Introduction: The Rome Foundation stated recommendations in 2016 to report confounding factors in clinical trials concerning functional gastrointestinal disorders (FGIDs). The aim of our study was to assess the reporting of different comorbidities and overlap syndromes in patients with functional dyspepsia (FD).
Methods: Randomised controlled trials (RCTs) that included adult patients with FD according to Rome criteria were selected via MEDLINE (PubMed®) and Scopus between 2006 and 2021. Characteristics of the trials and the patients, exclusion criteria, psychological factors, other FGIDs, somatic disorders, and non-gastrointestinal (GI) diseases were all recorded. We analysed the level of reporting of these comorbidities, focussing on the six most frequent. The study selection and data extraction were performed by FW; the systematic review was registered in PROSPERO (CRD42021235219).
Results: 108 articles were included in the final analysis. Clinical trials were mainly conducted in Asia (76.9%) and involved a complementary and alternative medicine treatment in 45.4% of the cases. The mean number of reported comorbidities was 2.44 (±1.23 SD). Only one paper reported all six comorbidities. 96.3% of the papers reported at least one comorbidity. 22.2% of papers reported anxiety, and 24.1% reported depression. 63.0% of the papers reported an overlap with gastro-oesophageal reflux (GOR) and 43.5% with irritable bowel syndrome (IBS). *H. pylori* gastritis and diabetes mellitus were reported in 54.6% and 37.0% of the papers respectively. There was no reported overlap with non-GI comorbidities. The reporting of overlaps and comorbidities during the study period remained unchanged.
Conclusions: The most reported comorbidities in FD trials are depression and anxiety levels, overlaps with GOR and IBS, *H. pylori* gastritis and diabetes mellitus. Overall, at least one of these comorbidities was reported in almost all articles, with a mean of about 2.5 comorbidities reported in each one.

Abstract Code: NGS15513-87 | **A combination of symptoms and visceral sensitivity are of importance for disease-specific quality of life in irritable bowel syndrome**

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Objective: Patients with IBS report reduced quality of life (QOL). However, it is not completely understood how different biopsychosocial factors influence QOL, and the relative importance of these factors. Factors of potential relevance include gastrointestinal (GI), psychological and somatic symptoms, GI motor and sensory abnormalities. Therefore, the aim of our study was to evaluate the importance of different factors and their effect on disease-specific QOL (IBS-QOL).
Methods: We included IBS patients (diagnosed according to Rome criteria) who completed the IBS-QOL questionnaire and validated questionnaires to assess stool form (BSF) and frequency, GI symptom severity (GSRS-IBS), general anxiety and depression (HADS), GI-specific anxiety (VSI), sense of coherence (KASAM), and overall somatic symptom severity (PHQ-12 & SCL-90R). Patients also underwent an oro-anal transit time (OATT) measurement and a rectal barostat examination. The average of the nine subscales of IBS-QOL was used as outcome variable, hereafter named overall IBS-QOL (range 0-100). Bivariate associations between IBS-QOL and the other factors were assessed using Pearson correlations. Variables significantly associated with IBS-QOL were entered into the general linear models (GLM), controlling for gender.
Results: We included 314 IBS patients (73.6% female, mean age 36.3 ± 12.2 years). Proportions of IBS subtypes included 22% IBS with constipation in, 42% with diarrhoea and 36% mixed or unsubtyped. Patients had a mean IBS duration of 11.6 ± 11.3 years. The overall IBS-QOL was 61.9 ± 17.8. Gender, stool frequency, GI and overall somatic symptom severity, general and GI-specific anxiety, sense of coherence, depression and rectal pain threshold were bivariately associated with overall IBS-QOL. These factors were included in the GLM analysis ($F(9,193) = 35.873$, $P < 0.001$, $R^2 = 0.608$) and stool frequency, GI and overall somatic symptom severity, depression, GI-specific anxiety and a lower rectal pain threshold were independently associated with reduced overall IBS-QOL (Table 1).
Conclusions: GI, somatic and psychological symptoms, and visceral sensitivity were found to be important determinants of overall disease-specific QOL in IBS. Hence, careful assessment of all these factors in patients with IBS is recommended as part of the management approach aiming towards QOL improvement.

Abstract Code: NGS15479-98 | **Characteristics of reflux episodes in patients with functional dyspepsia based on the Rome IV criteria**

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Objective: Overlap between dyspeptic and esophageal symptoms is commonly observed. In this study, we aimed to investigate the reflux

episodes using impedance-pH monitoring in patients with functional dyspepsia.

Methods: A total of 21 consecutive adult patients (12 female, 9 male) with functional dyspepsia by Rome IV criteria were included in this study. Patients whose predominant symptom was typical reflux symptoms were excluded from the study. All patients underwent ambulatory 24-h pH-impedance monitoring off-therapy. Reflux episodes were identified and classified as acid with a pH < 4, weakly acidic with a pH 4-7, or weakly alkaline reflux with a pH > 7. Acid exposure time (AET) was considered abnormal when pH is < 4 in the distal esophagus above 6% over 24 h, and borderline between 4%-6%.

Results: The median number of total reflux episodes was 51 (25th-75th percentile; 27-81). Four patients (19%) had pathological AET, and 1 patient (5%) had borderline AET. According to Rome IV criteria, %57 of the 21 patients included in the study had postprandial distress syndrome (PDS), %29 had epigastric pain syndrome (EPS), and %14 had an overlap. There was no difference between the three groups in the number of reflux episodes or the parameters of acid reflux (Table 1).

Conclusions: Although the number of reflux episodes in patients with functional dyspepsia was inconclusive, esophageal baseline impedance and lower esophageal sphincter pressure were found to be within the normal limits. The reflux episodes by ph-impedance monitoring and reflux characteristics were not different between the subgroups of functional dyspepsia.

Abstract Code: NGS15525-90 | Differences in IBS Care and Training across Europe (DICE) Study: A pan-European internet-based survey

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Objective: Significant variations in IBS care and education may exist around European countries. This can translate into a substantial additional misdiagnosis and economic burden. Therefore, we aimed to conduct the *Differences in IBS care and training across Europe* (DICE) study and to investigate the variations among countries.

Methods: The online survey was initiated by the European Society of Neurogastroenterology and Motility (ESNM) and run by Google Surveys. It consisted of 56 questions, divided into 5 sections: demographics, IBS Training, IBS Diagnosis, IBS Management, and organization. Results were compared according to human development index (HDI), for which countries were divided into two groups: low HDI < 0.880 and high HDI ≥0.880

Results: The survey was completed by 593 participants from 46 European countries, mainly specialists (72.8%) working in University hospitals (55.3%). Significant differences in availability of Neurogastroenterolgy Units (47.4% vs. 15.6%, $P < 0.001$), IBS-focused dietitians (37.5% vs. 14.3%, $P < 0.001$), and usage of telemedicine to consult/follow-up IBS patients (34.4% vs. 25.0, $P = 0.016$) were observed between responders from high and low HDI countries. In high HDI countries, IBS is diagnosed mainly by

R^2=0.608, n=203	Overall IBS-QOL	
	β	p-value
GI and somatic symptoms		
Stools/day, n= 228	-0.105	**0.025**
IBS severity (GSRS-IBS),n=309	-0.155	**0.011**
Overall somatic symptom severity (PHQ15 & SCL-90R), n=268	-0.158	**0.010**
Psychological symptoms		
General anxiety (HAD-A), n=312	0.000	0.997
Depression (HAD-D), n=312	-0.222	**0.001**
GI-specific anxiety (VSI), n=310	-0.343	**<0.001**
KASAM, n=268	0.050	0.209
GI sensorimotor function		
Rectal pain threshold, n=314	0.108	**0.025**

	PDS (n=12)		EPS (n=6)		Overlap (n=3)		
	mean ± SD	median	mean ± SD	median	mean ± SD	median	p
Age	44,7 ± 13,2	46,5	48,5 ± 14,0	54	35,3 ± 14,2	43	0,403[A]
BMI (kg/m²)	24,8 ± 3,2	25,2	28,7 ± 6,7	29,1	23,1 ± 2,4	22,0	0,140[A]
LES pressure (mmHg)	21,6 ± 12,9	19,0	18,5 ± 11,1	15,5	23,3 ± 3,1	24	0,491[K]
AET	8,1 ± 18,8	2,2	2,4 ± 1,9	2,0	16,5 ± 26,9	1,6	0,949[K]
DeMeester score	28,0 ± 67,5	8,3	8,0 ± 5,0	7,4	55,0 ± 95,2	1,7	0,780[K]
Acid reflux	29,0 ± 27,3	27,0	18,8 ± 17,9	14,5	27,0 ± 36,4	7,0	0,620[A]
Weakly acidic reflux	37,9 ± 35,1	26,0	17,2 ± 12,5	16,0	21,7 ± 22,7	18,0	0,743[A]
Weakly alkaline reflux	2,2 ± 1,9	2,0	11,8 ± 18,6	4	1,3 ± 2,3	0,0	0,341[A]
Total reflux	69,4 ± 58,4	60,5	47,8 ± 23,5	50,0	50,0 ± 20,5	51	0,557[K]
MNBI	2569 ± 1362	2498	1802 ± 901	1521	3221 ± 3287	2450	0,435[A]

AET, acid exposure time; BMI, body mass index; EPS, epigastric pain syndrome; LES, lower esophageal sphincter; MNBI, mean nocturnal baseline impedance; PDS, postprandial distress syndrome
[A] one-way ANOVA
[K] Kruskal-Wallis test

symptom-based diagnostic criteria and minimizing investigations (54.0% vs. 31.5%, $P < 0.001$), while in low HDI countries - by excluding organic disease after performing ultrasound, endoscopy, and other tests (64.6% vs. 41.4%, $P < 0.001$). Antispasmodics as first-line therapy for pain (91.6% vs. 67.4%, $P < 0.001$) and probiotics (68.5% vs. 41.8%, $P < 0.001$) are more used in low HDI countries. In high HDI more gastroenterologists are confident to use antidepressants compared to low HDI countries (51.2% vs. 22.7%, $P < 0.001$). IBS-specific training (OR 2.5), IBS fellowship (OR 2.33), general interest in IBS (OR 2.3), following IBS guidelines every time (OR 6.43), and access to a multidisciplinary IBSboard (OR 4.02) have a significant impact on responders' confidence to treat IBS patients.

Conclusions: Large variations in IBS training and management exist across Europe, with notable differences between high and low HDI countries. More efforts are needed to address these in order to improve IBS management and education in Europe.

Abstract Code: NGS15494-95 | Discrete choice experiment reveals strong preference for dietary treatment among patients with irritable bowel syndrome

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Background & Aims: Irritable Bowel Syndrome (IBS) is a highly frequent, chronic disorder of the Gut-brain interaction which significantly affects quality of life. Several treatments are available for the treatment of IBS, with comparable clinical efficacy. Patient preference can therefore be an important determinant of an effective management strategy. The treatment preferences of patients regarding decision-making remain unclear. We aimed to examine these current preferences and estimate trade-offs between different attributes.

Methods: 427 patients from the Maastricht IBS cohort were invited to participate. A labeled discrete choice experiment (DCE) survey, containing 9 scenarios with each three alternatives (medication, diet, psychotherapy), was developed in order to estimate preferences. The treatment scenarios were based on six attributes: effectiveness, time to response, time until recurrence, side effects, treatment burden, frequency of appointments. Semi-structured interviews of patients, a literature screen and an expert opinion meeting were used as input for the DCE. Statistical analysis was conducted with a mixed logit model, combined with interactions- and subgroup analysis including variables such as age, symptom severity and the presence of depression or anxiety.

Results: A total of 185 (43.33%) of 427 potential respondents completed the questionnaire (mean age 49.51, 69.20% female). The most preferred treatment was diet therapy (48.10%), subsequently pharmacological therapy (29.20%) and psychotherapy (22.70%). IBS patients preferred a high effectiveness, little time to response, long time until recurrence, no severe side effects and frequent appointments when attending psychotherapy. Heterogeneity in preferences among patients existed regarding effectiveness and time until recurrence. Younger patients (≤50 years) preferred dietary interventions and a long period until recurrence, whereas older patients (>50 years) were more inclined to choose pharmacotherapy and the period until recurrence was not important.

Conclusions: Dietary interventions were the most preferred IBS therapy. Identifying patients' treatment preferences during shared-decision making, will provide more optimal management strategies and could be the angle of approach to diminish disease burden.

Abstract Code: NGS15517-91 | Effect of fermented oat on colonic mucosal barrier in Irritable Bowel Syndrome

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Objective: Irritable Bowel Syndrome (IBS) is a debilitating disease lacking adequate treatment, since its pathophysiology remains obscure. Impaired intestinal permeability is one of the main pathophysiological mechanisms in IBS, as well as altered gut microflora. One of the vast studied bacteria strains is Lactobacillus plantarum 299v, showing some beneficial effects on symptoms in IBS. Short chain fatty acids (SCFA), bacterial metabolites built during the fermentation process, have shown to enhance intestinal barrier function. ReFerm is food product of oat gruel fermented with L. plantarum 299v containing high amounts of SCFA. We conducted a pseudo-randomized double blind experimental study to determine the effect of ReFerm on colonic barrier function in patients with IBS.

Methods: 30 patients with moderate to severe IBS with predominant diarrhea (IBS-D) and IBS-mixed (IBS-M) according to Rome IV criteria and symptom severity score, were allocated to ReFerm (18 patients, 2 men) or placebo (12 patients, 3 men) arms. The drop out was four (no men) and two (one-man) patients in both arms, respectively. The patients underwent sigmoideoscopy with biopsies taken from the distal colon before and after two weeks of enema treatment with ReFerm or placebo twice daily. The biopsies were mounted in Ussing chambers, and the paracellular permeability as well as the transcellular permeability was measured for 90 minutes using fluorescein isothiocyanate (FITC)-dextran 4000 and horseradish peroxidase (HRP), respectively. The transepithelial potential difference (PD) and the transepithelial resistance (TER) across the tissues were monitored throughout the experiments to ensure tissue viability.

Results: PD was stable in all biopsies mounted. The study showed significantly reduced paracellular permeability after intervention with ReFerm ($P < 0.05$), but not in the placebo arm (Figure 1). The difference in TER over time (30-90 minutes) was significantly decreased in the ReFerm arm after intervention in comparison to baseline ($P < 0.01$), indicating an improved barrier function. However, ReFerm showed no effect on transcellular permeability of colonic biopsies.

Conclusions: We demonstrated that ReFerm significantly reduces paracellular permeability in colonic biopsies of patients with IBS-D and IBS-M, confirmed by decreased TER changes. These results together indicate barrier-protecting properties of ReFerm, and suggest further studies of treatment effect and underlying mechanisms in IBS patients.

Abstract Code: NGS15605-89 | Functional GI diseases in children: Pharmaco-epidemiological data on an herbal therapeutic from the PhytoVIS database

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Objective: Data from pharmaco-epidemiological research can provide insight where clinical trials are difficult to conduct, as e.g. in the pediatric population. This also applies to the treatment of functional GI diseases by STW 5, a herbal therapeutic approved for use in children from an age of 3, based on several pro- and retrospective non-interventional studies in the paediatric population. To broaden this basis, data from the PhytoVIS study, presumably the world´s largest pharmaco-epidemiological study on the use of herbal medicinal products [1], were evaluated with regards to the use of STW 5 in the paediatric population.

Methods: The PhytoVIS database, consisting of 20,870 patients in total and 2063 data sets for the paediatric population, was screened for data on paediatric patients using STW-5. The data in this data base have been collected by means of a retrospective, anonymous survey in Germany [2].

Results: Overall, 77 datasets from the paediatric population were evaluated (60% female, 40% male). Dyspepsia-associated symptoms (FD) were the largest group (90%) while IBS-associated symptoms were described by 4%, and FD-/IBS associated by 6% of patients. In most cases, the therapeutic effect was perceived within 60 minutes after ingestion. The effect of the therapy was rated as very good by 60% of the FD patients, as moderate by 30% and as minimal by 10%. 65% of patients experienced slight adverse effects with no significant impairment while 93% experienced no adverse effects at all.

Conclusions: The data shed light on a still neglected field of the pharmacotherapy of functional GI diseases by giving information on the use of STW 5 in an unselected cohort of paediatric patients. Overall, studies based on this data base turn out to be a valuable tool to explore the pharmaco-epidemiology of children.

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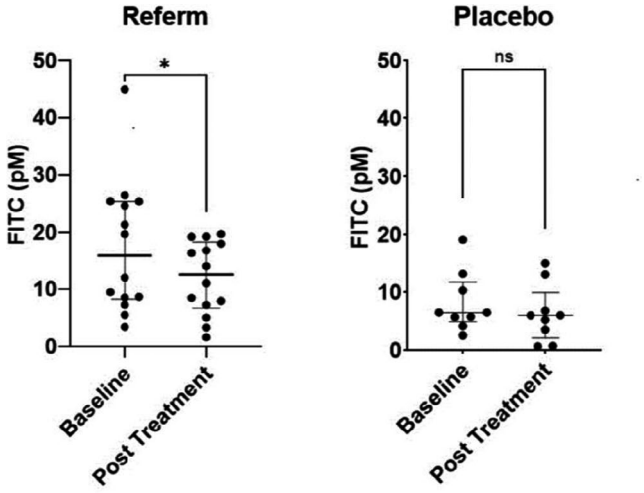

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Abstract Code: NGS15489-99 | IBS-like syndrome among medical students: Prevalence and associations

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Abdominal pain is the most common gastroenterological syndrome. A feature of young people is the predominance of functional disorders, for example irritable bowel syndrome (IBS). We can only assume the widespread prevalence of functional diseases in the youth environment, since we do not exclude organic diseases, which may also occur under these symptoms.

The aim is to study the prevalence of IBS-like syndrome in relation with the diet and the level of anxiety and depression.

Materials and method: An anonymous survey was conducted of 3634 students studying at the Omsk State Medical University and who gave informed consent to participate in the study, by filling out the online questionnaire forms GSRS, WHO CINDI program questionnaire, MINIMULT. The average age was 20.34 ± 3.68 years. 709 (19.51%) were males and 2925 (80.49%) females.

Results: The analysis of the questionnaire results revealed the following gastrointestinal symptoms: abdominal pain - in 2300 (63.29%), constipation - in 1353 (37.23%), diarrhea - in 1215 (33.43%) respondents. Persons with abdominal pain consumed coffee in a statistically significant amount (U = 1544300.5, $P = 0.0048$), they more often had an addiction to spicy food (2I = 7.76, $P < 0.001$), the habit of adding salt to cooked food (2I = 18.85, $P < 0.001$) and depressed mood background (2I = 17.49, $P < 0.001$). People with diarrhea are characterized by increased consumption of milky products (2I = 14.36, $P < 0.05$), addiction to salty foods and a high level of anxiety (2I = 101.0, $P < 0.001$). Persons with constipation are more likely to overeat (2I = 57.77, $P < 0.001$), addiction to flour products (2I = 27.8, $P < 0.001$), a tendency to depression (2I = 16.92, $P < 0.001$). All IBS-like symptoms were associated with low consumption of fruits and vegetables (U = 1391865.5, $P = 0.000$, U = 1340501.5, $P = 0.000$, U

= 1321122.5, P = 0.000 for abdominal pain, constipation and diarrhea, respectively). All respondents with gastrointestinal symptoms more often reported limited time for eating (2I = 13.91, P < 0.001), inability to eat at the same time (2I = 58.87, P < 0.001).

Conclusions: A high incidence of IBS-like syndrome was closely related with eating habits, levels of anxiety and depression.

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Abstract Code: NGS15533-89 | Meal-related abdominal pain and its association to disorders of gut-brain interaction and gastrointestinal symptoms

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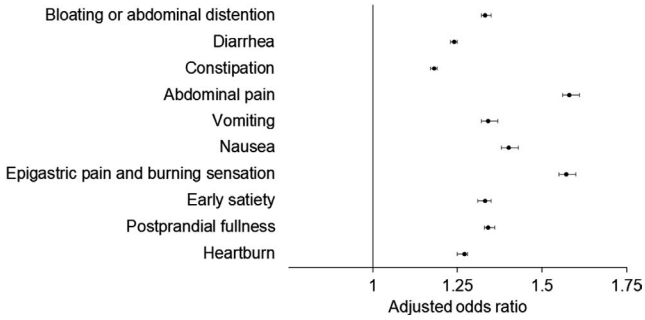
Objective: Patients with disorders of gut-brain interaction (DGBIs) can report meal-related gastrointestinal (GI) symptoms. However, this subgroup of DGBI patients is not well-characterized. We aimed to describe the global prevalence of meal-related abdominal pain in individuals without organic GI disorders and characterize this subgroup.

Methods: The data analyzed originated from the population-based Rome Foundation Global Epidemiology internet survey completed in 26 countries (N = 54,127) (Sperber et al. Gastroenterology 2021). Subjects were asked whether they had abdominal pain and how often this was meal-related. Respondents were categorized into three groups of meal-related abdominal pain; subjects who indicated 0% of the time with pain ('no'), 10-40% of the time with pain ('occasional'), and ≥50% of the time with pain ('frequent'). DGBI diagnoses and frequency of other GI symptoms (such as heartburn, constipation etc.) were assessed with the Rome IV diagnostic questionnaire. Mixed ordinal regression was used to assess associations between meal-related abdominal pain as outcome, other GI symptoms as independent variables and country as a random effect (accounting for inter-country variability).

Results: Overall, 11.0% [95% confidence interval: 10.7-11.2] of the subjects (13.1% [12.7-13.5] of females and 8.9% [8.5-9.2] of males) reported frequent meal-related abdominal pain. This was more common in younger age groups (18-29 years, frequent: 31.1% [29.9-32.3], occasional: 28.2% [27.4-29.0], no: 24.8% [23.9-25.7], P < 0.001). Having at least one bowel disorder was more common in the 'frequent' meal-related abdominal pain group compared to the 'occasional' and 'no' meal-related abdominal pain groups (67% [65.9-68.3] vs. 49% [48.0, 49.8] vs. 36% [34.6-36.5], P < 0.001). Having frequent meal-related abdominal pain was independently associated with having all other GI symptoms more frequently. The GI symptoms with the highest odds ratios were abdominal pain (OR = 1.58 [1.55-1.61], epigastric pain and burning sensation (OR = 1.57 [1.55-1.60], and nausea (OR = 1.40 [1.38-1.4]) (P < 0.001 for all) (Figure 1).



Conclusions: Subjects in the general population who report frequent meal-related abdominal pain experience more GI symptoms in general and more other types of pain symptoms in particular. They also fulfill diagnostic criteria for a bowel disorder more often. The impact of meal-related abdominal pain on diagnostic criteria, outcomes, and management needs to be evaluated.

Abstract Code: NGS15528-93 | Organic or functional in esophageal food impaction

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Aim: To assess the prevalence and characteristics of eosinophilic esophagitis (EE) in patients with esophageal food impaction (EFI).

Material and methods: Retrospective study, conducted over a period of 5 years (2016-2020), which included adult patients with EFI. Patients with esophageal disorders (stricture, cancer, hiatal hernia, Schatzki ring, motility disorders) or extra-esophageal disorders (diabetes, neurological disorders, psychiatric, disorders) were excluded.

Results: 146 patients were included in the study, 50 women (34.25%) and 96 men (65.75%), aged between 25 and 91 years (mean age 61.9 years). At the time of endoscopy, 96 patients (65.8%) presented associated digestive or extra-digestive lesions. Of these, 86 presented digestive lesions: 46 cases of benign stricture, 14 cases of esophageal cancer, 8 esophageal motility disorders, 10 cases of esophageal diverticula, 6 cases of hiatal hernia, 2 cases of esophagoplasty. In addition, 10 patients presented extra-digestive lesions: stroke - 3

cases, diabetes - 3 cases, Parkinson's disease - 2 cases, multiple sclerosis and Alzheimer's disease - 1 case. Performing endoscopy for EFI led to the detection of another 18 cases (12.32%) of associated digestive lesions: 6 cases of benign esophageal stricture, 4 cases of esophageal diverticulum, 4 cases of esophageal neoplasm, 2 cases of hiatal hernia and 2 cases of Schatzki ring. After performing endoscopy, 114 patients (78.08%) presented associated pathology. Biopsy was taked from 32 patients who did not have any associated pathology to detect EE. The diagnosis of EE was established in 14 patients (9.58% of patients with EFIA). Group A was characterized by a significantly lower mean age (42.64 vs 56.89; $P = 0.009$), normal endoscopic appearance in ¼ of the patients (21.4% vs 77.8%; $P = 0.005$), the presence of allergic diseases (64.3% vs 5.6%; $P = 0.036$), history of dysphagia (42.9% vs 16.7%; $P = 0.017$) and the presence of complications (21.4% vs 0%; $P = 0.042$).

Conclusions: According to the data obtained in our study, EE represented only 9.58% of the causes of EFI. Most patients with EE and EFI impaction were male, with a mean age of 42.64 years, associated with allergic diseases in 64.3% of the cases and a history of dysphagia.

Abstract Code: NGS15522-87 | Poor sleep quality predicts next day abdominal pain in irritable bowel syndrome using the experience sampling method

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Introduction: Sleep quality has the potential to impact symptom experience in Irritable Bowel Syndrome (IBS); a stress-sensitive disorder. We aimed to investigate the relationship between self-reported sleep indices and IBS symptoms using the Experience Sampling Method (ESM) as a real-time, repeated measurement method.

Methods: Single-centre, prospective, cross-sectional study conducted at the Wingate Institute of Neurogastroenterology, London, from March 2020 - May 2021. IBS patients recorded their symptoms on a smartphone application over 7 consecutive days. Two thirds of the sample were recruited from a community population and one third from our tertiary clinic. Self-reported sleep indices (sleep latency, number of awakenings, early morning awakening, sleep quality and nocturnal abdominal pain) were scored once daily to reflect the night before and IBS symptoms at ten random moments each day, using an 11-point numeric rating scale.

Results: 48 patients were included in the analysis (Female: 83%, median age; 35) with an IBS sub-type distribution of: IBS-D 70%; IBS-C; 20%; IBS-M; 17.5%; IBS-U; 12.5%. Linear mixed effect models showed a negative association between self-reported sleep quality (higher scores correspond to better sleep) and mean daily abdominal pain scores (higher scores correspond with worse pain). On average, a 1-point increase in sleep quality during the night was associated with a 0.05 decrease in abdominal pain the next day (SE: 0.013, $P < 0.001$). Reverse association was not significant, i.e. mean abdominal pain scores during the day did not predict sleep quality that night ($P = 0.59$). Number of awakenings at night was associated with mean nocturnal abdominal pain whereby an increase of 1 awakening lead to a 0.80 increase in nocturnal abdominal pain (SE: 0.120 $P < 0.001$). Additional relationships between sleep indices and IBS symptoms were not found to be significant.

Conclusions: Our results demonstrate a negative association between self-reported sleep quality and abdominal pain the next day. This study underlines the importance of considering the role of sleep quality as a lifestyle factor in the management of abdominal pain in the IBS population. It also supports the use of real-time patient reported outcome measures when interpreting potential influencers of IBS symptoms.

Abstract Code: NGS15515-89 | Quality of life in irritable bowel syndrome (IBS): Exploring mediating factors through structural equation modelling

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Objectives: IBS negatively influences mental and physical quality of life (QoL), but factors that explain this impact are still unclear. Mounting evidence has associated IBS severity, psychological distress, somatic symptoms, and gastrointestinal-specific anxiety with QoL in IBS. The aim of this study is to further explore these associations and to analyse potential mediating factors.

Methods: We included 183 adults with IBS (73% female, mean age 41.7 years) who completed validated self-report measures to assess factors of potential relevance for QoL: GI (GSRS or IBS-SSS[Z-score]) and overall somatic symptom severity (PHQ-15 or SCL-90[Z-score]), psychological distress (HADS), and GI-specific anxiety (VSI). Structural equation modelling was used to identify factors of importance for generic QoL, measured with SF-36.

Results: Our sample of IBS patients presented considerably lower scores on physical and mental QoL in comparison with Swedish normative data (Sullivan et al 1998). Correlation analyses demonstrated that both mental and physical QoL were significantly associated with IBS severity, depressive symptoms, GI-specific anxiety, and somatic symptom severity. Mental QoL was additionally associated with

general anxiety. A path analysis model examining the mediating effects of GI-specific anxiety and somatic symptoms in the association of IBS severity, general anxiety, and depressive symptoms with QoL was analysed while controlling for age and sex. The model was first analysed as a fully saturated model in which non-significant paths were progressively removed. Model fit was excellent (CFI = 0.96; $\chi2_{(20)}$ = 30.37, *P* = 0.064; RMSEA = 0.05, *P* = 0.406). The path analysis showed that the effects of IBS severity on mental (β = -0.05, *P* = 0.005) and physical QoL (β = -0.06, *P* = 0.007) were totally mediated by GI-specific anxiety. The effect of general anxiety on mental QoL was also totally mediated by GI-specific anxiety (β = -0.06, *P* = 0.005), and the effect on physical QoL was mediated by both GI-specific anxiety and somatic symptoms (β = -0.12, *P* = 0.001). Depressive symptoms presented a non-mediated, direct effect on mental QoL (β = -0.39; *P* < 0.001).

Conclusions: GI-specific anxiety and somatic symptom severity appear to be important mediators of the effects of IBS severity and psychological distress on QoL. Depressive symptoms appear to have an independent effect on mental QoL. Addressing GI-specific anxiety, and somatic and depressive symptoms seems to be important in IBS management.

Abstract Code: NGS15484-94 | Return on investment of internet delivered exposure therapy for irritable bowel syndrome: A randomized controlled trial

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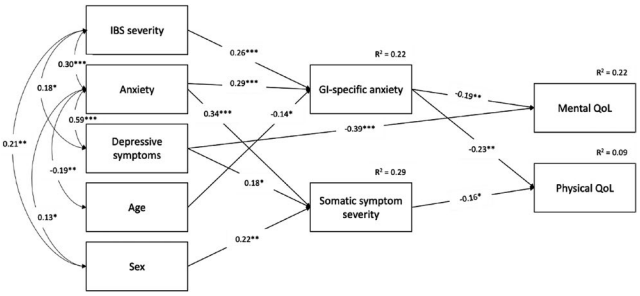
Background: Irritable bowel syndrome (IBS) is a debilitating and costly disorder. Cognitive behavior therapy (CBT) is effective in the treatment of IBS (1). CBT consists of different components and little is known about their relative importance. We have in an earlier study showed that inclusion of exposure in the CBT for IBS makes it even more effective. In the present study we wanted to evaluate the economic effects for society of inclusion vs exclusion of exposure in an internet delivered CBT for IBS.

Methods: We used data from a previous study with 309 participants with IBS. The study was conducted at the Internet Psychiatry Unit in Stockholm, Sweden. Participants were randomized to internet delivered CBT (ICBT) with or without exposure (ICBT-WE). We compared direct and indirect costs at baseline, after treatment, and 6 months after treatment (primary endpoint; 6MFU). Data was also collected on symptom severity and time spent by therapists and participants. The relative Incremental Cost Effectiveness Ratio (ICER) was calculated for the two treatment conditions and also the return on investment (ROI).

Results: Results showed that ICBT cost $213.5 (20%) more than ICBT-WE per participant. However, ICBT was associated with larger



cost and symptom reductions than ICBT-WE at 6MFU. The ICER was -301.69, meaning that for every point improvement on the Gastrointestinal Symptom Rating Scale – IBS version in ICBT, societal costs would be reduced with approximately $302. At a willingness to pay for a case of clinically significant improvement in IBS symptoms of $0, there was a 84% probability of cost-effectiveness. ROI analysis showed that for every $1 invested in ICBT rather than ICBT-WE, the return would be $5.64.

Conclusions: Composition of the treatment matters. Adding exposure to CBT for IBS is a cost-effective intervention from a societal perspective even though it may demand more therapist and patient time.

[1] Ballou S, Keefer L. Psychological Interventions for Irritable Bowel Syndrome and Inflammatory Bowel Diseases. Clinical and translational gastroenterology. 2017;8(1):e214-e.

Abstract Code: NGS15534-90 | Rifaximin therapy for patients with irritable bowel syndrome

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Background: Evidence suggests that gut flora may play an important role in the pathophysiology of the irritable bowel syndrome (IBS). We evaluated rifaximin, a minimally absorbed antibiotic, as treatment for IBS.

Methods: In this study patients who had IBS without constipation were randomly assigned to either rifaximin at a dose of 400 mg or placebo, two times daily for 2 weeks. The end point was the proportion of patients who had adequate relief of global IBS symptoms. Adequate relief was defined as self-reported relief of symptoms for at least 2 of the first 4 weeks after treatment.

Results: There were 47 patients included in group rifaximin and 38 patients in the placebo group. There were significantly more patients in the rifaximin group than in placebo group that reported an adequate relief of global IBS symptoms during the first 4 weeks after treatment (19/47vs 12/38; 40.4% vs. 31.5%, *P* = 0.01). In addition, more patients in the rifaximin group than in the placebo group had adequate relief of bloating (16/47 vs 9/37; 34.07% vs. 24.32%, *P* = 0.005), abdominal pain (15/47 vs8/37; 31.9% vs 21.6, *P* = 0.01) In

addition, significantly more patients in the rifaximin group had a response to treatment as assessed by daily ratings of IBS symptoms, bloating, abdominal pain, and stool consistency. There were no adverse events reported in the two groups.

Conclusions: Among patients who had IBS without constipation, treatment with rifaximin for 2 weeks provided significant relief of IBS symptoms, bloating and abdominal pain

Abstract Code: NGS15490-91 | State of intestinal permeability in irritable bowel syndrome

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The increased intestinal permeability is the most promising mechanism, which in the future may become a target for therapy of irritable bowel syndrome (IBS).

Purpose: To assess the effect of intestinal permeability on the course of the disease, to study the content of fecal zonulin in patients with IBS.

Materials and methods: The study included 55 patients with IBS (main group) and 40 healthy individuals (control group) who gave informed consent to participate in the study. Among patients with IBS were 39 (70.9%) women and 16 (29.1%) men aged 20 to 49 years (33.2 ± 5.5 years). Both groups were comparable by sex and age. Depending on the subtype of IBS, the main group subjects were divided into 4 subgroups: diarrhea-predominant IBS (n = 19), constipation-predominant IBS (n = 26), mixed-type IBS (n = 6), and not classified IBS (n = 4). 29 (52.3%) had a mild disease, 17 (30.9%) had a moderate, 9 (16.4%) had a severe. The level of fecal zonulin was carried out by enzyme immunoassay using the IDK Zonulin ELISA test system (Immundiagnostik, Germany).

Results: The average concentration of zonulin in feces in the control group was 61 ± 46 ng/ml. The average concentration of zonulin in feces among subjects with IBS was higher than the reference values. There were no statistically significant differences depending on gender and age in the groups. Statistically significant differences in the level of fecal zonulin were obtained among patients with IBS, depending on the subtype ($P < 0.001$) and the severity of the disease ($P < 0.01$). The average concentration of zonulin in feces in patients with diarrhea-predominant IBS was 248.0 [176.5; 658.0] ng/ml, with constipation-predominant IBS - 112.5 [94.8; 136.0] ng/ml, with mixed-type IBS - 186.5 [130.9; 223.4] ng/ml, with not classified IBS 87.3 [64.4; 197.9] ng/ml. The average content of fecal zonulin among patients with mild IBS was 116.5 [87.3; 142.1] ng/ml, moderate - 195.9 [142.2; 235.5] ng/ml, heavy - 301.5 [192.6; 673.4] ng/ml.

Conclusions: The identified associations suggest the influence of intestinal permeability on the severity and subtype of IBS.

Abstract Code: NGS15545-92 | Stratification of patients with hypermobile Ehlers-Danlos Syndrome according to presence of functional gastrointestinal disease, psycho-morbidity and quality of life

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Objectives: Studies have demonstrated a high prevalence of Functional Gastrointestinal Disorders (FGID) in Hypermobile Ehlers-Danlos Syndrome (hEDS) and hypermobility spectrum disorders (HSD). We aimed to determine the clusters of FGID overlap existing in patients with hEDS/HSD and evaluate psychomorbidity and quality of life between clusters.

Methods: Patients from dataset 1 were recruited from EDS UK and answered questionnaire data on ROME IV for assessment of FGID, PHQ-15 for somatization symptoms, SF-8 for quality of life, GAD-7 for anxiety, and PHQ-9 for depression. Patients from dataset 2 were recruited from primary, secondary, and tertiary care settings. A gastroenterologist assessed for hEDS/HSD and issued patients with ROME III FGID diagnoses. SCL-90 was used for assessing psychological symptoms, PHQ-15, and SF-36 for quality of life. The two datasets were merged, and functional GI diagnoses were used to cluster patients by applying a computational, non-linear, dimension reduction technique (UMAP). Thereafter, data was split into original datasets, and somatization, depression, anxiety, and quality of life compared amongst clusters. Results were analysed using the Kruskal-Wallis test.

Results: Three clusters of hEDS/HSD patients were formed, with IBS ($n = 499$) and FD ($n = 498$) presenting as the two most commonly occurring FGID. [(Cluster 0 (n = 489); 99% hEDS/HSD, 69% IBS and 100% FD: hEDS+IBS+FD),(Cluster 1 (n = 305); 100% hEDS/HSD, 0% IBS and 0% FD: hEDS alone),(Cluster 2 (n = 163); 99% hEDS/HSD, 100% IBS and 0% FD: hEDS+IBS-FD)].

Both datasets demonstrated an increase in somatization ($P < 0.0001$) and depression ($P < 0.0001$) in hEDS+IBS+FD and hEDS+IBS-FD versus hEDS alone.

Additionally, somatization and depression scores (both $P < 0.0001$) were higher in hEDS+IBS+FD vs. hEDS+IBS-FD.

In both dataset 1 and 2, anxiety disorders were increased in hEDS+IBS+FD versus hEDS+IBS-FD ($P < 0.008$, $P = 0.003$), and hEDS alone ($P < 0.0001$, $P < 0.0001$), and hEDS+IBS+FD demonstrated a worse quality of life versus hEDS+IBS-FD and hEDS alone.

Conclusions: This study demonstrates that within the wider hEDS/HSD population, patients with hEDS/HSD+IBS and hEDS/HSD+IBS+FD form subgroups with poorer health outcomes, including increased severities of somatization, psychological issues, and poorer quality of lives. This study demonstrates that these subgroups of patients require more recognition and would

benefit from psychological support and multidisciplinary approach to management.

Abstract Code: NGS15531-87 | The irritable bowel syndrome post Clostridium difficile Infection

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Background: The incidence of Clostridium difficile infection (CDI) is on the rise secondary to the treatments for SARS-CoV2 infections. Infectious enteritis is a commonly identified risk factor for irritable bowel syndrome (IBS). The are a few data on Post CDI (PCDI-IBS) irritable bowel syndrome incidence.
Aim: To determine the incidence for PCDI-IBS
Methods: The study inrolled 56 patients with CDI hospitalized in The Institute of Gastroenterology and Hepatology, Iasi, between May 2020 to March 2021. Participants completed the Rome IV IBS questionnaire and details on the CDI episode at three month after the CDI episode.
Results: From 56 patients, 14 patients represented 25% met the Rome IV criteria for IBS ≥3 months following CDI. The most common form was IBS-mixed in 8 patients followed by IBS-diarrhoea in 4 patients. In a regression analyze the patients with symptoms that lasted more than one week (nausea, vomiting, abdominal pain) were more in risk to develop PCDI- IBS. Also the PCDI- CDI was more frequent in patients who presented anxiety.
Conclusions: IBS is common after CDI. Longer CDI duration and anxiety are associated with the diagnosis of IBS post CDI. This should be considered for active management and follow-up of patients with CDI.

Abstract Code: NGS15520-85 | The hedonic heterogeneity of functional dyspepsia

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Background: In healthy subjects, ingestion of a comfort meal induces homeostatic sensations, e.g., satiety, fullness, with hedonic dimension, e.g., sensation of digestive wellbeing. Patients with functional dyspepsia and postprandial distress syndrome complain of early satiety and excessive fullness but their hedonic response to meal ingestion has not been investigated.
Aim: Our aim was to determine whether and to what extent in patients with postprandial dyspepsia their hedonic response is affected.
Methods: Randomized parallel trial in patients with postprandial distress syndrome functional dyspepsia (n = 17) and age-and-gender-matched healthy controls, comparing the sensations during and after stepwise ingestion of a comfort meal up to full satiation.
Results: Healthy subjects enjoyed the comfort meal with a peak of digestive well-being (3.6 ± 0.3 score) at 865 ± 99 Kcal; well-being decreased at full station (0.2 ± 0.7 score with 1287 ± 59 Kcal) with mild postprandial bloating (4.6 ± 0.9 score) but no abdominal discomfort (0.4 ± 0.3 score). As compared to healthy subjects, patients tolerated smaller meal loads and experienced early satiety (full satiation at 668 ± 65 Kcal; $P < 0.001$), more postprandial bloating (6.2 ± 0.5 score) and abdominal discomfort (5.8 ± 0.6 score; $P < 0.001$). Based on their hedonic response, two distinct categories of dyspepsia were recognized: whereas in a group of patients (n = 10) the meal impaired the sensation of digestive well-being after ingestion (-2.5 ± 0.2 score), another group (n = 7) enjoyed the meal and experienced digestive well-being during ingestion (3.3 ± 0.3 score at 498.5 ± 100 Kcal) that decayed after full satiation (-0.4 ± 1.0; $F(2,30) = 13.492$, $P < 0.001$ by RM-ANOVA). Interestingly, no differences in homeostatic sensations were detected between patients with positive and negative hedonic experience in terms of meal tolerance (691 ± 90 and 652 ± 95 Kcal, respectively; $P = 0.781$), postprandial fullness (6.2 ± 0.9 and 6.2 ± 0.7 score, respectively; $P = 0.991$) and abdominal discomfort (5.1 ± 1.0 and 6.3 ± 0.7 score, respectively; $P = 0.221$).
Conclusions: Despite their postprandial symptoms, a category of patients with dyspepsia enjoy the meal and experience satisfaction.

GASTRO-OESOPHAGEAL REFLUX DISEASE

Abstract Code: NGS15039-90 | Esophageal high resolution manometry abnormalities during gastroesophageal reflux disease

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Introduction: Gastroesophageal reflux disease (GERD) is a very common pathology. Functional explorations within esophageal high resolution manometry (HRM) find their place in particular in GERD refractory to treatment. It can highlight motor disorders associated with GERD such as inefficient motor skills or lower esophageal sphincter (LES) hypotonia.
Materials and methods: We have included retrospectively all patients who have benefited from HRM between January 2021 and April 2021 carriers of GERD held back by the presence of a typical heartburn.
Results: A total of 104 patients were included. He were 31 men and 73 women with a sex ratio M / F from 0.42. The most common

pathological history found were diabetes (13.5%) and dysthyroidism (9.3%). The average BMI was 26.4 Kg / m^2 [16-38] and 57.1% of patients had a BMI greater than 25 Kg / m^2. Dysphagia was associated with heartburn in 68.9% of patients and extra-digestive manifestations were found in 57.7% patients. Upper gastrointestinal endoscopy was normal in 55% of cases, found esophagitis in 21% of cases and a hiatus hernia (HH) in 19.1% of cases. Regarding the HRM results : the mean pression of the LES was of 15.26 mmHg [0-54], the average pression of rest in LES is 2.59 mmHg [0-7] Hypotonic LES was found in 48 patients (46%). HH was found on HRM in 56 patients (54.4%) with an average length of 1.3cm. Esophageal motor disorders were diagnosed : aperistalsis (n = 8, 3.2%) inefficient esophageal motor skills (n = 44; 43.1%), fragmented peristalsis (n = 2; 2%). The statistical study found that a low pression of the LES was associated with a longer duration of GERD (P = 0.048), the presence of endoscopic esophagitis (P = 0.037), the presence of a hiatus hernia (P = 0.003) and a short LES (P = 0.039).

Conclusions: Esophageal motor abnormalities were found in 53% of our patients. Ineffective esophageal motor skills were the most common motor trouble. Hypotonia of the LES was associated with an older GERD, with the presence of a hiatus hernia, esophagitis and shorter LES.

Abstract Code: NGS15477-96 | Identification of lower esophageal sphincter for gastro-esophageal reflux monitoring: to compare the method of esophageal manometry and the step-up method with use of basal impedance

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Objective: Esophageal manometry and radiological diagnosis are methods for accurate positioning of multichannel intraluminal impedance pH (MII-pH) monitoring. Esophageal manometry is the gold standard for accurate to locate the lower esophageal sphincter (LES). The basal impedance step-up method is the perspective method for accurate the LES location. Our aim was to compare the method of esophageal manometry and the basal impedance step-up method for the LES location for pH impedance probe positioning in gastroesophageal reflux disease (GERD) patients.

Methods: The study included 30 GERD patients: mean age was 43.7. 24-hour MII-pH-monitoring on the JSC RPE «Istok-Sistema». Patients with gastric baseline impedance < 500 Ω were excluded. Passage in the stomach was confirmed by a stable low impedance value (i.e. < 688 Ω). The probe was withdrawn gradually 1 cm every 15 seconds up to 5 cm above the step-up impedance point. Entry into the esophagus was deemed to have occurred when a sharp and stable impedance rise was seen, defined as an increase of > 50% with respect to gastric baseline. Esophageal high-resolution manometry (HRM) was used to control place of pH-impedance probe (Solar GI Laborie/MMS, The Netherlands). The statistical analysis was done using SPSS Statistics 17.0 (the Bland-Altman comparison method, Student's distribution, Wilcoxon signed-rank test and a linear regression model).

Results: The equation of linear regression didn't determine the differences between the impedance step-up and the method of esophageal manometry for accurate the LES location (r^2 = 0.309, P < 0.001). We not found difference between two groups by the Bland-Altman comparison method (M difference = 0.28, SD difference = 0.78). When we compared them as tested with Student's distribution and Wilcoxon's test, also no reliable differences (P = 0.52 and P = 0.051) were identified.

Conclusions: The impedance step-up method may be used for identification of the LES location for pH-impedance probe positioning in GERD patients.

Abstract Code: NGS15597-99 | Manometric findings in patients with suspected gastroesophageal reflux disease

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Introduction: High-resolution esophageal manometry (HREM) has an increasingly important role in the diagnostic assessment of gastroesophageal reflux disease (GERD), being formally indicated in the Lyon Consensus. Thus, the aim of this study was to describe the main manometric alterations identified in patients with suspected GERD.

Methods: Retrospective and single-center study, which included all patients who underwent HREM and 24-hour pH-metry study between January/2018 and December/2020. Four groups were defined: proven GERD [acid exposure time (AET) > 6% and/or number of reflux episodes (NRE) > 80], GERD with borderline diagnostic criteria [AET 4-6% and/or NRE 40-80], reflux hypersensitivity (RH) [AET < 4% and NRE < 40, symptom index > 50% and probability of symptom association > 95%] and functional heartburn (FH) [AET < 4% and NRE < 40, without symptomatic association].

Results: A total of 137 patients were included, mostly female (63.5%) with a mean age of 54 ± 13 years. 36 (26.3%) patients with GERD were identified, 23 (16.8%) with borderline criteria, 3 (2.2%) with RH and 75 (54.7%) with FH. Although patients with GERD had more frequent hiatal hernia, this association was not statistically significant (GERD = 11.1% vs. borderline = 8.7% vs. RH = 0.0% vs. PF = 6.7%; P = 0.819). The prevalence of hypotensive lower esophageal sphincter (LES) was less frequent in patients with functional heartburn compared to other groups (GERD = 27.8% vs. borderline = 34.8% vs. RH = 33.3% vs. PF = 14.7%; P = 0.002). Patients with GERD had a higher prevalence of ineffective esophageal motility (GERD = 13.9% vs. borderline = 0.0% vs. RH = 0.0% vs. FH = 2.7%; P = 0.045). There

Table 1. Manometric findings in patients with suspected GERD

	GERD	Borderline	Reflux hypersensitivity	Functional heartburn	
Hiatal hernia	4/36 (11.1%)	2/23 (8.7%)	0/3 (0.0%)	5/75 (6.7%)	$P = 0.819$
Hypotensive LES	10/36 (27.8%)	8/23 (34.8%)	1/3 (33.3%)	11/75 (14.7%)	$P = 0.002$
Ineffective esophageal motility	5/36 (13.9%)	0/23 (0.0%)	0/3 (0.0%)	2/75 (2.7%)	$P = 0.045$
Diminished contractile reserve	14/31 (45.2%)	10/22 (45.5%)	2/3 (66.7%)	29/67 (43.3%)	$P = 0.885$

were no significant differences in the multiple rapid swallows test between the 4 groups ($P = 0.885$).

Conclusions: HREM allows the assessment of certain parameters associated with reflux, namely esophageal hypomotility and hypotensive LES. Therefore, it can be a useful tool in the assessment of patients with suspected GERD, especially in the presence of borderline or inconclusive ph-metric findings.

Abstract Code: NGS15601-85 | **Provocative tests and gastroesophageal reflux disease – An additional parameter?**

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Introduction: The performance of provocative tests that infer contractile reserve in high-resolution esophageal manometry (HREM) is an important item in the preoperative evaluation of patients with gastroesophageal reflux disease (GERD). However, its impact on reflux exposure is not fully defined. Thus, the aim of this study was to assess whether diminished peristaltic reserve potentiates GERD.

Methods: Retrospective and single-center study, which included all patients who had undergone 24-hour pH-metry study esophageal and HREM with multiple rapid swallows (MRS) between January 2018 and December 2020. Individuals previously submitted to esophagogastric surgery were excluded. Diminished contractile reserve was defined as a ratio between the distal contractile integral (DCI) of the MRS and the mean DCI of simple swallows < 1.

Results: A total of 128 patients were included in the study, the majority female (63.3%) with a median age of 56 years (IQR 44-65). The main symptoms reported were heartburn and/or regurgitation (63.3%), cough (13.3%), chest pain (6.3%) and globus (3.1%). It was found that 55 (43.0%) patients had diminished contractile reserve. These individuals did not present, however, statistically significant differences in terms of duration concerning the exposure to acid (3.9% vs. 3.7%; $P = 0.484$) or the number of reflux episodes (33 vs. 42; $P = 0.680$) compared to patients with preserved contractile reserve. On the other hand, patients with GERD did not show a significant decrease in the esophageal body peristaltic reserve (45.1%), as well as patients with borderline diagnostic criteria (45.5%), hypersensitivity to reflux (66.7 %) and functional heartburn (43.3%) ($P = 0.885$).

Conclusions: In our population, MRS did not prove to be a useful tool in the diagnostic approach to GERD. Further studies are needed to assess the role of provocative tests in GERD, in addition to preoperative evaluation.

Abstract Code: NGS15577-97 | **The impact of patient education on GERD management in COVID-19 era**

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Introduction: The COVID- 19 pandemic has shown a disparity between patients and physicians regarding gastroesophageal reflux disease (GERD) management and its impact on quality of life. Patient satisfaction with prescription treatment can be overestimated by physicians and the severity of symptoms is underestimated when compared to patients' reports.

Aim: Diagnostic assessment in patients with heartburn, regurgitation in the Covid-19 pandemic.

Material and methods: The study includes 84 patients (64 women si 20 men), meanage 56 years with GERD symptoms, explored in the outpatient clinic between april 2020 - may 2021 by PCR, detailed anamnesis, biological tests, fecal antigen, abdominal ultrasound and endoscopy.

Results: 45 patients presented GERD and esophagitis (53.5%) at upper endoscopy: 25 class A, 14 class B și 6 class C, of which 20 were *H.Pylori* positive (44.4%) and 39 had endoscopic negative GERD (46.4%). All the patients were tested by PCR for SARS-COV-2 viral ARN, the positive cases being referred to the Infectious Diseases Hospital and those *H.Pylori* positive were treated with antibiotics and PPI to eradicate the infection and heal the esophagitis. Most patients had a comprehensive discussion of factors affecting GERD with their gastroenterologist, rather than family physician. The therapeutic response at PPI and antibiotics was efficient in most patients with eradication of *H.Pylori* infection and regression of esophagitis in classes B or C and its cure in class A.

Conclusions: GERD and H. Pylori coinfection is often present in the middle-aged adult. The treatment with PPI and antibiotics is useful in most patients with quality life improvement. These patients are also significantly more knowledgeable about when to take their

medication than those who did not have a comprehensive discussion with their physician. This emphasizes the need for better discussion between family physician and patient, or sending patients for endoscopic diagnosis and appropriate treatment to the gastroenterologist. The doctor-patient relationship was severely affected during the COVID-19 pandemic by avoiding or reducing patients' hospital visits, but keeping in touch by phone or email with the gastroenterologist.

Key words: gastroesophageal reflux disease, management, Covid- 19

Abstract Code: NGS15420-84 | The reliability of the Reflux Disease Questionnaire and the Gastro-esophageal Reflux Disease Quality of Life Questionnaire after translation to Arabic and Hebrew Languages

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Objective: Gastroesophageal reflux disease (GERD) negatively affects life quality. The Reflux Disease Questionnaire (RDQ), a 12-item assesses the frequency and severity of GERD symptoms. The GERD quality of life (QoL) questionnaire, a 16–item, assess the impact of GERD symptoms on physical and mental health. These two questionnaires are commonly used and were validated in various languages. The study aim was to assess the validity and reliability of these questionnaires in Arabic and Hebrew and GERD patients.

Methods: A validation study was conducted among patients with reflux esophagitis who underwent endoscopy at Nazareth hospital. The Arabic and Hebrew translations were assessed among experts in gastroenterology and epidemiology to assess its face and content validity. All translation and back translation progressions were achieved prior to study initiation.

Results: 149 patients (66.4% males) with a mean age 44.6 years were enrolled. 67 (45.0%) patients had esophagitis grade A, 32 (21.5%) had grade B, 41 (27.5%) had grade C and 9 (6.0%) had grade D 138 patients filled the Arabic version and 11 filled the Hebrew version. Face/content validity was accepted by experts. The reliability was excellent with Cronbach's alpha = 0.928 for RDQ. The reliability of the GERD QoL was good also for each domain, diet and food intake Cronbach's alpha = 0.751, daily activity Cronbach's alpha = 0.762. The QOL scores didn't differ between patients with esophagitis A/B compared to esophagitis C/D (P = 0.58).

Conclusions: The RDQ and GERD QoL Arabic and Hebrew versions are valid and reliable for implementation in clinical practice in Israeli population.

GASTROINTESTINAL MANIFESTATION OF SYSTEMIC DISEASE

Abstract Code: NGS15011-80 | Excess of the mortality rate associated with gastroparesis

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Introduction: Functional digestive disorders as digestive motor disorders are not traditionally not considered to be able to induce an excess in mortality rate. Gastroparesis is nevertheless associated in its severe cheeses to an alteration of nutritional status and may contribute to the deterioration of the underlying disease, such as diabetes. The objective of our work was therefore to determine whether gastroparesis was associated with an excess in mortality.

Methods: All subjects who performed a measurement of gastric emptying between 2018 and 2020 were studied (n = 32) with the exception (n = 14) of the minor subjects, who refused to participate in the study, or who could not perform the test (vomiting during the test meal, technical problem ...). Symptoms and quality of life were collected prospectively from 2020.

Results: A total of 32 patients (20 don't have gastroparesis (G-) and 12 have gastroparesis (G+)) were analyzed (mean age 43.4 ± 12.7 and 59.3% of women). The BMI was 28.1 kg / m2 for G+ and 24.7 kg / m2 for G- (P = 009). The symptoms and quality of life were no different between the two groups. Diabetes was significantly more present in G+ (16.7%) than G- (5%; P < 0.001). In 2020, 9.3% of patients had died (10% G + and 8.3% G-; P = 0.02). Comparisons of the curves of survival (G + and G-) by subgroup remained different in diabetic subjects (P = 0.02), in non-diabetics (P = 0.01), in women (P = 0.03) and in men (P = 0.01). In G-, the causes of death were linked to neoplasia (23.0%), a cardiovascular cause (24.3%), pneumonia (14.9%), undernutrition (5.5%), or worsening of the underlying disease (diabetes, scleroderma...; 5.5%) or other (25.7%). Among the G +, the causes of mortality were linked to neoplasia (38.2%; P = 0.17), a cardiovascular disease (17.6%), pneumonia (11.7%), undernutrition (5.8%), or other (21.1%).

Conclusions: The presence of gastroparesis authenticated by a slowing of gastric emptying is associated with an increased risk of mortality, regardless of the presence of diabetes or sex.

MICROBIOTA

Abstract Code: NGS15501-84 – Poster of Distinction | **Guidelines for Reporting on Animal Faecal Transplantation (GRAFT) studies: recommendations from a systematic review of murine transplantation protocols**

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Background/Objectives: Faecal microbiota transplant (FMT) is a powerful tool used to connect changes in gut microbial composition with a variety of disease states and pathologies. While FMT enables potential causal relationships to be identified, the experimental details reported in preclinical FMT protocols are highly inconsistent and/or incomplete. This limitation reflects a current lack of authoritative guidance on reporting standards which would facilitate replication efforts and ultimately reproducible science. We therefore systematically reviewed all FMT protocols used in mouse models of gastrointestinal disease with the goal of formulating recommendations on the reporting of preclinical FMT protocols.

Methods: Search strategies were applied across three databases (PubMed, EMBASE and Ovid Medline) until June 30, 2020. Data related to donor attributes, stool collection, processing/storage, recipient preparation, administration and quality control were extracted.

Results: A total of 1753 papers were identified, with 241 identified for data extraction and analysis. Of the papers included, 92.5% reported a positive outcome with FMT intervention. However, the vast majority of studies failed to address core methodological aspects including the use of anaerobic conditions (91.7%), storage (49.4%), homogenisation (33.6%), concentration (31.5%), volume (19.9%) and administration route (5.3%). To address these reporting limitations, we developed the *Guidelines for Reporting Animal Faecal Transplant (GRAFT)* framework that guide reporting standards for preclinical FMT (Figure 1).

Conclusions: The GRAFT recommendations will enable robust reporting of preclinical FMT design, and facilitate high quality peer review, improving the rigor and translation of knowledge gained through preclinical FMT studies.

FIGURE 1. Critical aspects of the GRAFT framework

Abstract Code: NGS15493-94 | **Duodenal dysbiosis is unrelated to proton pump inhibitor efficacy in functional dyspepsia patients**

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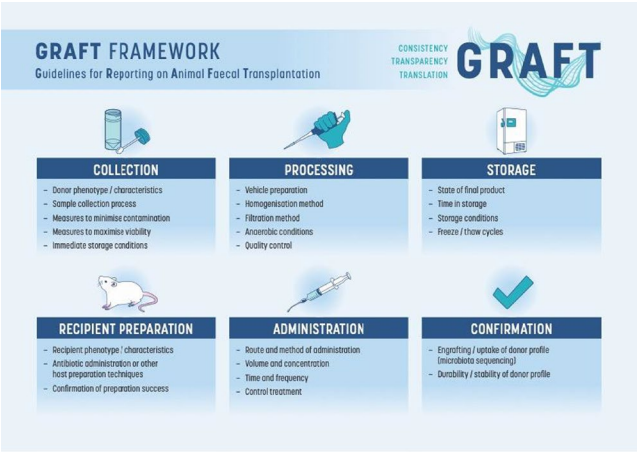
Objective: Proton pump inhibitors (PPI) improve functional dyspepsia (FD) symptoms through eosinophil-reducing effects (Wauters *et al.* Gastroenterology 2021). However, the contribution of the duodenal microbiome to FD-symptoms and interaction with PPI remains elusive.

Methods: Aseptic duodenal biopsies (mucosa) and brushings (lumen) were collected for 16S-rRNA sequencing before and after PPI-intake (4 weeks Pantoprazole 40mg daily) in FD patients and healthy controls. Symptoms (PAGI-SYM) and routine duodenal biopsies for eosinophils (H&E) were also collected at each visit. Genera abundance profiles were compared between and within groups with correction for multiple testing (FDR < 0.1). Next, genera of interest and alpha-diversity (Shannon-index) were studied using linear mixed models with treatment (off- or on-PPI) as within- and group (FD or control) as between-subject factors. Finally, correlations and associations between changes in microbiota and symptoms or eosinophils were assessed.

Results: In total, 28 FD (24 female, 31.7 ± 2 years, BMI 22.2 ± .7 kg/m^2) and 30 controls (21 female, 32.3 ± 2 years, BMI 23.2 ± 0.7 kg/m^2) were followed during PPI-therapy. Luminal *Porphyromonas*, *Neisseria*, *Haemophilus*, *Fusobacterium* and *Selenomonas* were lower in FD patients vs. controls and *Prevotella* decreased after PPI (FDR < 0.1). Mixed models confirmed lower luminal *Porphyromonas* (P = 0.001) and *Neisseria* (P = 0.02) in FD vs. controls off-PPI, with decreased *Porphyromonas* in controls and decreased *Prevotella* and increased *Streptococcus* in both groups after PPI (all P < 0.05) (Figure 1). Luminal diversity was similar and decreased in patients and controls after PPI (p < 0.01). No differences were found for mucosal samples. Luminal *Porphyromonas* was inversely correlated with symptoms (r = -0.35) and eosinophils (r = -0.43, both FDR = 0.04) off-PPI. In controls, luminal *Streptococcus* (r = 0.4, FDR = 0.06) correlated with



eosinophils. Although the reduction in symptoms or eosinophils was not associated with microbial changes in FD, increased eosinophils in controls were associated with changes in *Streptococcus* (F = 8.18, $P < 0.01$) after PPI.

Conclusions: Differential luminal but not mucosa-associated genera were found in FD, with a potential pathophysiological role of *Porphyromonas*. Previously observed effects of PPI were, however, not associated to changes in duodenal microbiota. In fact, increased *Streptococcus* and its association with potentially negative effects of PPI suggest a role for inadvertent microbiota changes after PPI.

Abstract Code: NGS15062-86 | **Enteroimmunology & Endocrinology: How dysbiotic gut inflammation leads to hormone imbalances, and how reversing them is the key to resolving chronic illness**

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Gut dysbiosis is associated with inducing a chronic inflammatory state that affects every organ and is implicated in the pathogenesis of multiple chronic conditions in the scope of internal medicine. Here we articulate relevance, diagnostic/therapeutic concerns of translational mucosal immunology ("Enteroimmunology") and articulate the impact on measured cortison secretion patterns as demonstrated by 24 hour salivary cortisol testing. Inflammatory cytokines stimulate cortisol secretion, and over time, an endocrinopathy develops: dysfunctional diurnal cortisol secretion, depletion of beneficial hormones such as testosterone, DHEA, progesterone, pregnenlone, thyroid hormone, and sometimes estrogens (although elevations of estrogens due to impaired excretion is more common) occur. These physiologic events are implicit in the process of aging. We will describe treatment approach and cases featuring gut microbiome repair and restitution of optimal hormone levels as essential to lessening physiologic/cellular aging and inflammation. We will review case studies including treatment of Crohns inducing remission, reversal of autoimmune inflammation, and reversal of prostate disease.

Abstract Code: NGS15518-92 | **Metabolic response of intestinal microbiota to guar guam consumption**

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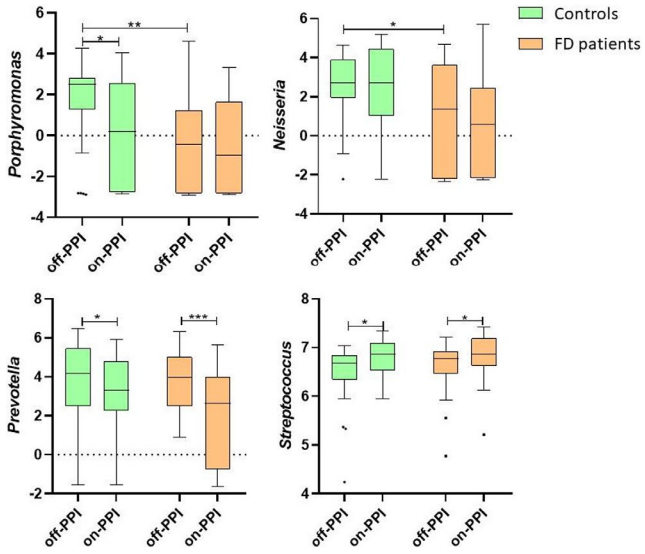
Background: Guar gum is classified as a fiber, but it remains uncertain whether and to what extent it is fermented by colonic microbiota and whether it has prebiotic properties.



Aim: To determine the metabolic reaction of intestinal microbiota in response to guar gum consumption, specifically, the extent of initial fermentation and subsequent adaptation.

Methods: Single-centre, single arm, open label, proof-of-concept study testing the effect of guar gum on microbiota metabolism and adaptation. Healthy subjects (n = 12) were administered gum guar (8 g/d) for 2 weeks. During 4-day periods immediately before, at the beginning and at the end administration, the diet was standardized and the following outcomes were measured: a) number of daytime gas evacuations for 2 days (by means of an event marker) as a surrogate marker of microbiota metabolic activity; b) digestive sensations (by daily scales).

Results: Before administration, participants registered 7.7 ± 1.0 anal gas evacuations per day with sensation of digestive well-being (3.3 ± 0.5 score on a -5 to +5 scale). At initial exposure, consumption of guar gum was associated with a small but significant increase in the number of anal gas evacuations (10.5 ± 1.9 evacuations/d; $P = 0.014$ vs pre-administration), impaired digestive well-being (2.2 ± 0.5 score; $P = 0.038$ vs pre) and mild abdominal symptoms. After 2 wk administration, anal gas evacuation decreased (7.1 ± 1.5 evacuations/d; $P = 0.013$ vs early administration), the sensation of digestive well-being improved (3.1 ± 0.5 score; $P = 0.003$ vs early administration) and initial symptoms tended to subside.

Conclusions: Guar gum is to some extent fermented by colonic microbiota releasing gas, and continuos consumption induces an adaptation of microbiota metabolism with beneficial effects to the host.

Keywords: intestinal gas, gut microbiota, prebiotics, fibre.

Abstract Code: NGS15509-92 | **The effects of human milk oligosaccharides on gut microbiota, metabolite profiles and host response in patients with irritable bowel syndrome**

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Human milk oligosaccharides (HMO) supplementation safely modulates fecal bifidobacteria abundance and holds the potential to manage symptoms in irritable bowel syndrome (IBS). Here, we investigated the role of a 4:1 mix of 2'-O-fucosyllactose and Lacto-N-neotetraose on the modulation of gut microbiota composition, metabolite profiles and mucosal host response in IBS patients.

Biological samples were collected at baseline and week 4 post supplementation as part of a previously published study of IBS patients (n = 58) receiving either a placebo (glucose) or 5g or 10g doses of HMO. The gut microbiota profile was determined in both feces and colonic biopsies by 16S rRNA sequencing. Liquid Chromatography-Mass Spectrometry was used to analyze metabolite profiles of feces, plasma and urine samples. The host gene expression of 86 genes related to innate immune response to bacteria and 5 genes involved in gut barrier function were determined by qPCR in biopsies.

The placebo, 5g and 10g HMO groups presented similar profiles of gut microbiota, metabolites and host response prior to the intervention. Neither the α- nor the β-diversity in fecal or mucosal samples differed between the groups before or post intervention. However, the change in fecal, but not mucosal, microbial dissimilarity (β-diversity) was higher within individuals receiving 10 g HMO than placebo. Both fecal and mucosal *Bifidobacterium* spp. increased after HMO intake, with increased proportions of *Bifidobacterium adolescentis* and *Bifidobacterium longum*. Moreover, the intervention modulated the fecal and plasma metabolite profiles but not the urine metabolite profile or the mucosal host response.

Supplementation with human milk oligosaccharides (HMO) modulated the fecal microbiota β-diversity, fecal and plasma metabolite profiles of IBS patients. Overall, these findings support that HMO supplementation modulate the intestinal microenvironment of patients with IBS, potentially supporting IBS symptoms.

Abstract Code: NGS15463-91 | The long-term efficacy and adverse events of fecal microbiota transplantation (FMT) for irritable bowel syndrome (IBS)

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Objective: The long-term efficacy and adverse events of FMT for IBS are unknown. The present study is a 3-years follow-up of patients included in our previous study to clarify this matter.

Methods: A total of 125 patients were included in this study. These patients included the placebo group (n = 38), the group that received 30-g donor´s feces patients (n = 42), and the group received 60-g of donor´s feces (n = 45). The patients provided a fecal sample and completed five questionnaires to assess symptoms and quality of life.at baseline, 2-years and 3-years after FMT. The fecal bacteria were analyzed using a predetermined targets method utilizing 16S rRNA 16S rRNA gene in PCR DNA amplification covering the variable genes V3–V9, and calculated a dysbiosis index (DI).

Results: The response rates for FMT after 2 years were 26.3%, 68.9% and 77.8% in the placebo, 30-g and 60-g groups, respectively. The corresponding figures after 3 years were 27.0%, 67.6% and 72.5%. The response rates in 30-g and 60-g groups were significantly higher than placebo 2- and 3-years after FMT. Patients in the 30-g and 60-g groups had significantly lower IBS symptoms and fatigue and higher quality of life at both 2-, and 3-years after FMT. The response rates were higher and Severity Scoring System (IBS-SSS) scores were significantly lower in females than males. The DI decreased significantly in the 30-g and 60-g groups but not in the placebo group, 2- and 3-years following FMT. The levels of 10 bacteria that changed after FMT in actively treated groups were significantly correlated with the total scores of IBS-SSS, and Fatigue Assessment Scale (FAS). No adverse events were reported.

Conclusions: A single FMT using the present protocol improves the symptoms and quality of life of IBS patients up to 3 years without any long-term side effects. The study identified 10 bacteria groups that are correlated to symptoms.

NUTRITION AND DIET

Abstract Code: NGS15527-92 | Effect of a targeted nutritional intervention on symptom control and modulation of the fecal microbiota in patients with IBS-C

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Background: 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.

Methods: 10 IBS-C patients 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 nutritional protocol was elaborated respecting the macronutrient percentage and the quantity of fiber indicated by LARN 2014 guidelines.

Results: Symptoms Questionnaires showed a significant reduction in pre – evacuation abdominal pain ($P = 0.0206$), in the daily frequence of abdominal pain ($P = 0.0057$) and in the abdominal pain during the evacuation ($P < 0.0001$) following the 4-week nutritional protocol. About diet, % 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 ($P = 0.0199$; from 2.33 ± 1.12 to 4 ± 0.5). Actually, in IBS patients the MD index (MDSS) was significantly altered compared to the nutritional protocol based on MD parameters ($P < 0.001$). Following nutritional protocol an increase of Bacteroidetes and a decrease of Firmicutes at phylum level was observed. In particular, at family level a decrease of Ruminococcacae, Lachnospiraceae, Clostridiales, Prevotellaceae and an increase of Bacteroidaceae were present. Alfa- and beta-diversity of GUT microbiota did't shown statistical significance differences following the nutritional protocol.

Conclusions: These preliminary results show the significant role of a right dietary lifestile in controlling IBS symptoms, with a modulation of the intestinal microbiota composition; further investigations, increasing the number of patients, are needed to confirm these data.

Abstract Code: NGS15564-93 | Effectiveness and convenience of dietary therapies in irritable bowel syndrome: A randomised control trial of traditional dietary advice, the low fodmap diet and the gluten-free diet

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Objectives: Various diets are proposed as first-line therapies for irritable bowel syndrome (IBS) despite insufficient or low-quality evidence. No study has directly compared traditional dietary advice (TDA) against the low FODMAP diet (LFD) and gluten-free diet (GFD). We performed a randomized controlled trial to address this issue.

Design: Patients with Rome IV-defined IBS diarrhoea or mixed subtype were recruited via two centres in the United Kingdom, and block randomised in groups of up to 5 to receive TDA, LFD or a GFD (the latter allowing for minute gluten cross-contamination). The primary endpoint was clinical response after 4 weeks of dietary intervention, as defined by ≥ 50-point reduction in IBS symptom severity score (IBS-SSS). Secondary endpoints included i) acceptability and food-related quality of life with dietary therapy, ii) changes in nutritional intake, iii) alterations in stool dysbiosis index, and iv) baseline factors associated with a clinical response.

Results: 101 patients commenced dietary intervention (TDA = 35, LFD = 33, GFD = 33); median age 34 years, 70% female, and mean baseline IBS-SSS of 301. On modified intention-to-treat analysis, the primary endpoint of ≥ 50-point reduction in IBS-SSS was met by 46% undertaking TDA, 55% for LFD, and 58% for GFD; $P = 0.59$. Individuals found TDA significantly cheaper, tastier, less time-consuming to shop, easier to implement, and socially more convenient than the GFD and LFD. Changes in micro- and macro- nutrient intake, and alterations in stool dysbosis index, were similar between the diets. Baseline characteristics and stool dysbiosis index did not predict clinical response.

Conclusions: TDA, GFD and LFD demonstrate similar efficacy in IBS but differ with regards to their cost and convenience. TDA is the most patient-friendly and should be recommended as the first choice dietary therapy in IBS, with a GFD and LFD reserved according to specific patient preferences and specialist dietetic input.

Clinical trials number: NCT04072991

Abstract Code: NGS15570-90 | Effects of whey protein on energy intake, gastric emptying and glycaemia in obese, older and younger men

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Background: A strategy to reduce energy intake in obese, young adults is to increase dietary protein. It is not clear if this works in obese, older individuals; we have reported that a 30 g whey protein drink suppresses energy intake less in older than young non-obese men. The whey protein slowed gastric emptying, more in the older than younger men. The aim of this study was to determine the effect of a whey-protein drink on energy intake, gastric emptying and glycaemia in obese, older and younger men.

Methods: In randomised, double-blind order, 10 younger (age: 27 ± 2yrs; body mass index: 36 ± 2kg/m^2) and 10 older (72 ± 1yrs; 33 ± 1kg/m^2) obese men ingested a 30g whey protein (120kcal) and control (2kcal) drink on separate study days. Gastric emptying, as measured by antral area (ultrasonography), blood glucose concentrations (t = 0-180min), and *ad libitum* energy intake (t = 180-210min) were determined following overnight fasting. Data were analysed using repeated measure mixed-effect model.

Results: Energy intake was not altered by the whey-protein drink ingestion, when compared to control, in either the older (decrease 2 ± 8%) or younger (decrease 3 ± 8%) obese men ($P > 0.05$). There was a trend for energy consumption to be lower in the older than younger men on both study days ($P = 0.16$) (Figure 1A, B). Whey

protein ingestion slowed gastric emptying, compared to control, to a similar degree in both age groups (gastric emptying half time: older and younger combined protein vs. control: 40 ± 13vs. 20 ± 1min, $P < 0.001$) (Figure 1C, D). Fasting and postprandial blood glucose concentrations were higher in the older than younger obese men (protein and control day combined old vs. young; fasting: 6.2 ± 0.1 vs. 4.9 ± 0.6mmol/l and postprandial (area under the curve 1110 ± 30 vs. 992 ± 20mmol/l/180min, $P < 0.05$). There was no effect of whey-protein ingestion on glycaemia in either age group (Figure 1E, F).

Conclusions: Obesity may blunt/abolish the age-related effect of whey protein on suppression of energy intake and slowing of gastric emptying.

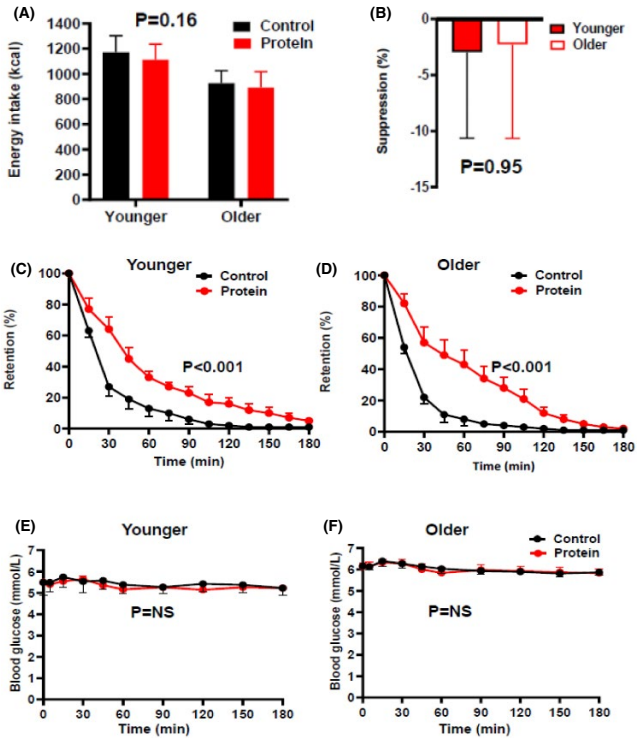

FIGURE 1. Energy intake (A, B), Gastric emptying (C, D) and blood glucose concentrations (E, F) following whey-protein (30g) and control intake in obese, younger and older men

Abstract Code: NGS15556-94 | **Is the activity-based anorexia (ABA) model a reliable method of presenting clinical features of anorexia?**

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Anorexia nervosa (AN) is a severe condition affecting 1% of adult females in developed countries. Severe restriction of energy intake, intense fear of gaining weight and distortion of the body image characterize the disease. A reduction in food intake/loss of appetite and hyperactivity/increased anxiety as observed in AN are also the core features of the ABA model. Our aim was to assess how accurately the standard acute ABA protocol mimics some of the most common AN complications including cardiac changes and gonadal dysfunction, and how it corresponds with basic biochemical parameters, depending on gender, age and initial body weight.

The ABA model was adopted, and voluntary physical activity, body weight gain and food intake were assessed daily. Electrocardiography, heart rate variability and systolic blood pressure (SBP) were measured one day before the start and on the last day of the experiment. Immediately after euthanasia, tissue fragments from rat's uterine horns and ovaries were collected for H&E staining and histological assessment of telocytes and sex hormone receptors. The concentration of female gonadal hormones (LH, FSH), glucose, transaminases and lipid profile were measured in the blood serum.

ABA rats showed a significant weight loss and remarkably increased activity from the first day. ABA rats developed severe hypoglycemia, had increased ALT and AST levels as well as decreased total cholesterol, triglycerides, LDL and HDL. The weight of the uterus was two times lower in ABA female rats. Microscopic analysis of ABA ovarian tissue revealed a reduction in the number of antral follicles and decreased expression of estrogen receptors. A decrease in heart rate, an increase in systolic blood pressure, a prolongation of both the QRS complex and the QT interval was characteristic for ABA rats.

The ABA model is a reliable research tool for presenting the breakdown of adaptation mechanisms observed in severe AN. Cardiac and hormonal features of ABA with underlying altered neuroendocrine pathways integrated with numerous appetite regulating hormones create a clear preclinical phenotype of a human disease.

Abstract Code: NGS15549-96 | **Patterns of dairy products and confectionnaries consumption correlates with number of gastroesophageal refluxes**

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Association between dietary patterns with types and number of gastroesophageal refluxes has not been studied yet.

Aim: To perform the analysis of the association between dietary patterns and number of gastroesophageal refluxes detected with esophageal multichannel intraluminal pH-impedance (MII).

Methods: Subjects referred to esophageal pH-impedance examination were invited to participate in the study, approved by LEC (https://rscf.ru/contests/search-projects/19-76-30014/). In case of agreement, they were asked to provide data of their usual diet - this information was collected with the use of food frequency questionnaire (Nutrilogic, Russia). The data on quantities and frequency of

foods and products consumption were assessed in accordance with the Healthy eating index for the following main groups of products: grains, fruits, vegetables, dairy products, meats, fats and confectioneries. The results were shown as a quotient of dividing the actual values by the recommended. We used Ohmega recorder (Laborie, the Netherlands) and 2pH-6impedance catheters (MMS, the Netherlands) to perform MII, and manufacturer's software to analyze the obtained records. Spearman rank R was used to analyze correlation between the number of gastroesophageal refluxes (GERs) detected with esophageal MII and dietary patterns.

Results: Data of 40 consecutive patients (12 of them with confirmed gastroesophageal reflux disease, 28 females, age (Mean ± SD): 52.2 ± 12.9 y.o.) served as the source for the study. Mean energy value of the diet was 2302 ± 1391 kcal/day. Dietary patterns for main food groups were as follows: grains 1.4 ± 0.7, vegetables 1.1 ± 0.7, fruits 0.8 ± 0.9, dairy products 0.6 ± 0.6, meats 1.7 ± 1.0, fats 0.6 ± 0.8, confectioneries 0.3 ± 0.5. Mean total number of GERs was 43.8 ± 24.4 per day, acid GERs 26.2 ± 20.5 per day. Direct medium-strength correlation was found between *pattern of dairy products* consumption and the *total number of GERs* (Spearman R = 0.47, $P < 0.05$), *weak-acid GERs* (R = 0.49, $P < 0.05$), *non-acid GERs* (R = 0.62, $P < 0.05$). *Pattern of confectioneries* consumption correlated directly with the *number of high GERs* (that reached proximal oesophagus, ~17 cm above lower oesophageal sphincter): R = 0.47, $P < 0.05$. No other correlations were identified.

Conclusions: This study shows that dietary patterns may have impact on the number and type of gastroesophageal refluxes. The obtained results may be a basis for larger comparative trials and for diet modification in patients with GERD.

Abstract Code: NGS15049-91 | Region specific effects of fennel tea on gastric motility

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Objective: Fennel tea is a folk remedy for gastrointestinal complaints like nausea, bloating and indigestion in many countries worldwide. Fennel stem extracts significantly reduced spontaneous activity of isolated rat ileum. Scientific data on the effect of fennel tea on stomach motility is lacking. We aimed to determine the effects of fennel tea on the motility of guinea pig stomach preparations.

Methods: Guinea pig circular and longitudinal smooth muscle strips from the antrum, corpus and fundus were mounted in organ bath. Different amounts of fennel tea (15.6, 31.25, 62.5, 125, 250, 500, 1000 and 2000 µL, corresponding to a final dose of 0.78, 1.56, 3.13, 6.25, 12.5, 25, 50 and 100 µL/mL, respectively) were added to the chambers and the changes in muscle force and (in case of antrum) in the amplitude and frequency of phasic activity were measured.

Results: Fennel tea had no effect on the muscle force or on the frequency of phasic contractions of antrum circular and longitudinal muscle strips at any of the tested doses. However, it increased the amplitude of spontaneous phasic contractions significantly at an applied dose of 1000 and 2000 µL (corresponding to 50 and 100 µL/mL tea in the chamber, respectively) in antrum longitudinal preparations ($P < 0.05$ at both doses). In antrum circular preparations all applied doses between 15.6-2000 µL were effective (all $P < 0.05$). In the fundus, fennel tea induced a significant relaxation in both circular and longitudinal muscle strips at all applied doses (all $P < 0.05$). Fennel tea also caused a significant relaxation in corpus circular and longitudinal preparations at all tested doses ($P < 0.01$ for all). The effect was reversible by wash out in all regions.

Conclusions: Fennel tea causes a reversible relaxation in the fundus and the corpus, while in the antrum it increases the amplitude of spontaneous phasic contractions. Our data may support its claimed beneficial effects in conditions like indigestion.

OBESITY

Abstract Code: NGS15488-98 | Effect of obesity on the expression of nutrient receptors and satiety hormones in the human colon

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Background: Nutrient-sensing receptors located on enteroendocrine cells (EECs) of the colon bind specific nutrients. Receptor binding leads to cell activation and release of specific hormones/peptides, such as peptide (PYY), GLP-1 and serotonin, which regulate appetite and satiety. We assessed the effect of obesity on the expression of G-protein coupled receptors (GPCRs), the neuropeptide and satiety hormone PYY and serotonin, at both mRNA and protein level.

Methods: qPCR and immunohistochemistry were used to examine colonic tissue from cohorts of patients from the Netherlands (proximal and sigmoid tissue) and the United Kingdom (tissue from across the colon) and patients were grouped by body mass index (BMI) value into BMI < 25 (healthy) and BMI ≥ 25 (overweight/obese).

Results: The mRNA expression of serotonin and PYY was not significantly different between BMI groups. GPR40 mRNA level significantly increased in sigmoid colon of BMI ≥25 ($P = 0.0464$), but not proximal colon. GPR41, GPR109a, GPR43, GPR120, GPRC6A and CaSR mRNA levels were unaltered between BMI groups. Serotonin- and PYY-immunopositive cell numbers were not different the two BMI groups. Serotonin-containing enterochromaffin cells (EC) showed a high degree of co-expression (95-99%) with the amino acid sensing receptor, CaSR, whereas L-cells expressing PYY rarely co-expressed (5-6%) CaSR, in the colon.

Conclusions: BMI does not affect the mRNA or cell expression of the nutrient receptors GPR41, GPR109a, GPR43, GPR120, GPRC6A and CaSR, PYY, serotonin or enterochromaffin and L cells in our cohort of human colon samples. Therefore, obesity may alter other functions such as hormone release

Abstract Code: NGS15487-97 | Gut microbiota markers of efficacy of lifestyle interventions in obese subjects

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Obesity is a risk factor for chronic diseases including metabolic syndrome placing an enormous global economic burden. Diet and lifestyle interventions are the first line strategies to treat obesity, but their efficacy varies among individuals. The gut microbiome also varies among individuals; hence it may play a role in inter-individual differences in response to treatment.

Objective: The objective of this study was to identify gut microbiome markers of inter-individual differences in response to a comprehensive lifestyle intervention program in obese adults.

Methods: The study was approved by institutional IRB and included 14 obese volunteers enrolled in a 10-week comprehensive lifestyle intervention program. The volunteers provided fecal samples, completed diet questionnaires, and underwent body composition analysis at baseline, 10 weeks, and 6 months after the program. All correlations were done using spearman correlation and FDR corrected significant values are reported.

Results: The study included 14 subjects [average age 50.6, (95% CI: 45.9-55.4 years); average BMI 31.5 kg/m^2 (95% CI: 30.0-33.1 kg/m^2); 57% female). Nine subjects lost > 5% of their baseline weight (average 7.84 kg, 95% CI: 6.43-9.25 kg) after the 10-week intervention, while the remaining 5 subjects lost < 5% baseline weight. There were no significant differences among the two groups at baseline for demographic and clinical characteristics. Alcohol, fruit, and aspartame consumption exhibit significant negative correlation while caffeine, vegetable servings and alpha/beta carotene exhibit significant positive correlation with weight loss. The baseline Bray-Curtis distance metric-based microbial beta diversity was significantly correlated with weight loss and decrease in percent body fat loss. The baseline abundance of *Phascolarctobacterium* was significantly correlated with > 5% weight loss while abundance of *Parasutterella* was corelated with inability to achieve at least 5% weight loss. Interestingly, *Phascolarctobacterium* was also significantly corelated with beta carotene intake and negatively correlated with fruit consumption.

Conclusions: This pilot study suggests baseline microbiome may be predictive of response to a comprehensive lifestyle intervention, but these findings need to be validated in a larger cohort.

Abstract Code: NGS15537-93 | Long-term effect of Laparoscopic Roux-en-Y gastric bypass on GERD symptoms

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Background and aim: Laparoscopic Roux-en-Y gastric bypass (LRYGB) is the second most performed bariatric procedure and it is usually considered the procedure of choice to treat patients with both severe obesity and gastroesophageal reflux disease (GERD). However, some authors described the new onset or the recurrence of GERD symptoms after RYGB and data at long-term were scanty. Aim: to evaluate the prevalence of GERD symptoms in a cohort of patients at minimum 5 years after RYGB.

Methods: We enrolled 50 patients (37 women, mean age 41.1 ± 10.3 years, mean BMI 42.1 ± 5.8 kg/m^2, 5 with BMI ≥50 kg/m^2) who underwent LRYGB at least 5 years before (mean follow-up 98 ± 23 months, range 60-130). Retrospective analysis of a prospectively maintained database was carried out to evaluate weight loss, GERD symptoms, resolution of comorbidities type 2 diabetes mellitus (T2D), hypertension (HTN), dyslipidemia, and complications before RYGB and at long-term follow up.

Results: Twenty-five/50 patients (50%) referred preoperative GERD symptoms; among them, 12 patients (48%) showed an intraoperative hiatal hernia (HH) and underwent LRYGB with concomitant HH repair (HHR). At long term follow-up (97.8 ± 23.1 months) mean BMI was significantly lower compared to baseline (30.4 ± 5.5 kg/m^2; P < 0.001). Among patients with preoperative GERD, 18/25 (72%) had GERD resolution; however, 7/25 (28%) reported postoperative GERD symptoms. Furthermore, 4/25 patients (16%) without preoperative GERD referred postoperative GERD new onset.

Conclusions: LRYGB provides satisfactory weight loss and is associated to a high percentage of GERD symptoms resolution. However, about 11/50 (22%) of patients complained GERD symptoms at long-term follow-up. The pathophysiology of GERD after RYGB, de novo or persistence, is not completely understood and further studies are needed.

Abstract Code: NGS15031-82 | Ultrasound assessment of colonic wall: Is thickness decreasing a marker of gut function and metabolic health?

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Introduction: Metabolic syndrome (MetS) is associated with alteration gut function. The mucosal and submucosal layers of colonic wall are the place of interaction with gut microbiota triggering mucosal

immunology pathways [1]. Ultrasound (US) can help detect gut motility and evaluate colonic wall. Bowel-wall thickening is the most commonly used sign of bowel wall pathology detected on ultrasound, decreasing of colonic wall thickness has not been considered and may be reliable sign of disorders in gut mucosal immunology.

The Aim was to evaluate the relevance of ultrasound measurements of colon wall thickness, inflammatory and vascular markers in obese patients.

Materials and Methods: We included 75 overweight subjects (age 26-75 years; 42 females), BMI > 30, waist circumference (WC) > 110. 30 healthy volunteers were controls. All patients underwent general clinical, lab tests; abdominal ultrasonography using multiparameter abdominal US. Colonic wall thickness has been evaluated on ultrasound imaging of anterior wall in transverse, ascending and descending colon and in small intestine, also M-mode was used to analyze peristaltic waves. We did standardized Doppler spectral analysis of mesenteric blood flow evaluation velocity criteria in superior & inferior mesenteric arteries.

Results: We observed decreased colonic wall thickness to 2-3.5 mm in obese individuals (up to 1-3 mm in DMT2 patients) vs 3-5.5 mm in controls. Microbiota alteration was in 86 patients (54 patients demonstrated cholestasis). Mesenteric blood flow Doppler detected increasing PSV in superior & inferior mesenteric artery was in obese (up to 130-178 cm / sec vs 106-134 cm/sec in controls, $P < 0.05$), abdominal aorta atherosclerosis, aneurisms. Microsplenia and increased VF correlated with thinning colonic wall ($r > 0.7$).

Conclusions: Decreasing colonic wall thickness is associated with constipation symptoms, metabolic syndrome, diabetes and altered mesenteric blood flow.

References

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OESOPHAGEAL MOTILITY DISORDERS

Abstract Code: NGS15546-93 – Poster of Distinction | **No increase in oesophageal dysmotility or hiatus hernias in patients with hypermobility spectrum disorders and dysphagia compared to non-hypermobile controls: A two-centre case-control study**

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Introduction: Dysphagia is prevalent in patients with hypermobile Ehlers-Danlos Syndrome/Hypermobility Spectrum Disorder (hEDS/HSD)[1]. Dysmotility is hypothesized as the underlying mechanism, particularly in patients with postural tachycardia syndrome (PoTS)[2]. No large studies using high resolution manometry (HRM) have been conducted to characterise the oesophageal motility patterns in hEDS/HSD patients with non-obstructive dysphagia.

Methods: Consecutive patients with hEDS/HSD referred for HRM from tertiary neurogastroenterology clinics at two different institutions for investigation of endoscopy negative dysphagia between January 2010 to January 2021 were included. Consecutive non hEDS/HSD patients referred for the same reason were also included as controls. Patients were categorised as hEDS/HSD cases if they satisfied the 2017 diagnostic classification for hEDS/HSD. Patients with incomplete motility data, surgery to the gastro-oesophageal junction, inflammatory connective tissue disorder or outside ages 18-80 were excluded. Oesophageal manometric parameters were obtained from either MMS (water-perfused), Manoview or Sandhill HRM traces. Motility diagnoses were made using the Chicago classification v4.0.

Comparisons between cases and controls was made using the t-test for continuous variables, or Chi-square test/Fisher's exact test for categorical variables. A p value < 0.05 denoted statistical significance. Stata (version 12.1) was used for analysis.

	hEDS n=140	Controls n-167	P value
Female N (%)	133 (95)	98 (59)	<0.001
Mean age (SD)	38.5 (14.1)	44.5 (13.9)	<0.001
Mean Eckardt score (SD)	4.2 (2.8)	5.0 (6.0)	0.36
Opiate use N (%)	48 (34.3)	17 (10.2)	<0.001
PoTS N (%)	67 (47.9)	1 (0.6)	<0.001
Oesophageal motility:			
Normal N (%)	86 (61.4)	74 (43.7)	0.002
Disorders of peristalsis N (%)	47 (33.6)	66 (39.5)	0.001
Absent peristalsis N (%)	5 (3.6)	19 (11.4)	0.01
Ineffective oesophageal motility N (%)	39 (27.9)	42 (25.2)	0.6
Hypercontractile oesophagus N (%)	2 (1.4)	1 (0.6)	0.4
Distal oesophageal spasm	1 (0.7)	4 (2.4)	0.4
Disorders of outflow N (%)	7 (5.0)	28 (16.7)	0.001
Achalasia	2 (1.4)	20 (12.0)	<0.001
OGJ outflow obstruction	5 (3.6)	8 (4.8)	0.6
Rapid drink challenge:			
Abnormal inhibition of peristalsis N (%)	3 (4.6)	21 (26.6)	<0.001
Abnormal after contraction N (%)	23 (32.9)	43 (55.1)	0.007
Multiple rapid swallow			
Abnormal inhibition of peristalsis N (%)	4 (8.3)	10 (16.4)	0.2
Abnormal after contraction N (%)	11 (22.4)	17 (28.3)	0.5
Small hiatus hernia (<2cm) N (%)	21 (15.0)	34 (20.4)	0.2
Large hiatus hernia (>2cm) N (%)	9 (6.4)	10 (6.0)	0.8

Results – Table 1: 307 patients were included. 140 patients (46%) had hEDS/HSD. hEDS/HSD patients were significantly more likely to be female (95% vs 59%), taking opiates (34% vs 10%) and have PoTS (48% vs 0.6%), all $P < 0.001$. Severity of dysphagia (Eckardt score) was similar between the two groups ($P = 0.36$). The most common diagnosis in hEDS/HSD was normal motility (61.4%) followed by ineffective oesophageal motility (27.9%), however compared to controls they were significantly less likely to have a motility disorder (38.6% vs 56.3%, $P = 0.002$), even after adjusting for opiates, PoTS and age (OR: 0.41, CI:0.22-0.71, $P = 0.003$). With a rapid drink challenge hEDS/HSD patients were significantly less likely to have

abnormal peristaltic inhibition ($P < 0.001$) and abnormal after contraction ($P = 0.007$). 21% of hEDS/HSD patients had a hiatus hernia but this was less than the incidence in controls (26%, $P > 0.5$).

Conclusions: Patients with hEDS/HSD who present to tertiary neurogastroenterology centres with dysphagia are not at increased risk of suffering from a major oesophageal motility disorder or hiatus hernia compared to patients without hEDS/HSD.

TABLE 1. Demographics and HRM findings of hEDS/HSD patients vs controls with dysphagia

Abstract Code: NGS15547-94 – Poster of Distinction | **POEM improve the esophageal body distension in type III achalasia**

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Background and aims: Although peroral endoscopic myotomy (POEM) is reported to be effective especially type III achalasia, its effect on esophageal body peristalsis was poorly understood. The aim of this study is to evaluate the morphologic change in esophageal body peristalsis after POEM according to the subtypes of achalasia by analyzing intraluminal ultrasound (US) images temporally correlated with high-resolution impedance manometry (HRIM) data.

Methods: Intraluminal US images and impedance values from 17 achalasia patients who underwent POEM and pre- and post-POEM HRIM and intraluminal US examination (mean age, 48.47 years (22 – 76): 7 males, 10 females) (four patients for type I, seven for type II and six for type III achalasia) and eight normal subjects (mean age, 45.13 years (27 – 57): 3 males, 5 females) were analyzed. Intraluminal US images parameters included esophageal muscle thickness (MT), muscle cross-sectional area (MSCA) and lumen cross-sectional area (LCSA), swallow-to-distension time and distension duration.

Results

MT increased and LCSA decreased significantly, but esophageal body contractility was not improved after POEM in type I achalasia. MT increased and LCSA decreased significantly after and muscle thinning during distension and lumen-occluding esophageal contractility improved after POEM in type II achalasia. On the contrary to type I and II achalasia, MT decreased and LCSA increased after POEM in type III achalasia. Swallow-to-distension shortened and distension duration increased after POEM in type III achalasia.

Conclusions

POEM decreased esophageal LCSA by lower esophageal sphincter and intrabolus pressure decompression in type I and II achalasia, and improved esophageal body distensibility and inhibitory function during primary peristalsis in type III achalasia.

Key words: Achalasia, POEM, Morphologic change, Peristalsis

Abstract Code: NGS15014-83 – Poster of Distinction | **Yield of Provocative maneuvers in Non Achalasia dysphagia patients**

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Introduction: Provocative maneuvers solid swallows, multiple rapid swallows (MRS) and rapid drink challenge (RDC) test complement and enhance HRM evaluation however, difficult to perform in achalasia patients. There is paucity in literature depicting simultaneous comparison of water swallows and provocative test metrics in patients with dysphagia and pressure abnormalities during the swallow period in non achalasia patients.

Methods: This is a retrospective study done in non achalasia dysphagia during the year July 2017 to December 2019. HRM testing was done with ten swallows of 5mL water followed by five solid swallows of equal size followed with MRS and RDC. Intrabolus pressure (IBP) (mm Hg), Distal contractile integral (DCI) (mmHg cm^{-1} s^{-1}), Contractile front velocity (cms^{-1}). Distal latency (DL) (sec) and 4s IRP (mm Hg) was recorded in water and solid swallow. Post MRS and RDC after contraction was calculated. Results were presented as percentage and Mean ± SE (SD).

Results: Patients with non-achalasia dysphagia have elevated 4s IRP (mm Hg) in solid swallow (10 ± 0.5) as compared to water swallows (8 ± 0.3) and faster ($P = 0.02$) and CFV was faster in solid swallow (9 ± 1.2 vs 6 ± 0.5; p value = 0.02). Other parameters were comparable in between the two swallows. Abnormal water and solid swallow were 55% (297/540) and 82% (200/245). Abnormal peristalsis pattern in water swallow was identified in 50% (27/54) with another 5% increased diagnostic yield with addition of solid swallow (30/54). The use of MRS and RDC identified abnormal contractile augmentation in 13% (7/54) and 20% (11/54) in patients with normal liquid and solid swallow peristalsis pattern respectively resulting in diagnostic yield to 90. MRS or RDC as adjunctive tests described abnormal pressure patterns in all forty nine symptomatic patients The distribution of Hypo-repressive, prolonged hyper-repressive and non obstructive hyper-contractile was seen in 18/49 (37%), 2/49 (4%) and 29/49 (59%) patients during MRS swallowing period and 14/49 (29%), 8/49 (16%) and 27/49 (59%) during RDC.

Conclusions: **N**on achalasia patients have predominant distal esophageal body contraction abnormality. MRS or RDC pressurization patterns identify all symptomatic dysphagia patients but should be complementary in HRM evaluation.

Abstract Code: NGS15007-85 | **A case report of a patient with Eosinophilic Esophagitis**

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Introduction: Eosinophilic esophagitis is a chronic, antigen-triggered inflammatory disease of the esophagus. The disease is discovered in the 1990s and it has a continuous rise in incidence. It can affect children and adults and is caused by allergens which are common ingredients of food (1). It can manifest as dysphagia and odynophagia or in rare cases the first manifestation of the disease can be obstruction of the esophagus with a bolus of food. The eosinophilic esophagus has non-specific changes of the mucosa of the esophagus like mucosal swelling, white deposits, or narrowing of the lumen of the esophagus (2). Treatment of a disease includes diet restrictions, therapy with oral corticosteroids, and treatment of complications of disease.

Case report: 43-year old man seeks help in the Emergency department of General County Hospital Vinkovci because of food impaction in esophagus what happens during lunch last day. Because of that patient could not drink anything during the 24-hour period. The patient underwent emergent gastroscopy during which food impaction was found. Food was moved to the stomach and fragmented into small particles. Because specific changes of esophageal mucosis like transversal lines were noticed through the whole circumference of the esophagus control gastroscopy was done. Biopsy of the esophagus was done and it was found a high number of eosinophilic granulocytes. Because of a number of eosinophilic granulocytes, higher than 15 in tissue sample patient was diagnosed with eosinophilic esophagitis. We started treatment of the disease with oral corticosteroids in order to stop the newly exacerbation of symptoms. The aim of this case report was to show that obstruction of the esophagus can be the first manifestation of the eosinophilic esophagitis and in that case, after sollwing of food impaction, it is essential to undergo control gastroscopy and biopsy of esophageal mucosis because of patohistologycal examination and adequate treatment of a disease.

Keywords: Eosinophilic esophagitis, esophageal food impaction

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Abstract Code: NGS15472-91 | Can esophageal symptoms be associated with sleep disorders in esophageal rare diseases? A retrospective case-control study across achalasia, eosinophilic esophagitis and gastroesophageal reflux disease

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Objective: The association of gastroesophageal reflux disease (GERD) with sleep disorders has been revealed in several studies. Conversely, the quality of sleep in patients with eosinophilic esophagitis (EoE) and Achalasia (Ach) is still poorly investigated, although the presence of typical GERD symptoms is common in these rare diseases. Therefore, the aim of this study is to evaluate the prevalence of sleep disturbances across EoE and Ach compared to GERD patients and their correlation with esophageal symptoms and quality of life.

Methods: 30 Ach and 20 EoE patients were enrolled and compared to a control group of 20 GERD patients. All patients underwent a standardized questionnaire investigating the intensity-frequency scores (0-6) of esophageal symptoms, Pittsburgh Sleep Quality Index (PSQI) questionnaire to assess sleep quality, a SF-36 survey to investigate quality of life (physical (PCS) and mental (MCS) component), Beck Depression Inventory-II (BDI-II) and State Trait Anxiety Inventory (STAI) to assess the presence of depression and anxiety.

Results: The prevalence of sleep disturbances was 66.7% in Ach, 50% in EoE, and 60% in GERD patients ($P = 0.5$). PSQI, PCS, MCS, STAI Y1; STAI Y2, and BDI II scores did not significantly differ among the three groups ($P > 0.05$ in all cases). PCS and MCS significantly correlated with depression and anxiety levels (Figure 1). Ach patients showed significantly higher intensity-frequency scores of dysphagia for solids (Scheffè $P < 0.001$ and $P = 0.003$) and liquids (Scheffè $P = 0.001$ and $P = 0.01$) than EoE and GERD patients. No differences were found in the intensity-frequency scores of the esophageal symptoms among the three groups. Furthermore, a higher intensity-frequency score of regurgitation was significantly associated with worst quality of sleep.

Conclusions: Sleep disturbances are common with Ach and EoE, similar to GERD patients. Moreover, there is a significant association between poor quality of sleep and regurgitation, a typical GERD symptom, independent from diagnosis. Conversely, no correlation was found between sleep disturbances and dysphagia both for solids and liquids, the main symptoms of Ach and EoE. Our results should encourage the physicians to screen for the presence of sleep abnormalities to provide a more comprehensive and effective management of these patients.

Abstract Code: NGS15574-94 | Clinical symptoms, endoscopic findings, and lower esophageal sphincter characteristics in patients with absent contractility

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Objectives: We investigated the clinical symptoms, upper gastrointestinal endoscopy findings, and lower esophageal sphincter (LES) characteristics in adult patients diagnosed with absent contractility on high resolution manometry and factors associated with erosive esophagitis that were found on endoscopy in these patients.

Methods: A cross-sectional study was conducted in patients with absent contractility who were examined at the Institute of Gastroenterology and Hepatology, Vietnam between March 2018 and August 2020. Clinical symptoms, endoscopic findings, and LES metrics were collected and compared between individuals with and without erosive esophagitis. Logistic regression analysis was used to examine a variety of factors associated with erosive esophagitis.

Results: Among 7,519 patients who underwent HRM, 204 (2.7%) were diagnosed with absent contractility. The mean age of the study sample was 45.9 years, 65.7% were women, and none had systemic sclerosis. The most common symptoms were regurgitation, belching, epigastric pain, and bloating. On endoscopy, 50% had erosive esophagitis, mostly Los Angeles grade A (42.9%). On manometry, 44.6% of the patients had LES hypotension and 68.1% had low integrated relaxation pressure in 4 seconds (IRP4s). Male sex (adjusted OR = 2.01, 95% CI: 1.04-3.89) and an IRP4s < 5 mmHg (adjusted OR = 2.21, 95%CI: 1.12-4.37) were significantly associated with erosive esophagitis.

Conclusions: Absent contractility was present in many patients without known systemic diseases. Erosive esophagitis was common and associated with male sex and low IRP4s.

Keywords: absent contractility, esophageal motility disorders, high resolution manometry

Abstract Code: NGS15485-95 | COVID-19 pandemic perception in achalasic patients: Impact on gastrointestinal symptoms and use of Telemedicine

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Achalasia is a primary motor disorder of the oesophagus characterized by absence of peristalsis and insufficient lower oesophageal sphincter relaxation. Currently, there are no data available on the perception of COVID-19 pandemic in achalasic patients and the impact of COVID-19 lockdown on their upper gastrointestinal symptoms. The aim of this study was to evaluate these aspects as well as the attitude towards Telemedicine.

64 achalasic patients followed up at our outpatient clinic devoted to rare disease at the University of Salerno participated in this study. COVID-19 perception was assessed using a previously published survey. Moreover, upper gastrointestinal symptoms were assessed by a standardized intensity-frequency questionnaire and the results were compared to those obtained before COVID-19 pandemic. The survey and the gastrointestinal questionnaire were administered by telephone or video (social media) calls during the II Italian lockdown. Fifty-one patients (79.7%), 66% men, mean age 61 ± 15.4, responded to the survey. One patient was diagnosed with COVID-19 and was excluded from the analysis. At the question "On a 0 to 100 scale, how much are you worried because of the COVID-19 pandemic?" The mean score was 72.8 ± 27.1 and 64.7% achalasic patients answered more than 60. In addition, those who considered themselves more vulnerable to COVID-19 than the general population and who were more anxious about contracting the infection showed a significantly higher score for COVID-19 worry compared to those who considered themselves less vulnerable and anxious (79.7 ± 27.6 vs 62.5 ± 23.6, P = 0.027 and 80.9 ± 19.6 vs 57.1 ± 33.1, P = 0.002 respectively). Moreover, in the selected patients (n = 29) who did not undergo any change in medical or surgical treatment at least one year before COVID-19 pandemic, there was a significant worsening of the intensity-frequency score of regurgitation, heartburn, odynophagia, water brush, and epigastric burning during COVID-19 lockdown (Wilcoxon test < 0.05). Additionally, 75% of patients were very interested in using Telemedicine.

In conclusion, achalasic patients showed that the COVID-19 lockdown had a significant impact on their psychological aspects and several upper gastrointestinal symptoms. Telemedicine can represent a new strategy to follow up achalasic patients.

Abstract Code: NGS15500-83 | Demographics and follow-up of Hypercontractile esophagus: single tertiary center experience

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Hypercontractile esophagus is defined as excessive esophageal peristaltic vigor in the absence of mechanical obstruction. As it is an infrequent diagnosis and its clinical presentation and outcome remain uncertain, we intend to describe the population diagnosed with this entity in the last 6 years in our department.

We included all patients diagnosed with hypercontractile esophagus as classified by Chicago Classification (CC) version 3.0, from 01-01-2015 until 30-04-2021. Esophageal HRM was performed in our department using a water-perfused system (MMS).

We identified 32 patients with 20% or more hypercontractile swallows in HRM but 4 of them presented esophagogastric junction outflow obstruction and are excluded from the following description. From the remaining 28 patients, 16 were female (57.1%) and mean age was 63 years (±10.9). Considering the overall number of HRM performed in our department, we estimate an incidence of 1.3% of this manometric finding (28/2240). HRM was performed for: dysphagia and/or retrosternal pain in 20, gastroesophageal reflux symptoms in 7 and systemic sclerosis in 1. From the 10 patients who underwent barium esophagram, 8 had findings compatible with hypercontractile esophagus.

Nineteen patients (67.9%) maintained follow-up and 4 underwent medical treatment: isosorbide in 2, nitroglycerin in 1 and nifedipine in 1. Only in the patients under isosorbide, symptoms alleviated. No patient repeated HRM over the abovementioned period.

As per CC version 4.0, clinically relevant hypercontractile esophagus should only be considered in the presence of important symptoms therefore excluding 1 patient out of the 28 with the manometric diagnosis (96.4% had clinically relevant hypercontractile esophagus).

In conclusion, 1.3% of HRM identified hypercontractile esophagus, considered clinically relevant in 96.4%. We identified a female predominance (57.1%) and mean age of 63 years, comparable with the published literature. Limitations of this study are attributable to its retrospective design and small number of patients.

Abstract Code: NGS15562-91 | Development of a score that predicts Manometric alterations in patients with systemic sclerosis

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Introduction: In patients with systemic sclerosis (SS) esophageal manometry (EM) is generally reserved for patients with symptoms refractory to empirical therapy. However, 30% of patients with abnormal MS are asymptomatic. Our aim was to evaluate the relationship between findings in MS and different clinical and laboratory findings in patients with SSc and to build a predictive model for altered MS.

Methods: Retrospective study of 71 SSc patients who underwent EM over a 12-year period (2008-2020). SSc-related EM changes were defined as lower esophageal sphincter hypotension, ineffective motility, or absent contractility.

Results: The population studied had a median age of 54 (42-64) years; female in 88%. Diffuse cutaneous SSc in 10.5%, limited cutaneous SSc in 39.5% and overlap syndrome with SSc in 42.1%. Gastrointestinal (GI) symptoms present in 82% of patients (dysphagia in 63%). EM showed changes in 40.8% of patients. In univariate analysis, altered MS presented in relation to Raynaud's syndrome (RR3.6; 95%CI 1.3-5.3; P = 0.024), diffuse cutaneous SSc (RR2.5; 95%CI 1.5-4.5 ; P = 0.007), antinuclear antibody (RR3.6; 95%CI 1.8-4.6, P = 0.034), abnormal cardiac study (RR2.2; 95%CI 1.3-4.7, P = 0.045) and abnormal CO diffusion capacity (RR1.8; 95%CI 1.3-3.2, P = 0.021). Altered MS no presentation with the presence of GI symptoms (RR1.4; 95%CI 0.6-3.4, P = 0.234). We built a model using diffuse cutaneous SSc, antinuclear antibody, cardiac study and CO diffusion capacity, with an area under the curve of 0.748 (P = 0.002). This model has a sensitivity of 86% and a specificity of 74% for EM changes.

Conclusions: In our population, gastrointestinal symptoms unrelated to EM changes. Other findings should be considered for changes that are predictive of MS. Our model is able to alter MS prediction in patients with SSc. External validation is required.

Abstract Code: NGS15478-97 | Dysphagia and normal esophageal motility: Can Upper Esophageal Sphincter analysis help?

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Introduction: Recently the protocol for high-resolution pharyngeal manometry and impedance was released. The consensus group, regarding the Upper Esophageal Sphincter (UES) relaxation analysis, considered that UES integrated relaxation pressure (IRP) was the better metric to measure. Currently the protocol and software for esophageal high-resolution manometry (HRM) can characterize the UES.

Objective: Evaluate UES in patients with dysphagia and normal esophageal motility.

Methods: Retrospective study of dysphagic patients with a normal esophageal motility accessed by HRM, according to Chicago classification, from 2018 to May 2021. The exam was performed by the same operator, with a water perfusion catheter (MMS catheter G-90500). The results for UES resting pressures (rP) were analyzed according to the manufacturer's normative values. UES IRP of 0.2 second was automatically determined by the MMS software, and for a 5 mL liquid swallow, IR P > 13 mmHg was considered abnormal (according to Nativ-Zeltzer et al. 2016).

Results: We analyzed a total of 164 dysphagic patients, 56% (n = 92) had abnormal findings with outflow obstruction or major/minor peristalsis disorders. One paediatric patient with normal esophageal motility was excluded. We evaluated a total of 71 patients, mean age 54.2 ± 15.5 years, mainly women (66.2%, n = 47). The mean UES rP was 72.3 ± 68.5 mmHg, 66.2%(n = 47) patients had normal rP, 23.9% (n = 17) had hypercontractile and 9.9%(n = 7) had hypocontractile UES. Mean UES IRP was 7.3 ± 6.7 mmHg, 11.3%(n = 8) had abnormal IRP, with no sex predominance, of these, 37.5% (n = 3) had normal or hypocontractile and 25% (n = 2) had hypercontractile UES.

Conclusions: (a) We found that more than 10% of dysphagic patients with normal esophageal motility have abnormal UES IRP, and more than 30% have abnormal tone of the UES. (b) The characterization of the UES, including the UES IRP, could be relevant to measure in dysphagic patients.

Abstract Code: NGS15536-92 | Effect of water bolus temperature and sparkling water on esophageal motor function in Rapid drink challenge in high resolution manometry

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Background: Patients with motility disorders associate the intake of water at different temperature with the worsening or improvement of esophageal symptoms. On the other hand, the use of provocative tests such as the rapid drink challenge (RDC) increase the sensitivity for the diagnosis of esophageal motility disorders.
Our aim, was to determine changes in esophageal motility, in integrated relaxation pressure (IRP) and the development of typical esophageal symptoms during RDC with the administration of cold (CW), hot (HW) or sparkling water (SW)
Methods: 108 patients referred for high resolution manometry (HRM) were randomized into 4 groups, RDC consisting in free drinking of 200 mL of water as quick as possible, every group drank 200 mL of CW at 11 °C, HW at 42°C, SW at 22.3°C. Both pressure patterns and symptoms induced by the RDC were analyzed and compared with a control group.
Results: CW, HT and SW in RDC compared with controls didn´t show significative differences in the IRP (CW 3.19 ± 0.9 vs 2.4 ± 0.67, HT 2.4 ± 1.02 vs 2.4 ± 0.67, and SW 3.1 ± 1.5 vs 2.4 ± 0.67, *P* = NS). Comparing the IRP of SWS with the IRP of the RDC in the CW group there´s a significative difference (9.04 ± 0.97 vs 3.19 ± 0.94, *P* = < 0.001) without difference in DCI (2871 ± 462 vs 2170 ± 1090 *P* = NS). In the HW group the IRP of SWS showed a significant difference with the IRP RDC (8.0 ± 1 vs 2.4 ± 1, *P* = < 0.001), without difference in DCI (2132 ± 455 vs 2765 ± 895, *P* = NS). In the SW group the IRP of SWS showed a significant difference with the IRP RDC (9.9 ± 2 vs 3.1 ± 1.5, *P* = < 0.001) and also with DCI (2879 ± 428 vs 1488 ± 689, *P* = < 0.001). No patient showed usual esophageal symptoms with RDC.
Conclusions: RDC with normal water at room temperature seems sufficient for evaluation of symptoms, complete inhibition of contractility and complete relaxation of the LES. We didn't find a clear contribution in changing water temperature or composition.

Abstract Code: NGS15592-94 | Esophageal epithelial barrier function in patients with Achalasia

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Objective: The pathogenesis of Achalasia is not well-known. Eventhough the disease effects the muscular layer, long-term food accumulation and as result of this, lactic acidosis as well as possible reflux related changes following therapeutic modalities might have an effect on epithelium. Our aim is to evaluate epithelial barrier functions of Achalasia patients (before and after baloon dilatation) compared to healthy volunteers (HV) and GERD groups.
Methods: Naive Achalasia patients before and after baloon dilatation (n = 23), HV (n = 15) and GERD (NERH (non-erosive reflux disease) (n = 15), ERD (erosive reflux disease) (n = 15)) patients were evaluated. Ussing chamber system was used to determine the electrophysiological properties of the esophageal epithelium and permeability properties were examined by fluorometric method. In addition, e-cadherin, caludin 1, claudin 4, occludin, zonula occludens 1and zonula occludens 2 gene and protein expression levels which are related with the tissue integrity were analysed. The qRT-PCR method was used to determine gene expression levels, and protein expression levels were investigated with ELISA.
Results: The electrophysiological properties of the Achalasia groups (187.3 Ω) were similar to the HV (166.8 Ω) group. On the other hand transepithelial resistance (TEER) of Achalasia patients was significantly higher than GERD groups(141.8 Ω), and the fluorescein permeability was significantly lower. There was no significant difference between the pre-treatment and post-treatment groups. Tight junction-related gene expression levels of the Achalasia groups were significantly higher than HV and GERD groups. Additionally, the protein levels of the same molecules were examined, it was concluded that only zonula occludens 2 protein level was significantly higher than the HV and GERD groups. The claudin 4 level of the Achalasia group after treatment was significantly higher compared to the HV and GERD groups. The protein level of e-cadherin, which is an important cell adhesion molecule, was significantly higher than the ERH group.
Conclusions: It has been determined that long-term food accumulation and lactic acidosis in Achalasia does not have any detrimental effect on the esophageal epithelial barrier. We believe that our study will contribute the understanding of pathogenesis of Achalasia at molecular level.

Abstract Code: NGS15598-00 | Esophageal motility disorders - the importance of proper therapeutic guidance

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Introduction: Esophageal motility disorders can have a significant impact on patients' quality of life. Despite this, these pathologies are little recognized in clinical practice. Thus, the aim of this study was to assess the prevalence and impact of unrecognized primary esophageal motility disorders.
Methods: Retrospective and monocentric study, which included all individuals diagnosed with esophageal motility disorders in high-resolution manometry between January 2018 and December 2020.

Patients who had previously undergone esophageal-gastric surgery were excluded.

Results: A total of 160 individuals were included, mostly female (63.8%), with a median age of 57 years (IQR 46-66 years). The most frequently reported symptoms were dysphagia (52.6%), heartburn and/or regurgitation (27.8%), cough (8.6%) and chest pain (6.3%). The esophageal motility disorders diagnosed were esophagogastric junction outflow obstruction (34.4%), hypercontractile esophagus (28.8%), achalasia (15.6%), ineffective esophageal motility (8.1%), absent contractility (6.9%) and distal esophageal spasm (6.3%). In one third of the cases, there was no subsequent therapeutic orientation of the identified motility disorder. Most of these situations (74.4%) were followed by specialties other than Gastroenterology (Table 1). The lack of clinical guidance was found mainly in cases of hypercontractile esophagus (58.3%) and esophagogastric junction outflow obstruction (37.5%). It was also found that, 6 months after performing high-resolution manometry, most of these individuals had symptoms, unlike those who had been correctly followed and treated (62.3% vs. 29.4%; $P < 0.001$).

Conclusions: In our cohort, one third of patients were not adequately treated, in most cases with persistent symptoms at follow-up. Therefore, we would like to encourage clinicals to find strategies to identify these individuals in order to optimize medical management and their quality of life, especially when they are followed by specialties other than Gastroenterology.

TABLE 1. Specialties that followed patients with esophageal motility disorders without adequate therapeutic guidance

Specialties	n = 43
General Surgery	15 (34.9%)
Gastroenterology	11 (25.6%)
Internal medicine	6 (14.0%)
Pneumology	5 (11.6%)
Rheumatology	3 (7.0%)
Endocrinology	1 (2.3%)
Orthopedics	1 (2.3%)
Otolaryngology	1 (2.3%)

Abstract Code: NGS15599-01 | Esophageal motility disorders in systemic sclerosis: A high-resolution manometry study

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Introduction: The classic manometric findings in systemic sclerosis are aperistalsis of the esophageal body with hypotensive lower esophageal sphincter. However, there is underrecognized heterogeneity of manometric features in this population. The aim of this study was to characterize esophageal motility disorders in systemic sclerosis using high-resolution esophageal manometry and to determine predictive factors of esophageal involvement.

Methods: Retrospective and single-center study, which included all individuals with systemic sclerosis referred for high-resolution esophageal manometry between April 2018 and December 2020. Esophageal motility disorders were reclassified according to the Chicago V3.0 classification.

Results: A total of 48 patients with systemic sclerosis were included, most of them female (91.7%) with a median age of 54 years old (interquartile range 45-64). The most frequent symptoms were dysphagia (75.0%), heartburn (20.8%) and regurgitation (10.4%). Only 7 (14.6%) patients were asymptomatic at the time of high-resolution esophageal manometry. The presence of esophageal symptoms was not predictive of esophageal dysmotility (58.5% vs 57.1%, $P = 0.945$). Absent contractility was presented in 8 (16.7%) patients and ineffective esophageal motility in 6 (12.5%). There was hypotensive lower esophageal sphincter in 16 (33.3%) cases. In addition, 7 (14.6%) patients had esophagogastric junction outflow obstruction, 4 (8.3%) distal esophageal spasm, 3 (6.3%) hypercontractile esophagus and there was one case each of type I and type II achalasia. The presence of anti-Scl70 antibodies (Scl70) was associated with esophageal involvement (62.5% vs 7.5%, $P < 0.001$). On the other hand, no association was found between cutaneous involvement and manometric changes (50.0% vs 72.2%, $P = 0.322$).

Conclusions: The present study confirms that esophageal motility alterations detected by high-resolution esophageal manometry are frequent in systemic sclerosis patients. However, they may be more related to the autoantibody profile than to the cutaneous involvement or gastrointestinal complaints of patients. Therefore, high-resolution esophageal manometry should be considered in all patients with systemic sclerosis, even in the absence of clinical manifestations. Furthermore, clinicians should expect to see heterogeneous manometric patterns in this population; otherwise, they might mistakenly dismiss the diagnosis of systemic sclerosis.

Abstract Code: NGS15470-89 | Guidewire-assisted probe placement for water-perfused high-resolution manometry in patients with achalasia

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Introduction: High resolution manometry (HRM) is the gold standard for the diagnosis of esophagogastric junction (EGJ) outflow disorders like achalasia, providing essential information for the patient management. However, blind positioning of the probe across the EGJ is not always possible in patients with achalasia.

Aims & methods: This retrospective study aimed to assess the success rate of gastric insertion of a water-perfused HRM probe in patients with suspected achalasia. We report our experience using guidewire-assisted HRM probe insertion when blind positioning failed. For this purpose, a 22-channel water-perfused probe with central lumen was advanced on a guidewire previously inserted into

the gastric cavity using an ultra-slim nasoendoscope. Data from all patients, who underwent a water-perfused HRM between January 2011 and June 2020 and were diagnosed with achalasia, were analysed.

Results: Overall, 227 patients (119 females; 53 ± 18 years) were included. The rate of successful gastric insertion was 74.9% (95%CI: 69.2-80.5). When blind positioning failed, the suspected diagnosis of achalasia subtype was based on esophageal body analysis during HRM and barium swallow features. Achalasia type I, II or III was diagnosed in 80 (35%), 104 (46%) and 43 (19%) patients, respectively. Gastric insertion success rate according to achalasia subtypes was 55% in type I, 88% in type II and 81% in type III. Achalasia type I was significantly associated with failure of gastric insertion (OR ≥ 3.57; $P \leq 0.005$). In 12 of the 57 patients with gastric insertion, the wire-guided technique was used when accurate EGJ assessment was judged important to guide treatment. Guidewire-assisted HRM was successful in all 12 patients and type I, II or III achalasia was diagnosed in 4 (33.3%), 3 (25%) and 5 (41.7%) patients, respectively. Nine of these patients were treated either by pneumatic dilation (1 patient with type I, 3 with type II achalasia) or by peroral endoscopic myotomy (POEM) (5 patients with type III achalasia).

Conclusions: Failure of gastric intubation during water-perfused esophageal HRM occurs frequently in achalasia, especially among patients with type I. Guidewire-assisted HRM allowed manometric EGJ assessment in all patients in whom the technique was used.

Disclosure: Nothing to disclose

Abstract Code: NGS15590-92 | High resolution esophageal manometry measurements: Is it a question of age or gender?

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Background: The impact of age and gender on esophageal motility is not completely established.

Aim: To evaluate the effect of age and gender on manometry parameters measured with high resolution esophageal manometry (HREM).

Methods: Retrospective study that included consecutive patients submitted to HREM with Manoscan® using a 36-channel solid state catheter between September 2019 and October 2020. Patients with a confirmed disorder of esophagogastric junction outflow obstruction or disorder of peristalsis based on Chicago Classification v3.0 were excluded from further analysis. Patients were stratified regarding age in < 60 years and ≥60 years groups.

Results: Seventy-two patients were included, 59% were female gender, with mean age of 55.5 ± 14.2 years, and 50.0% were over 60 years. The most common indications were refractory gastroesophageal reflux disease (62.5%) and dysphagia (29.2%). There were no statistically significant differences in HREM parameters with gender, including presence of hiatal hernia ($P = 0.53$), mean hernia size ($P = 0.60$), upper esophageal sphincter (UES) ($P = 0.72$) and lower esophageal sphincter (LES) ($P = 0.74$) mean basal pressures, median integrated residual pressure ($P = 0.65$), mean distal latency ($P = 0.89$), and distal contractile integral ($P = 0.73$). Regarding age, patients with ≥60 years had more frequently hiatal hernia (66.7% vs 38.9%; $P = 0.02$), and larger mean hernia size (1.0 ± 1.1 vs 0.5 ± 0.8 cm; $P = 0.03$), and had significantly higher mean distal contractile integral (2200 ± 1243 vs 1670 ± 723 mmHg.cm.s; $P = 0.049$). There were no statistically significant differences in other HREM parameters with age, including UES ($P = 0.33$) and LES ($P = 0.11$) mean basal pressures, median integrated residual pressure ($P = 0.73$), and mean distal latency ($P = 0.40$). Regarding multiple rapid swallows test parameters, older and male patients had a higher mean distal contractile integral (3179 ± 2189 vs 1968 ± 1070 mmHg.cm.s, $P = 0.02$; 3216 ± 2077 vs 2186 ± 1514 mmHg.cm.s, $P = 0.046$; respectively), but there were no significant differences in median integrated residual pressures ($P = 0.70$; $P = 0.22$), and distal latency ($P = 0.98$; $P = 0.99$).

Conclusions: Older patients presented higher frequency and dimensions hiatal hernia and a higher esophageal contractile vigor. Older and male patients seem to have a higher esophageal contractile reserve.

Abstract Code: NGS15040-82 | High-resolution esophageal manometry: Influence of body mass index on retention pressure of LES and the transdiaphragmatic pressure gradient

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Introduction: The lower esophageal sphincter (LES) retention pressure (PR) is the difference between the resting pressure of the LES (PSIO) and the trans-diaphragmatic pressure gradient (TDPG). Obesity is a known factor of risk of GERD and could be responsible by increasing TDPG and decreasing PR.

Patients and methods: We included retrospectively all patients who have benefited from HRM between January 2021 and April 2021.

Results: A total of 108 patients were included. They were 40 men and 68 women with a sex ratio M / F of 0.58. The average age was 58.3 years old. Antecedents most frequently found diabetes (14%) and dysthyroidism (8.6%). The diagnosis of GERD was retained for typical heartburn in 56 patients (51.8%). Upper gastrointestinal endoscopy was normal in 65% of cases. The average BMI was 25.31 Kg / m2 [16-35], 26 patients were obese with a BMI ≥ 30 Kg / m2. At MHR, the mean TDPG was 16.3 mmHg [-5-93] and PR average of -0.02 mmHg [-8.3-61]. An Hiatus Hernia was found in 58 patients with an average length of 2.6cm [2-6]. Esophageal motor skills were normal in 45 patients and ineffective in 34 patients. The statistical study showed that in obese patients (BMI ≥ 30Kg / m2), the PR was lower (-12.7 vs 5.01 mmHg; $P = 0.003$) and the higher GPTD (25.19 vs 12.8 mmHg; $P = 0.001$). These same data were also significantly associated with the presence of GERD and HH greater than 2 cm. There was no association between the TDPG and PR and

motor disorders of the esophagus. The GERD and HH were also significantly associated with Low pression of LES with a $P = 0.039$ and 0.004 respectively.

Conclusions: PR allows a more precise assessment of the state of the esogastric junction by integrating both the TDPG and the pressure of the LES. In our study, low PR and high TDPG appear to be associated with obesity, symptoms of GERD and HH.

Abstract Code: NGS15600-84 | Hypercontractile esophagus - Clinical presentation, manometric findings and therapeutic results

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Introduction: Hypercontractile esophagus is an esophageal motility disorder recently defined in the Chicago criteria (version 3.0) as the presence of at least 20% hypercontractile supine swallows. However, the pathophysiology and treatment of this entity are not fully established. Thus, the aim of this study was to describe our experience regarding clinical presentation, manometric findings and therapeutic results of hypercontractile esophagus.

Methods: Retrospective and single-center study, including patients diagnosed with hypercontractile esophagus in high-resolution esophageal manometry (HREM) between January 2018 and December 2020. Patients previously submitted to esophagus-gastric surgery were excluded.

Results: Among the 289 patients who underwent HREM, 46 (15.9%) were diagnosed with hypercontractile esophagus, the majority female (67.4%), with a median age of 61 years (IQR 51-69). The most frequently reported symptoms were dysphagia (34.8%), heartburn (28.3%), regurgitation (23.9%) and chest pain (8.7%). More than half of the patients had at least 50% hypercontractile supine swallows and a quarter had 100%. Most patients without targeted treatment (60.0%) maintained symptoms at follow-up. Excluding cases of gastroesophageal reflux disease documented on 24-hour pH-metry study, eighteen patients started treatment, most with proton pump inhibitors (44.4%), followed by calcium channel blockers (33.3%), injection of botulinum toxin (11.1%) and nitrates (11.1%). Of these, only 33.3% had complete resolution of symptoms, with injection of botulinum toxin, nitrates and calcium channel blockers being the treatments with the highest response rates (50%, 50% and 33.3%, respectively).

Conclusions: The majority of patients with no targeted treatment maintained symptoms during follow-up. Furthermore, the effectiveness of the different therapies performed was, in general, discouraging. Thus, it is essential to investigate new approaches in the treatment of hypercontractile esophagus.

Abstract Code: NGS15548-95 | Lower amount of assessed swallows may be sufficient to obtain reproducible results of high-resolution esophageal manometry

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Aim: To calculate the number of wet swallows necessary for correct interpretation of the results of integrated relaxation pressure (IRP) with low probability of type I and II errors.

Methods: Retrospective analysis of the HREM (Laborie) results obtained in sitting position in 100 recent consecutive patients with solid-state 10 Fr catheter (Unisensor) was performed. Cases were assessed for technical quality before inclusion. The patients were divided to the group with disorders of EGJ outflow (IR $P > 15$ mm Hg, cohort 1) or to the cohort 2 (controls). The set of individual measurements (swallows #1, 2...10) obtained from each subject was consequently assessed for the mean result of IRPs. At each time point (after n number of measurements) the mean of n IRPs were assessed for conclusion (disorder presence/absence). The results of the obtained averages were characterized as false positive (mean IR $P >$ 15 mm Hg, no disorder of EGJ outflow by 10 measurements), false-negative (mean IR $P < 15$ mm Hg, disorder of EGJ outflow present by 10 swallows), true-positive, and true-negative. Diagnostic accuracy was calculated. Association of the diagnostic accuracy from recall was studied with the use of receiver operating characteristic curve analysis. For the study purposes, thresholds of the number of IRP measurements were calculated based on the acceptable number of diagnostic accuracy ≥95%.

Results: Cohort 1 consisted of 25 subjects; 75 subjects were in cohort 2. Mean IRP by 10 water swallows differed significantly between the cohorts: (Mean ± SD) 21.8 ± 6.0 in cohort 1, 9.1 ± 4.6, in cohort 2, $P < 0.01$). The probability that conclusions made after 10 wet swallows and the lower number of them match was high. Actual probability to obtain false-positive results was 2 times lower then "allowed" rate of 5%. The probability to make false-negative results did not exceed 10% in any number of measurements. The area under receiver operating characteristic curve after 2 measurements for the cohort 1 was 0.9584, and for the cohort 2 - 0.9652.

Conclusions: The recommended number of water swallows measurements is excessive for correct conclusion on disorders of esophago-gastric outflow presence is excessive. The probability to make same conclusion based on IRP values after 2 swallows and after 10 swallows is 95%.

Abstract Code: NGS15480-90 | Our clinical experience concerning Esophagogastric junction outflow obstruction

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Esophagogastric junction outflow obstruction (EGJOO) is characterized by impaired swallow induced low esophagogastric sphincter relaxation with preserved peristalsis. Its etiology and natural history remain uncertain. We intend to describe the population diagnosed with EGJOO in the last 6 years in our department.

We included all patients diagnosed with EGJOO as classified by Chicago Classification (CC) version 3.0, from 01-01-2015 until 30-04-2021. Esophageal HRM was performed in our department using a water-perfused system (MMS).

We identified 34 patients, 26 (76.5%) females with median age of 67 years (±22.75). HRM was performed for: dysphagia in 22, systemic sclerosis in 7 and gastroesophageal reflux in 5. Three (10.7%) had no esophageal symptoms. From the 17 (50%) who underwent barium esophagram, 11 (64.7%) had abnormal findings compatible with EGJOO. Nine patients (26.5%) had secondary EGJOO: 5 had a hiatal hernia, 2 previous Nissen fundoplication, 1 esophageal diverticulum and 1 chronic opiate use. Twenty patients (62.5%) maintained follow-up. Nine underwent treatment: 3 botulinum toxin injection, isosorbide in 3, nifedipine in 1, 1 pneumatic dilation and the 1 patient with an esophageal diverticulum underwent surgical diverticulectomy. Five patients (14.7%) underwent 2 HRM over time: 3 maintained EGJOO and 2 had a previous normal HRM. None developed achalasia in the abovementioned period.

Considering the total of HRM performed, EGJOO was diagnosed in 1.5% (34/2240). As per CC version 4.0, clinically relevant EGJOO would be considered in the 11 patients (32.4%) presenting abnormal barium esophagram, as all presented dysphagia. Four patients presented EGJOO with hypercontractile features (1 of them the opioid user).

Regarding secondary *versus* functional EGJOO, age and gender did not differ but hypercontractile features were significantly more frequent in secondary EGJOO (44.4% *versus* 4%, $P = 0.019$) and therapeutic success was more frequent in functional EGJOO (100% *versus* 25%, $P = 0.048$).

Considering CC version 4.0, only 32% of our patients should be considered as having a clinically relevant EGJOO and 27% had a secondary cause for this finding. Therapeutic challenge with botulinum toxin injection and/or watchful waiting are the best supported treatment options for primary EGJOO, but further studies are needed to define its natural history and definitive approach.

Abstract Code: NGS15589-00 | Primary achalasia in relation to pseudoachalasia - Clinical challenges

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Introduction: In everyday clinical practice, it is difficult to distinguish primary achalasia from pseudoachalasia, as seen in this case report.

Material and methods: The case of a 39-year-old patient who was referred for treatment to the National Reference Center for Functional Gastrointestinal Disorders due to dysphagia is presented. For several months now, he has had difficulty swallowing painfully, initially solid foods and then liquids, and he feels the food getting stuck behind his sternum with vomiting.

In less than a year, he lost 20 kilograms. He hadn't been seriously ill before. The patient has a reduced body mass index (BMI 19.6 kg/m^2), in nutritional (NRS2002 = 3) and risk of developing sarcopenia (SARC-F score = 6). Laboratory findings were without significant deviations. On the upper endoscopy, a dilated esophagus with food retention and with narrowing in the distal part of the esophagus was seen (biopsies were taken without signs of malignancy). High-resolution esophageal manometry (HREM) showed a finding typical of achalasia type II. The MSCT of the thorax was normal but on ultrasound and MSCT of the abdomen the tumor formations on both kidneys were verified. The patient was presented at a multidisciplinary council that decided to perform pneumatic balloon dilatation (PBD) of the lower esophageal sphincter (LOS) due to dominant dysphagia, followed by radical left nephrectomy and finally, at the request of the patient, only an enucleation of the tumor (bilateral pathohistological diagnosis: Adenocarcinoma renis). Due to residual discomfort, PBD was repeated. Since then, for more than 3 years, the patient is regularly monitored (upper endoscopy, MSCT, PET/CT) and there are no signs of recurrence/metastatic malignancy. During this period, clinical improvement was achieved (no dysphagia) and he gained significantly on body weight.

Conclusions: Based on the findings of HREM, it is not possible to distinguish idiopathic achalasia from pseudoachalasia (which may be caused by malignant disease or nonmalignant obstruction). As shown in this case, in order to exclude malignant pseudoachalasia, it is necessary to identify risk factors and perform additional diagnostic processing (CT and/or endoscopic ultrasound).

Abstract Code: NGS15595-97 | Therapeutic approach to idiopathic esophagogastric junction outflow obstruction

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Introduction: Idiopathic esophagogastric junction outflow obstruction (EGJOO) is an esophageal motility disorder defined in the Chicago criteria (version 3.0) as an elevated median integrated relaxation pressure and preserved esophageal peristalsis. However, the therapeutic approach to this entity is not fully defined. Thus,

the aim of this study was to describe our experience regarding the therapeutic results of idiopathic EGJOO.

Methods: Retrospective and single-center study, which included patients diagnosed with EGJOO in high-resolution esophageal manometry (HREM) between January 2018 and December 2020. Patients with anatomical alterations of the gastroesophageal junction (e.g., hiatal hernia or surgical history) were excluded.

Results: Among the 289 patients who underwent HREM, 55 (19.0%) had EGJOO, most were female (67.5%), with a median age of 55 years (IQR 47-65). The most frequently reported symptoms were dysphagia (50.9%), heartburn (23.6%), regurgitation (12.7%), cough (9.1%) and chest pain (7.3%). Excluding cases of gastroesophageal reflux disease documented on 24-hour pH-metry study, sixteen patients started treatment, most with proton pump inhibitors (43.8%), followed by injection of botulinum toxin (37.5%), calcium channel blockers (12.5%) and laparoscopic Heller myotomy (6.3%). Patients submitted to botulinum toxin injection showed the best response to treatment (100% vs. 34.4%; $P = 0.003$). On the other hand, 59.1% of patients without targeted treatment showed spontaneous improvement in symptoms.

Conclusions: Most patients with EGJOO showed symptomatic improvement without any targeted treatment, so we suggest that these patients should be monitored, namely with a reassessment HREM at follow-up. In case of persistence or worsening of symptoms, the injection of botulinum toxin seems to be particularly effective in selected cases. Prospective studies that assess the risk of disease progression to achalasia may have an additional impact on the therapeutic management of these patients.

Abstract Code: NGS15516-90 | Water temperature determines pressure responses to the rapid drink challenge test

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Background: The rapid drink challenge test (RDC) has been included in the last version of the Chicago criteria (CC4.0) for high resolution esophageal manometry (HREM) as a complementary test to assess obstruction across the esophagogastric junction. The normal response to the RDC test is a complete inhibition of esophageal body pressure and relaxation of the lower esophageal sphincter.

Aim: To analyze the effect of water temperature on pressure responses to the RDC in patients with normal or ineffective esophageal motility (expected to have a normal inhibitory response).

Methods: At the end of the CC4-0 protocol, two consecutive RDC were performed in random order, by drinking 200 ml of mild-cold water (median temperature 15.3°C[IQR 5-95; 13.5 – 20]) and mild-hot water at body-temperature (37 °C [IQR 5-95; 35.5 - 40]). Pressure responses to each RDC were compared using the Mano View 3.3 software.

Results: 108 consecutive patients (normal motility 61; ineffective motility 47) were included (65 F; age range 33-80 yrs). Median esophageal pressure during RDC was significantly lower with mild-cold: 6 mmHg (IQR 5-95; 9.6-26.5) compared to mild-hot water: 14.3 mmHg (IQR5-95; 1.9-36); $P < 0.001$. Complete inhibition of esophageal pressure was observed in 97.2% of patients with mild-cold water, but only in 32(65.8%) patients with mild-hot water($P < 0.001$). In the 32 patients with pressurization during the RDC, 20 produced peristaltic contractions, 5 produced only abnormal panesophageal pressurizations, and 7 had both peristaltic contractions and panesophageal pressurizations. Only 4(3.7%) patients had abnormal LES relaxation (IR $P > 15$ mmHg) during the RDC (2 with mild-cold and 2 with mild-hot water). Two patients with abnormal LES relaxation had also panesophageal pressurizations during hot water, but not during cold water. There was no association between incomplete inhibition with the Eckard score or with any individual symptom.

Conclusions: In a significant proportion of patients with normal or ineffective motility, performing a RDC test with mild-hot water (at body temperature) may abolish the normal inhibitory response to RDC. These data shows that control of water temperature during the RDC may be crucial for the outcome of the test, and opens the possibility to find alterations in the inhibitory pathways that may pass undetected using the standard protocols.

VİSCERAL PAİN MECHANİSMS

Abstract Code: NGS15529-94 | Evidence for engagement of the nucleus of the solitary tract in processing intestinal chemonociceptive input irrespective of conscious pain response in healthy humans

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Background and aims: Neuroimaging studies have revealed important pathomechanisms related to disorders of brain-gut interactions, such as irritable bowel syndrome and functional dyspepsia. More detailed investigations aimed at neural processing in the brainstem, including the key relay station of the nucleus of the solitary tract (NTS), have hitherto been hampered by technical shortcomings. To ascertain these processes in more detail, we used multi-echo multi-band 7T functional magnetic resonance imaging (fMRI) and a novel translational experimental model based on a nutrient-derived intestinal chemonociceptive stimulus.

Methods: In a randomized cross-over fashion, subjects received duodenal infusion of capsaicin (the pungent principal in red peppers) and placebo (saline solution). During infusion, fMRI data and concomitant symptom ratings were acquired.

Results: Eighteen healthy female volunteers were included in the final analysis. Significantly increased brain activation over time during capsaicin infusion, as compared to placebo, was observed in brain regions implicated in pain processing, including several cortical areas, the thalamus and NTS. Brain activation in the thalamus, cingulate cortex and insula were more pronounced in subjects who reported abdominal pain (visual analogue scale > 10mm), as compared to subjects who experienced no pain. On the contrary, activations at the level of the NTS were independent of subjective pain ratings.

Conclusions: The current experimental paradigm allowed us to demonstrate activation of the principal relay station for visceral afferents in the brainstem, the NTS, which was engaged irrespective of the conscious pain response. These findings contribute to understanding the fundamental mechanism necessary for developing novel therapies aimed at correcting disturbances in visceral afferent pain processing. Clinicaltrials.gov (NCT02551029)

Abstract Code: NGS15010-79 | Management of abdominal pain in emergency rooms: epidemiological aspects and clinical impact

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Introduction: Abdominal pain is a frequent reason for consultation in the emergency room. Several studies have highlighted the impact of epidemiological data on the diagnostic and therapeutic approach as well as on the prognosis of abdominal pain. Our objective was to study the epidemiological characteristics of patients attending the emergency department for abdominal pain.

Material and Methods: Retrospective study including patients consulting in the various medical and surgical boxes. The study period was three days. Data were entered and analyzed using SPSS.

Results: 76 patients were collected, of which 54% were women and 46% were men. The mean age was 39.7 ± 20 years. 74% of patients had a medical history and 34% surgical. Signs associated with abdominal pain were abdominal bloating (68%), vomiting (66%), diarrhea (53%), and constipation (20%). The site of pain was epigastric (32%), right hypochondrium (12%), hypogastric (13%), left hypochondrium (13%), right iliac fossa (15%), left iliac fossa (10%), and diffuse (5%). At initial examination: mean respiratory rate at 22 ± 5 c / min, heart rate at 83 ± 18 bpm, systolic blood pressure at 123 ± 4 mmHg and diastolic at 82 ± 4 mmHg. 15. 54% were febrile. Additional examinations performed were ECG in 62% of patients, Abdomen x-ray in 34%, chest x-ray in 50%, laboratory workup in 68%, abdominal ultrasound in 30% and abdominal CT scan in 7%. The diagnoses retained were gastroenteritis (55%), simple gallstones (13%), diabetic ketoacidosis (3%), acute coronary syndrome (1%). 4% presented a digestive neoplasia and 11% a surgical emergency such as acute appendicitis (8%) and intestinal obstruction (3%). 55% received symptomatic treatment. 84% were discharged at home and 16% were hospitalized, including 10% in the visceral surgery department and 6% in Emergency.

Conclusions: The management of abdominal pain requires special attention with regard to the patient's background and the clinical picture to identify medical and surgical emergencies. In our study, 16% of patients with abdominal pain required hospitalizati

OTHERS

Abstract Code: NGS15530-86 | Digital instruments for reporting of gastrointestinal symptoms in clinical trials: Comparison of end-of-day diaries versus experience sampling method

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Background: We previously reported on the excellent adherence to a smartphone app used as symptom diary in a clinical trial. Other sampling methods, such as the experience sampling method (ESM), are better equipped for measuring symptom variability over time, provide useful information regarding possible symptom triggers and are free of ecological and recall bias. The high frequency of measurements, however, could limit the feasibility of ESM in clinical trials.

Objective: This study aimed to compare compliance rates to a smartphone-based diary and ESM for symptom assessment in irritable bowel syndrome (IBS) and functional dyspepsia (FD).

Methods: Data from multiple studies was included. Patients with IBS participated in a randomized controlled trial, which involved a smartphone diary of 2+8 weeks (pre-treatment + treatment period), and an observational study, during which patients completed ESM assessments using a smartphone for one week. Patients with FD participated in a randomized controlled trial, which involved a smartphone diary of 2+12 weeks (pre-treatment + treatment period), and an observational study, during which patients completed ESM assessments using a smartphone for one week. Compliance

rates were compared between these two symptom monitoring/sampling methods.

Results: Twenty-five patients with IBS and fifteen patients with FD were included. Overall compliance rates for the end-of-day diaries were significantly higher than for ESM (92.7% and 90.1% versus 69.8% and 61.4%, respectively).

Conclusions: We here demonstrate excellent compliance rates for smartphone application-based end-of-day diaries as used in two separate clinical trials. Overall compliance rates for ESM were significantly lower, rendering it more suitable for intermittent sampling periods rather than continuously during longer clinical trials.

Abstract Code: NGS15476-95 | From men and pigs: colonic distension-evoked mucosal secretion

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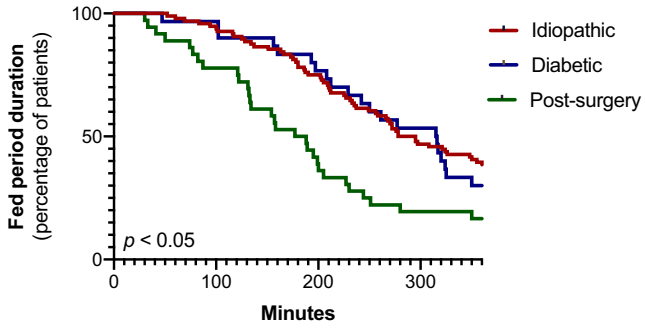
Distention evoked intestinal secretion is mainly studied in rodents, while, due to nutritional and physiological similarities, the porcine intestine appears to be a valuable model for the human one. Our objective was to investigate porcine and human colonic distension-induced secretion.

Transverse colonic tissue preparations (n = 42) from 23 pigs and intestinal specimens (n = 534) from the colon of 108 patients were mounted in Ussing chambers and short circuit currents (I_{sc}) were measured. Tissue distension was evoked by pressure application from the serosal and mucosal side (60 s, 60 mmHg (porcine) and 20 mmHg (human)). Amplitude of secretory response was calculated in control tissues and compared in a paired manner to responses in tissues treated (a) with chloride (Cl^-)-free solution, (b) with tetrodotoxin (TTX, 1 µM), (c) with cyclooxygenase inhibitor piroxicam (10 µM) and (d) with a filter placed on the mucosal side.

Differently from the pig, in human colonic tissues distension induced secretory response was larger after serosal than mucosal distension. In addition, in porcine tissue a higher pressure was necessary to evoke similar secretory responses. In both species, secretory response was significantly reduced after change to Cl^-free buffer (porcine: 24.87 ± 11.41 vs. 0.42 ± 2.50 ΔµA/cm², $P < 0.01$; human 27.82 ± 19.37 vs. -8.08 ± 5.82 ΔµA/cm², $P < 0.001$), by pre-treatment with piroxicam (porcine: 19.28 ± 8.94 vs.7.20 ± 5.54 ΔµAs/cm², $P < 0.05$; human: 26.51 ± 14.44 vs. 16.40 ± 9.81 ΔµA/cm², $P < 0.001$) and by a mucosal placed filter (porcine: 25.30 ± 3.94 vs. -0.03 ± 3.68 ΔµAs/cm², $P < 0.05$; human: 11.59 ± 9.32 vs. 2.56 ± 2.31 ΔµA/cm², $P < 0.01$). However, pre-treatment with TTX significantly reduced secretory response only in porcine colonic tissue (19.49 ± 6.10 ΔµAs/cm² vs.27.26 ± 8.41, $P < 0.05$).

In conclusion, in both species, distension of the colonic wall evokes secretion, which is (1) Cl^- dependent, (2) partly mediated by prostaglandins and (3) mainly induced by tensile forces. However, in porcine colon this response is induced by higher pressure compared to human colon and it is (partly) nerve-mediated.

Abstract Code: NGS15532-88 | Measurement of antroduodenal motility identifies characteristic patterns in gastroparesis according to different etiologies



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Objective: Gastroparesis (GP) is a gastrointestinal disorder associated with significant morbidity and health care costs. GP patients form a heterogeneous population with diverse etiology. Treatment is often challenging due to a poorly understood underlying pathophysiology. The aim of this study is to assess antroduodenal motility patterns among the different GP etiologies.

Methods: In this retrospective analysis, we reviewed antroduodenal manometry (ADM) recordings of patients with confirmed GP between 2009-2019. ADM was performed using a 36-channel high-resolution manometry catheter. After 30 minutes recording in fasting conditions, patients were given a standardized meal. During the following 6 hours ADM measurements were evaluated for antral and duodenal amplitudes (mmHg) and motility index (MI), fed period duration (min), number and duration of phase III contractions and migrating motor complexes (MMCs), and presence of neuropathic patterns (i.e. bursts, retrograde peristalsis, clustered contractions, absence of phase III contractions).

Results: A total of 167 GP-patients (142 women, median age 45 [31-57]) with confirmed delayed gastric emptying were included. The following GP etiologies were identified: idiopathic n = 101; post-surgery n = 36; diabetes n = 30. A lower percentage of female patients was found in the post-surgery GP-group compared to the other groups ($P < 0.01$). No differences were found between GP-groups regarding age, BMI, gastric half emptying time, antral and duodenal amplitudes, and MI. Fed period duration was significantly longer in idiopathic ($P < 0.01$) and diabetic GP-patients ($P < 0.05$) compared to post-surgery GP-patients. Furthermore, the number and duration of phase III contractions, and the number of MMCs was significantly lower in idiopathic and diabetic patients compared

to post-surgery GP-patients ($P < 0.01$). Likewise, absence of MMCs were more often observed in idiopathic and diabetes GP-patients compared to post-surgery GP-patients (resp. $P < 0.01$ and $P < 0.05$). No significant differences between GP-subgroups were found regarding the presence of neuropathic patterns.

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

Abstract Code: NGS15563-92 | Predictive factors for roux stasis syndrome after distal gastrectomy with Roux-en-Y reconstruction in gastric cancer patients

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Introduction: Roux-en-Y (R-Y) reconstruction after distal gastrectomy in gastric cancer patients can cause Roux stasis syndrome (RSS), the pathogenic mechanism of which is unclear. This study retrospectively evaluated the risk factors for RSS.

Methods: Patients who were pathologically diagnosed with gastric cancer and underwent distal gastrectomy with R-Y reconstruction between March 2014 and March 2021 were retrospectively analysed. RSS occurrence was evaluated and examined for correlations with demographic and clinicopathological data. A nomogram was built using "R" package.

Results: RSS was observed in 20/220 patients (9.1%). The median time to RSS occurrence was 9.2 days (9.2 ± 3.5) after surgery. Patients with RSS had a significantly longer postoperative hospital stay ($P < 0.001$) and higher hospitalization costs. There was a significant difference between males and females (11.9% vs. 3.9%, $P = 0.049$). The incidence of RSS tended to be higher in underweight (body mass index (BMI) < 18.5 kg/m^2) and obese (BMI ≥ 28.0 kg/m^2) patients ($P = 0.043$). The rates of smoking and nerve invasion were higher in patients with RSS, but statistical significance was not reached. There were no significant differences in other factors. A nomogram was built in which sex, BMI group, nerve invasion and smoking were incorporated to predict RSS (AUC = 0.71).

Conclusions: Both male sex and a polarized BMI are independent risk factors for RSS after distal gastrectomy with R-Y reconstruction in gastric cancer patients. A nomogram including sex, BMI group, nerve invasion and smoking can predict RSS occurrence.

Keywords: stasis syndrome, distal gastrectomy, anastomosis, Roux-en-Y, gastric cancer

Abstract Code: NGS15504-87 | Quality of care of patients undergoing analysis for gastrointestinal motility disorders in the Netherlands: a patient hotel model

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Aim: There is growing demand for improving healthcare services for patients globally. Patient hotel models can be applied to allow shorter inpatient stays. From patients' perspective regarding satisfaction and experience it is unknown how to structure testing and analysis in tertiary referral centers and whether a patient hotel model can improve patients' quality of care. The aim of our study was to investigate patient experience and satisfaction and healthcare costs in a patient hotel model in patients referred for analysis of complex gastrointestinal motility disorders.

Methods: All consecutive patients referred for analysis of gastrointestinal motility disorders at Maastricht UMC+, Maastricht, the Netherlands, that stayed overnight in the patient hotel between June 2017 and July 2018 were asked to complete a questionnaire (with open ended and closed questions) on patient satisfaction and quality of care. The patient hotel is located in the immediate vicinity to our hospital. Costs of overnight stay were calculated.

Results: During the study period, forty-six patients stayed in the patient hotel, of whom sixteen patients completed and returned the questionnaire. Patients were largely to absolutely satisfied with the quality of care, regarding coordination, information, courtesy of nurses and staff and privacy. Eighty-eight percent of patients preferred to stay in the hotel over the hospital. Several patients responded and stated that staying in the hotel was pleasant and made them feel less as a patient as the stigma of 'hospitalization' was not present. Consultation with other caregivers was greatly valued as patients felt that their symptoms and complaints are being taken seriously. A single patient commented on practical issues regarding use of wheelchair in the hotel and the distance between hotel and hospital. Cost savings between 48,433 and 74,613 euros for one year were achieved, amounting to 613 to 944 euros per patient.

Conclusions: Positive patient satisfaction by using a patient hotel model for analysis of gastrointestinal motility disorders was achieved. Patients perceived their quality of care as high with a positive experience regarding coordination, information, courtesy of nurses and staff and privacy. We show that moving overnight stays from inpatient to an outpatient hotel provides substantial financial savings for hospitals, healthcare providers and insurance companies.

Abstract Code: NGS15514-88 | STW 5 protects human intestinal epithelial barrier function upon inflammatory stimulus

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Background: The herbal preparation STW 5 (Iberogast®) is clinically used in managing the symptoms of functional dyspepsia and irritable bowel syndrome (IBS) and has been shown to possess properties that may protect intestinal epithelial barrier (IEB) in inflammatory bowel disease models (Malfertheiner, 2017, Wadie et al., 2012).

Objective: This evidence reinforces the role of this herbal preparation on IEB protection in IBS. Nevertheless, the effect of STW 5 on intestinal epithelial gene expression and overall pathways in both basal and inflammatory conditions has not been described in humans.

Methods: In this study, we have tested the hypothesis that STW 5 reinforce human IEB function by modulating gene expression and pathways related to intestinal epithelial permeability. To address our hypothesis, we used both human intestinal enteroids generated from healthy patients and human intestinal enteroid-derived monolayers. Human enteroids were pre-treated with STW 5 before being stimulated with a pro-inflammatory cocktail for 16 hours. The enteroids were collected for bulk RNA sequencing and analyzed. To further demonstrate the functional role of STW 5 on human intestinal epithelial cells, we performed a permeability assay on human enteroids derived monolayers. Similarly, human enteroids monolayers were pre-treated with STW 5 before being stimulated with a pro-inflammatory cocktail for 16 hours. Transepithelial resistance was monitored overtime and permeability assays were carried out at the end of the experiments.

Results: STW 5 pretreatment did not dampen the inflammatory process occurring in enteroids treated with inflammatory cytokines when compared to control. However, the transcriptomic analysis suggested that genes involved in both adherent and tight junction regulation were upregulated. Human enteroids monolayers pretreated with STW 5 and stimulated with inflammatory cytokines demonstrated a higher resistance and lower permeability when compared to human enteroid monolayers treated with cytokines alone.

Conclusions: Overall, our results suggest that the herbal preparation STW 5 protects human intestinal epithelial barrier function upon inflammatory stimulus. This could be one of the STW 5 mechanisms on leaky gut induced low-grade inflammation in IBS.

Abstract Code: NGS15523-88 | Telemedicine consultations during the COVID-19 pandemic are associated with a high degree of satisfaction and reduced anxiety in patients with disorders of gut-brain interaction

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Objective: Telemedicine is a technological tool that can supplement in-person healthcare delivery. There is no data on whether telemedicine consultations of patients with disorders of gut-brain interaction (DGBI) impact anxiety and the degree of satisfaction.

Methods: Forty-one consecutive patients, preliminarily diagnosed with irritable bowel syndrome (IBS), were consulted by a telemedicine platform (Healee, Bulgaria) in January – March 2021. DGBI were classified using the Rome IV criteria, The general anxiety disorder – 7 (GAD-7) questionnaire evaluated anxiety at the time of consultation and one month later. The short assessment of patient satisfaction (SAPS) scale assessed the degree of satisfaction. The patients were divided into two subgroups based on the improvement of their symptoms one month after the telemedicine consultation.

Results: Of 41 patients (mean age = 37.5 years, SD = 6.8, 51.2% females), 15 (36.6%) fulfilled the Rome IV criteria for IBS and 26 (63.4%) had other DGBI (functional dyspepsia, functional diarrhea, functional constipation and functional bloating). Symptom improvement was reported by 32 (78%) patients. Mean SAPS was 24.1 (16-18, SD = 3.4), 15 (36.6%) patients were very satisfied, 22 (53.7%) were satisfied, 4 (9.8%) were dissatisfied, and no one was very dissatisfied. GAD-7 scores were significantly lower one month after online visit ($t = 14.38$, $df = 40$, $P < 0.001$). In the group of patients with symptom improvement, GAD-7 scores were significantly lower after one month ($t = 22.61$, $df = 31$, $P < 0.001$). In the group who had no symptom improvement, GAD-7 scores were significantly higher one month after the consultation ($t = 7.30$, $df = 8$, $P < 0.001$). In regression, analysis the majority found the telemedicine clinic satisfactory with no difference between men and women, young and old, and patients with IBS or other DGBI.

Conclusions: Telemedicine consultations during the COVID-19 pandemic are associated with a high degree of satisfaction and reduced anxiety in patients with DGBI. Patients with IBS referred to online visits have frequently been misdiagnosed with other DGBI that may require further investigation and /or different treatment. Anxiety is significantly reduced one month after telemedicine consultation in patients with DGBI and symptom improvement.

Abstract Code: NGS15503-86 | The prognostic significance of the neuronal markers NF and PGP9.5 in colorectal cancer

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Background & aims: Colorectal cancer (CRC) is the third most common cancer and the second leading cause of cancer-related deaths worldwide. Although the TNM (tumor-lymph node- metastasis) staging classification system is still regarded as one of the main prognostic factors, clinical outcome can vary considerably for patients diagnosed in similar stages. Recent developments revealed that neurons within the CRC tumor stroma could affect clinical outcome in CRC patients. In this study, we aim to investigate the prognostic value of the neuronal markers neurofilament (NF) and protein gene product 9.5 (PGP9.5).

Methods: Formalin-fixed, paraffin-embedded (FFPE) tumor tissues (n = 204) from the Netherlands Cohort Study on diet and cancer (NLCS) were immunohistochemically (IHC) stained for NF and PGP9.5. Slides were scanned and made available for digital histological evaluation. Two different methods for histological assessment were applied: 1) random sampling using systematically positioned rectangular measurement sites, and 2) whole slide evaluation. Two independent observers assessed the presence of NF or PGP9.5 expression within the tumor. Associations between NF and/or PGP9.5 expression and multiple clinical and pathological characteristics were investigated using Pearson chi-square test, long-rank tests and Kaplan-Meier. Multivariate analyses were performed with Cox proportional hazard models, adjusted for potential confounders and known prognostic factors.

Results: NF and PGP9.5 positive nerves were found within the tumor stroma. A substantial agreement (NF κ = 0.608 ; PGP9.5 κ = 0.620) was found between the two different methodologies. Whole slide evaluation was used for all further analyses, as it is less time-consuming. Positive staining with NF as single marker was statistically significantly associated with a poorer overall survival (log-rank$_{NF}$ P = 0.0028). Patients with positive staining for both markers also had a statistically significantly lower survival compared to the patients with negative staining (Log-rank$_{combined\text{-}model}$ P = 0.0170 ; HR$_{double\text{-}positive}$ = 2.23; 95%-CI 0.55-8.99).

Conclusions: Both NF as single marker and the combined marker panel NF and PGP9.5 were statistically significantly associated with poorer survival in CRC. These findings provide new evidence for a potential prognostic role of neuronal markers in CRC.

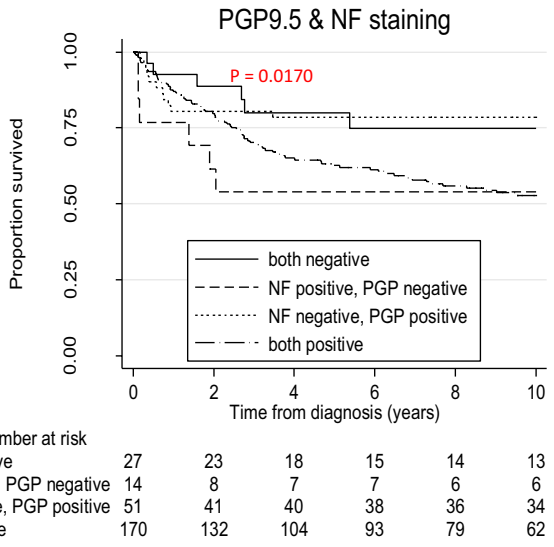

FIGURE 1. 10-year cancer-specific survival curve for the combined model of potential neuronal prognostic markers, NF and PGP9.5 in a population-based CRC series