
# Neurogastroenterology and Motility update DDW 2018

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# Objectives

- Esophageal disorders:
- GERD,
- Spastic esophageal disorders and Botox
- Cannabis effect on HRM
- Gastroparesis
- Abdominal bloating and pelvic floor dysfunction

# INTERIM RESULT OF A PROSPECTIVE MULTI-CENTER REGISTGRY OF LOWER ESOPHAGEAL SPHINCTER STIMULATION FOR GERD: THE LESS-GERD REGISTRY.


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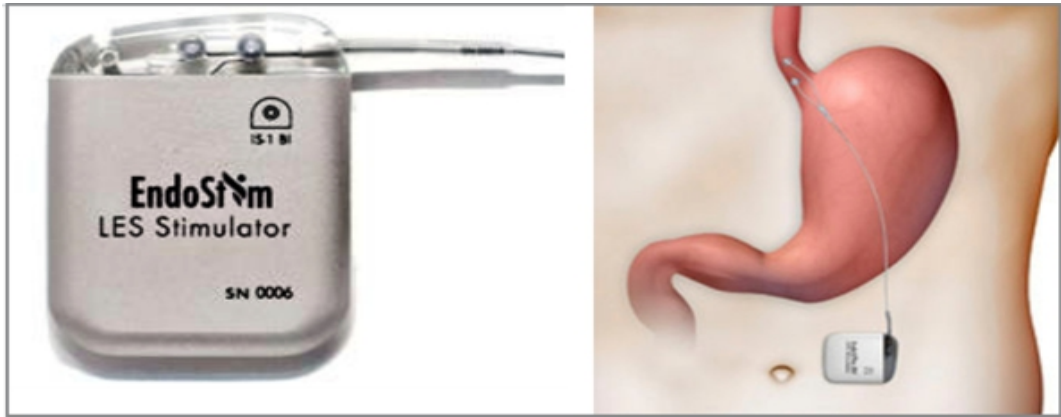
# Aims and Methods

- Safety and efficacy of electrical stimulation of the lower esophageal sphincter (ES-LES) using the EndoStim® LES Stimulation System (Nijmegen, The Netherlands) has been demonstrated in clinical trials in up to 4 years.
- This is prospective international multicenter web-based registry of patients with GERD treated with ES-LES.
- Data is collected at baseline and at routine follow-ups for 5 years.
- Demographics, adverse events, GERD symptoms, GERD health related quality of life (GERD-HRQL) heartburn and regurgitation scores, use of proton pump inhibitors (PPIs) and physiological data (esophageal pH/manometry) are collected when available.

# Results

- Data are available from 223 patients from 16 sites in Europe and Latin America. Mean age at time of implant was 50 ±14; 59% were males.
- Paired GERD-HRQL Heartburn data are presented in Table 1. Paired GERD-HRQL Regurgitation data are presented in Table 2.
- Post-implant esophageal pH testing was performed by a few sites either as standard of care or in patients with residual symptoms.



# Table 1: Paired GERD-HRQL Heartburn

| | N | Pre-Implant Median (Q1, Q3) | Post-Implant Median (Q1, Q3) | Change Median (Q1, Q3) | P-value † |
|---|---|---|---|---|---|
| 12 Months | 96 | 24.00 (16.50, 28.50) | 6.50 (2.00, 13.00) | -14.50 (-22.50, -6.00) | <.001 |
| 24 Months | 38 | 23.50 (17.00, 28.00) | 7.00 (2.00, 12.00) | -15.50 (-21.00, -7.00) | <.001 |
| 36 Months | 12 | 20.00 (18.50, 27.00) | 3.00 (0.50, 13.50) | -16.00 (-24.00, -6.50) | .0034 |

† P-values result from Wilcoxon Signed Rank Test of change from Baseline

# Table 2: Paired GERD-HRQL Regurgitation

| | N | Pre-Implant Median (Q1, Q3) | Post-Implant Median (Q1, Q3) | Change Median (Q1, Q3) | P-value † |
|---|---|---|---|---|---|
| 12 Months | 94 | 18.50 (11.00, 27.00) | 6.00 (1.00, 12.00) | -9.00 (-18.00, -2.00) | <.001 |
| 24 Months | 37 | 18.00 (10.00, 24.00) | 5.00 (1.00, 12.00) | -10.00 (-14.00, -4.00) | <.001 |
| 36 Months | 13 | 17.00 (9.00, 20.00) | 4.00 (0.00, 10.00) | -9.00 (-14.00, -3.00) | .0020 |

† P-values result from Wilcoxon Signed Rank Test of change from Baseline

# Results:

- In patients with pre-implant, and 3-6 month (n=32) and 12 month (n=7) post-op, median 24-hour esophageal acid exposure (pH) improved from 8.0% pre-implant to 4.5% at 3-6 months (p=NS) and from 6.2 % pre-implant to 4.5% at 12 months (p=NS), respectively.
- Eight serious adverse events (8/223) in seven patients were reported to be possibly or definitely-related to the device.

These included:  gastroparetic symptoms, lead dislodgement, palpitations, pain, and dysphagia. All events resolved; four patients had the device explanted.

## Conclusion:

ES-LES is an effective in treating GERD patients in routine clinical practice with acceptable safety profile.

# BOTULINUM TOXIN INJECTIONS FOR THE TREATMENT OF HYPERCONTRACTILE ESOPHAGUS: A RANDOMIZED PLACEBO CONTROLLED TRIAL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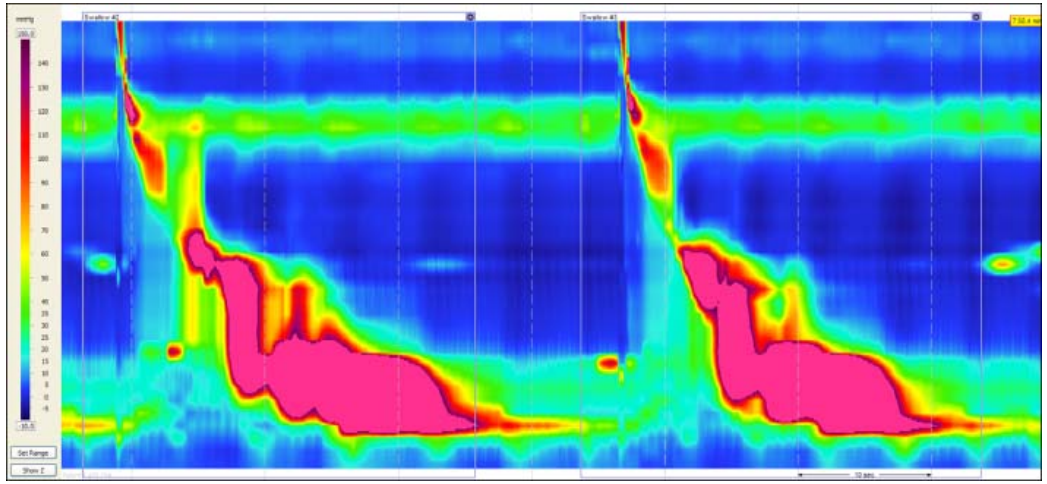

# Background

- Botulinum toxin (BT) injections have been shown to be efficient for the treatment of achalasia, and only 1 study showed a possible effect on distal esophageal spasm (DES) or nutcracker.
- The goal of this randomized study was to assess the efficacy of Botnulinum toxin vs placebo in patients with symptoms associated with DES or jackhammer esophagus (JH), identified by esophageal high resolution manometry, according to the Chicago classification v3.0.

# Methods

- **Inclusion criteria** were: patients with dysphagia and/or thoracic pain for at least 6 months, and DES or JH on HRM.
- **Exclusion criteria** were past history of esophago-gastric surgery, gastroesophageal malignancy/tumor, large hiatal hernia or severe esophagitis.
- **Randomization**: Botulinum toxin (100 IU injected in several points at the level of the cardia and in the esophageal wall), vs no injection.
- The endoscopic intervention was blinded to the patient and the physicians involved in the follow-up.
- HRM and Eckardt score were performed 3 months later.
- The patient could then choose for a second (or first) injection of BT.
- The last manometric and clinical follow-up were performed at 6 months after the initial procedure.

# Results

- 23 patients (13 women, mean age: 60 years (31-75)) were included: 10 in the control group, and 13 in the BT group.
- mean Eckardt score was similar (BT: 6 (3-10) vs 7 (4-10) in the control group, p=0.47).
- The initial manometric diagnoses were 12 Jackhammer esophagus (9 in the BT group), 9 DES, and 2 atypical cases.
- The Eckardt score was significantly improved at 3 months (-1.9, p=0.0036), without any difference between the 2 groups (p=0.3).
- The clinical improvement seemed more noticeable in DES patients than in JH (decrease of the Eckardt score: -4 vs -0.5, p=0.11).
- Interestingly, most of the cases resolved to normal manometry or ineffective esophageal motility at 3 months, whatever the treatment administered.
- No complication related to the endoscopic procedures occurred.

# Conclusion

- This randomized study did not confirm the efficacy of Botulinum toxin injection for the treatment DES or JH.
- The symptoms associated to these disorders may improve over time without treatment.
- The evaluation of other endoscopic procedures such as POEM should take into account this possibility of spontaneous remission of symptoms.

# CHRONIC CANNABIS USE AND GASTROINTESTINAL SYMPTOMATOLOGY, ENDOSCOPIC AND HIGH-RESOLUTION MANOMETRY FINDINGS: A RETROSPECTIVE CASE-CONTROL STUDY


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# Introduction

- Recreational cannabis use is increasing with its legalization in many states, and medical marijuana is prescribed for a variety of upper gastrointestinal (GI) complaints.
- Animal studies suggest cannabis can reduce TLESRS, reflux and vomiting; in 2016, Cannabinoid Hyperemesis Syndrome was added to the Rome criteria for functional GI disorders.
- Human studies report conflicting effects on visceral sensation, and in turn, abdominal pain.
- There are currently no large studies investigating GI symptoms in patients presenting to a Gastroenterology practice with chronic cannabis use.

# Methods

- A retrospective case-control study was conducted from 2006-2017 comprising 2371 patients (772 cases, 1599 controls) in a diverse, inner-city outpatient Gastroenterology office.
- The cases consisted of those with documented cannabis use, and non-cannabis users served as randomly selected controls.
- Main presenting complaint, demographics, frequency and duration of cannabis use, endoscopic and high-resolution (HR) manometry with impedance findings were recorded.

# Results

- The most common complaint in cannabis users was abdominal pain, and in non-cannabis users was heartburn.
- Cannabis users were more likely to be male, African American, and younger (age 49 vs 59 p<0.0001), and 64% endorsed daily use. They were more likely to complain of abdominal pain (25% vs 8%, p<0001), heartburn (15% vs 9%, <p 0.001) and nausea with vomiting (7% vs 1% P<0.001).
- Esophagitis (8% vs 3% p 0.0003), non-erosive gastritis (30% vs 15% p 0.0001) and erosive gastritis (14% vs 3% p<0.0001) were significant findings in cannabis users compared to controls.
- Intra-esophageal stasis by HR impedance manometry (65% vs 17% p 0.001) and a hypertensive LES by HR manometry (27% vs 8% p 0.02) were significant findings in cannabis users compared to controls.
- Cannabis users likely to have abnormal manometry study (20% vs 52% p 0.03), although no specific pattern by Chicago classification could be identified.

# Conclusions

- abdominal pain was the most common complaint in cannabis users
- The significant manometric findings of a hypertensive LES with intra-esophageal stasis may explain the complaint of increased heartburn and vomiting in cannabis users.
- cannabis use may exacerbate, or initiate, a variety of GI symptoms which goes against current knowledge.
- Future studies should focus on the true clinical effects of cannabis in chronic users as our study calls into question the therapeutic role of cannabis for GI symptoms.

# GASTRIC EMPTYING CHANGES OVER TIME IN GASTROPARESIS: COMPARISON OF INITIAL AND 48 WEEK FOLLOW UP GASTRIC EMPTYING TESTS IN THE GASTROPARESIS REGISTRY OF THE GASTROPARESIS CONSORTIUM

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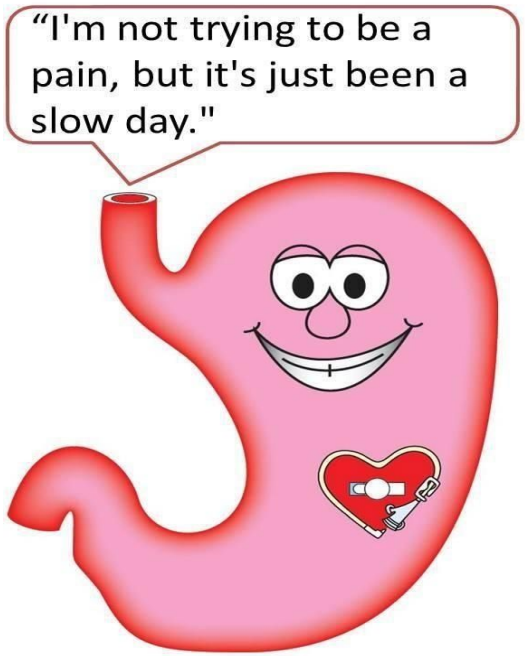


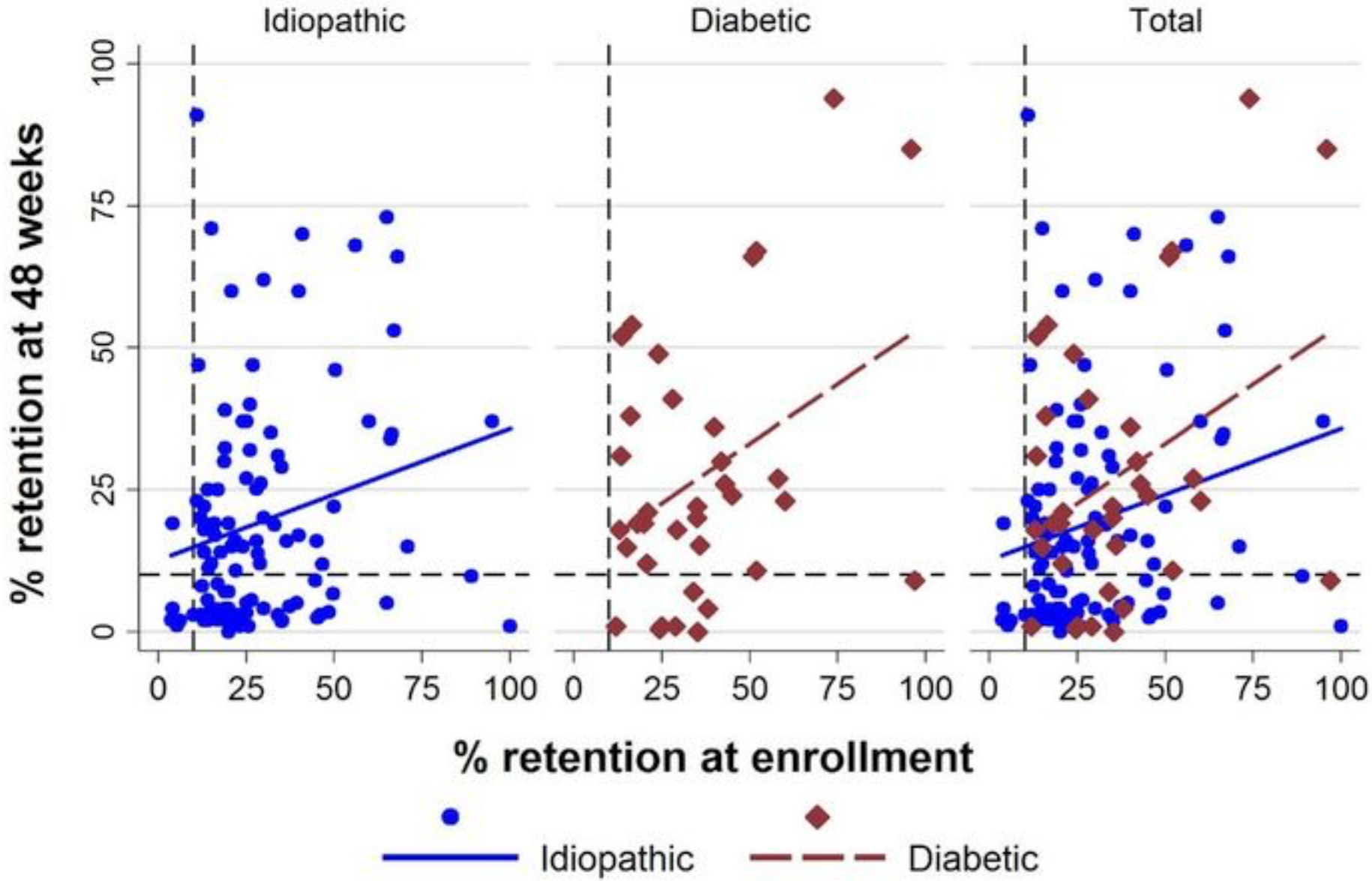
- Gastric emptying (GE) tests are used to diagnose gastroparesis but not usually obtained in follow up.
- Changes to GE over time are not known in patients with Gastroparesis.

**Aims:**

1) Determine if changes in GE occur over time in gastroparesis;
2) Determine characteristics of gastroparesis patients whose GE changes over time;
3) Determine symptom changes over 48 weeks in gastroparesis patients who have changes in GE.

# Methods:

- Patients with symptoms of gastroparesis were enrolled into the NIDDK Gastroparesis Registries from December 2010 to November 2016.
- Patients had idiopathic or diabetic gastroparesis had GE at enrollment and a follow-up GE at 48 weeks.
- GE scintigraphy was performed with standard protocol
- Symptom severity was assessed with Patient Assessment of Upper Gastrointestinal Symptoms (PAGI-SYM).
- Patients received Standard of Care during follow-up.
- Worsening GE was defined >12% more retention and improved GE was >12% reduction in retention at 4 hrs.
- Logistic regression models comparing improved retention to no improvement were assessed.


Idiopathic
Diabetic
Total
% retention at 48 weeks
0
25
50
75
100
% retention at enrollment
Idiopathic
Diabetic
Graphs by Etiology: 0=Idiopathic,1=Diabetic

## Results:

- 142 patients with gastroparesis were included; 36 diabetic and 106 idiopathic.
- GCSI decreased from 2.8±1.1 at enrollment to 2.5±1.0 at 48 weeks (p=0.01).
- Gastric retention 4 hr decreased from 30.9±20.0% at enrollment to 21.4±21.1% at 48 weeks (p<0.01).
- Overall, 22 patients (15%) had worsening, 59 (42%) had no change, and 61 (43%) had an improvement in GE.
- 36% of patients normalized their GE at 48 weeks.
- Gastric emptying worsen in patients with diabetic Gp compared with patients with idiopathic Gp (25% vs 12%; p=0.06).

# Results:

- Worsened GE was associated with greater duration of symptoms ($p<0.01$), lower SF-36 physical component ($p=0.08$), and having a gastric electric stimulator ($p=0.05$).
- Improved GE at 48 weeks was associated with increased gastric retention at enrollment ($p<0.001$), higher symptoms of GERD ($p=0.02$), initial use of narcotics ($p<0.01$), but not related to acute onset of symptoms or initial infectious prodrome.
- Improved GE over 48 weeks was associated with improvement in nausea ($p=0.02$), upper abdominal discomfort ($p=0.04$) and increased weight ($p=0.08$).
- Independent enrollment characteristics associated with improved GE were younger age ($p=0.07$), chronic-progressive symptoms ($p<0.001$), use of narcotics ($p<0.001$), increased CRP levels ($p=0.01$), and lower depression scores ($p=0.04$).

# Conclusions:

- Gastric emptying can change over time in gastroparesis patients;
- Most patients improve or remain the same.
- Improved GE was associated with initial increased gastric retention, narcotic use, less depression, more severe GERD, elevated CRP.
- Improved GE was associated with decreased nausea and upper abdominal discomfort, weight gain at follow up.

# LONGITUDINAL SYMPTOM AND QUALITY OF LIFE OUTCOMES IN PATIENTS WITH SUSPECTED GASTROPARESIS IN RELATION TO DELAYS IN GASTRIC EMPTYING AND GENERALIZED GUT TRANSIT: A PROSPECTIVE, MULTICENTER EVALUATION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# Background

- Gastric scintigraphy (GES) and wireless motility capsule (WMC) tests facilitate diagnosis of gastroparesis and may influence clinical decisions.
- The impact of gastric emptying testing on longitudinal symptom outcomes and quality of life is unknown.

**Hypothesis:**

(i) delayed gastric emptying as assessed by GES and WMC is associated with worse gastroparesis symptom and quality of life outcomes

(ii) delayed generalized transit on WMC also relates to worse symptoms and impaired quality of life at 3 and 6 month follow-up.

## Methods:

- 167 patients with ≥2 gastroparesis symptoms (nausea, vomiting, early satiety, bloating, fullness) x >12 wk at 10 centers underwent concurrent GES and WMC.
- Based on results, management plans were devised to change drug and diet therapy and order further diagnostic tests.

- Gastroparesis symptoms were quantified by GCSI and PAGI-SYM scores (0=none, 5=very severe); quality of life was measured by PAGI-QOL surveys (0=poor, 5=excellent) before and at 3 and 6 month follow-up.

- Delay in GE and delay in generalized gut transit was defined:
- GES: >10% 4 hour retention
- WMC: >5 hour retention
- delayed generalized transit in ≥2 gut regions (stomach, small bowel, colon) by WMC.

## Results:

- GCSI scores decreased from 2.66±0.99 at baseline to 2.26±1.20 and 2.03±1.11 at 3 and 6 month follow-up (P<0.001).
- PAGI-QOL increased from 2.68±1.25 to 3.00±1.26 and 3.21±1.23 at 3 and 6 months (P<0.001).
- Gastric emptying was delayed by GES in 39/159 (25%) and WMC in 53/153 (35%).
- Delayed gastric emptying on GES and WMC was associated with worse symptom outcomes at 3 and 6 months (Table 1).
- Of individual symptoms, only postprandial fullness GCSI sub scores related to emptying delays.
- Fullness scores severity were better if patients had normal emptying by GES and WMC
- Some QOL measures were worse with delayed gastric emptying on GES and WMC at 6 months (Table 2).
- Delayed generalized WMC transit was associated with worse symptom outcomes (Table 1).

Table 1: RELATIONSHIP OF SYMPTOM OUTCOMES TO GUT TRANSIT PARAMETERS

| Transit Parameter | GCSI Symptom Measure | 3 Month Follow-Up | | | 6 Month Follow-Up | | |
|---|---|---|---|---|---|---|---|
| | | Delayed Transit | Normal Transit | P Value | Delayed Transit | Normal Transit | P Value |
| Gastric emptying by GES | GCSI score ≤2 (mild or better) on follow-up | 11/33 (33.3%) | 53/110 (48.2%) | 0.14 | 13/32 (40.6%) | 60/106 (56.6%) | 0.11 |
| | GCSI score worsening on follow-up | 14/33 (42.4%) | 26/110 (23.4%) | 0.03 | 10/32 (31.2%) | 24/106 (22.6%) | 0.32 |
| Gastric emptying by WMC | GCSI score ≤2 (mild or better) on follow-up | 17/51 (33.3%) | 47/92 (51.1%) | 0.04 | 20/48 (41.7%) | 53/90 (58.9%) | 0.05 |
| | GCSI score worsening on follow-up | 17/51 (33.3%) | 23/92 (25.0%) | 0.29 | 15/48 (31.2%) | 19/90 (21.1%) | 0.19 |
| Generalized transit by WMC | GCSI score ≤2 (mild or better) on follow-up | 11/33 (33.3%) | 51/106 (48.1%) | 0.14 | 12/32 (37.5%) | 58/102 (56.9%) | 0.06 |
| | GCSI score worsening on follow-up | 14/33 (42.4%) | 24/106 (22.6%) | 0.03 | 12/32 (37.5%) | 21/102 (20.6%) | 0.05 |

Table 2: RELATIONSHIP OF QUALITY OF LIFE OUTCOMES TO GASTRIC EMPTYING

| Transit Parameter | PAGI-QOL Measure | 3 Month Follow-Up | | | 6 Month Follow-Up | | |
|---|---|---|---|---|---|---|---|
| | | Delayed Transit | Normal Transit | P Value | Delayed Transit | Normal Transit | P Value |
| Gastric emptying by GES | PAGI-QOL score <2 (impaired to poor) on follow-up | 12/33 (36.4%) | 25/110 (22.7%) | 0.12 | 10/32 (31.2%) | 14/106 (13.2%) | 0.02 |
| | PAGI-QOL score worsening on follow-up | 11/33 (33.3%) | 32/110 (29.1%) | 0.64 | 14/32 (43.8%) | 23/106 (21.7%) | 0.01 |
| Gastric emptying by WMC | PAGI-QOL score <2 (impaired to poor) on follow-up | 17/51 (33.3%) | 20/92 (21.7%) | 0.13 | 11/48 (22.9%) | 13/90 (14.4%) | 0.21 |
| | PAGI-QOL score worsening on follow-up | 18/51 (35.3%) | 24/92 (26.1%) | 0.25 | 17/48 (35.4%) | 17/90 (18.9%) | 0.03 |

# Conclusions:

- Patients with gastroparesis symptoms reported improved symptoms and quality of life at 3 and 6 month follow-up after transit testing in a prospective study.
- Documentation of delayed gastric emptying either by scintigraphy or WMC was associated with worse symptom (especially fullness) and quality of life outcomes.
- Generalized transit delay was also associated with worse symptom outcomes, illustrating a potential advantage of measuring transit in all gut regions with suspected gastroparesis.
- Further study of management decisions after evaluating gut transit could refine treatments and influence clinical outcomes in gastroparesis.

# OUTLET DYSFUNCTION IS PREVALENT IN SEVERE FUNCTIONAL BLOATING: PRELIMINARY REPORT FROM A MULTICENTER ITALIAN STUDY

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# Introduction

- Bloating and abdominal distension are common and bothersome complains in patients with functional gastrointestinal disorders (FGID).
- Recent studies have provided evidence of impaired handling of bowel gaseous content as relevant etiology in functional bloating.
- Aim of the study was to evaluate relationship between defecation pattern, symptoms and abdominal girth measure in FGID patients consulting GI office for bloating as main complain.

# Methods:

- prospective, multicenter study on 76 patients of Italian heritage consulting for severe bloating (VAS score >24 on a 100-mm scale) as primary complain with/without subjective report of visible abdominal distension.
- Comorbid FGID were grouped according to Rome III criteria.
- All patients were prescribed two weeks of NICE dietary advice for IBS augmented by lactose abstinence.
- A belt around the abdomen at standardized sites was used to assess the abdominal girth.
- During run-in, patients completed a daily diary log including abdominal bloating score (100-mm VAS), Bristol stool scale and stool frequency.
- At randomization visit, all patients filled in a questionnaire on subjective adequate relief of bloating on a Likert scale and a further bloating 100-mm VAS. A belt around the abdomen at standardized sites was used to assess the abdominal girth two hours after a meal.
- All patient reporting no relief of bloating at the end of run in underwent a standardized balloon expulsion test (BET, 16F Foley Catheter) scored as either successful or failed if the balloon could not be evacuated within 2 minutes.

# Results

- 76 patients completed the run-in period.
- FGID comorbidities were as follows: 6 IBS-D, 6 IBS-M, 30 IBS-C, 9 IBS-U, 6 functional constipation, 3 functional dyspepsia, and 16 functional bloating.
- A significant negative correlation was found between subjective relief of bloating and both bloating VAS score and abdominal girth changes (Pearson's r=.53 and .52, respectively, $p<0.001$).
- 53/76 (69%) patients reported worst or no bloating improvement after diet advice.
- Among the 53 non-responders, the majority (68%) failed the balloon expulsion test.
- Multiple regression analysis showed that Balloon expulsion test (successful or failed) as dependent variable, was significantly related to bloating severity ($p<0.001$) while no relationship was found for abdominal girth changes, and FGID diagnosis.

## Conclusions:

- In this prospective, multicenter trial a modified NICE diet advise was associated with subjective benefit in approximately 30% of patient consulting for severe bloating.
- In the non-responder population, outlet dysfunction was prevalent and correlated with bloating perception supporting a potential role of biofeedback to improve defecation effort.