

Gastric peroral endoscopic pyloromyotomy for decompensated gastroparesis: comprehensive motility analysis in relation to treatment outcomes



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ABSTRACT

Background and study aims There are no reliable data to predict which patients with gastroparesis (GP) would benefit the most from gastric peroral endoscopic pyloromyotomy (G-POEM). The aim of the present study was to assess whether antro-duodenal motility patterns and pyloric distensibility can predict the outcome of G-POEM in patients with decompensated GP.

Patients and methods In an open-label study, patients with GP and refractory symptoms were eligible for treatment with G-POEM if treatment attempts according to a standardized stepwise protocol had failed. Baseline assessment included Gastroparesis Cardinal Symptom Index (GCSI), C13-octanoic gastric emptying breath test and high-resolution antro-duodenal manometry. Pyloric distensibility using EndoFlip measurements was assessed at baseline and 3 months after the procedure. Explorative analyses were performed on potential predictors of response using logistic regression analyses.

Results Twenty-four patients with decompensated GP underwent G-POEM. At baseline, 78.3% and 61.9% of patients showed antral hypomotility and neuropathic motor patterns, respectively. The technical success rate was 100% (24/24). Mean GCSI improved significantly at 3, 6, and 12 months after G-POEM ($P=0.01$). Median distensibility index (DI) improved significantly as compared with baseline (7.5 [6.9;11.7] vs. 5.3[3.1;8.1], $P=0.004$). A significant correlation was found between clinical response at 6 months and pyloric DI improvement ($P=0.003$). No potential predictors of clinical response after G-POEM could be identified in an explorative analysis.

Conclusions G-POEM improved pyloric distensibility patterns in patients with decompensated GP. Clinical response at 6 months after G-POEM was associated with pyloric distensibility improvement. However, no potential predictors of response could be identified from either antro-duodenal motility patterns or pyloric distensibility.

Introduction

Management of patients with gastroparesis (GP) refractory to medical treatment is challenging as these patients often require nutritional support [1]. In our tertiary referral center, patients with GP are treated with a stepwise approach, starting with dietary advice and prokinetics, followed by nasoduodenal tube feeding for 3 months (gastric rest) in case of decompensated GP. When oral reintroduction fails, placement of a percutaneous endoscopic gastrostomy with jejunal extension (PEG-J) is offered for long-term nutritional support [2].

Gastric peroral endoscopic pyloromyotomy (G-POEM) was introduced in 2013 as an alternative therapeutic modality for GP patients with refractory symptoms [3]. In recent years, several groups have reported promising data on G-POEM in terms of safety and efficacy outcomes in the short- and midterm [4–13]. In a recent pooled analysis of 10 studies and 292 patients with a mean follow-up of 7.8 months, a significant symptomatic improvement was achieved after 84% of G-POEM procedures [14]. In our tertiary referral center, G-POEM is available for patients with decompensated GP (grade 3) who have followed the different treatment steps.

In the absence of well-designed randomized controlled trials (RCTs) to determine the efficacy of G-POEM, it is important to obtain reliable data on certain patient characteristics to help in predicting which of them would benefit most from G-POEM. In a recent systemic review, no relationship was found between G-POEM efficacy and patient characteristics, GP etiology, preprocedural evaluation or previous pylorus-directed treatment [14]. Therefore, objective parameters such as antro-duodenal manometry and pyloric distensibility have been proposed as tools for outcome prediction [14,15]. For this purpose, further controlled clinical trials have been suggested with patient selection using high-resolution antro-duodenal manometry or EndoFlip assessment of pyloric function in combination with long-term follow-up [1].

Antro-duodenal manometry (ADM) provides information about coordination of gastric and small-intestine motor function in both fasting and postprandial periods [16]. However, there are limited data on the role of antro-pyloro-duodenal dysmotility in patients with GP. In the 1990s, it was suggested that antral hypomotility is the major cause of delayed gastric emptying and abnormalities in pyloric and small-intestine motility were reported in patients with GP [17]. Recently, small bowel motor abnormalities were reported in the majority of patients with symptoms suggestive of GP [18].

Physiological evaluation of pyloric function can be assessed using an endoscopic functional luminal imaging probe (EndoFlip) by measuring pyloric distensibility [19–21]. Recently, preliminary data have been reported on the association between EndoFlip measurements and short/mid-term clinical success after G-POEM, suggesting that EndoFlip measurements have the potential to be used as a tool for predicting G-POEM clinical outcome [12,22].

The aim of the present study, therefore, was to assess whether antro-duodenal motility patterns and pyloric distensibility can predict the outcome of G-POEM in patients with de-

compensated GP. We hypothesized that: 1) a disturbed antro-duodenal motility would be associated with a poorer clinical response to G-POEM and; 2) an increased post-intervention pyloric distensibility would be associated with a better clinical response to G-POEM.

Patients and methods

Study design

In a prospective open-label study from September 2017 to September 2019, all patients referred to Maastricht University Medical center with GP and refractory symptoms were screened for treatment with G-POEM.

Inclusion criteria were: >18 years old and decompensated GP (grade 3, defined as refractory symptoms, nutritional status unable to be maintained via oral intake, and frequent hospital admissions), exposure to all conservative treatment entities, including gastric rest, [2] and failure of oral reintroduction.

Exclusion criteria were: <18 years old, medical history of stomach surgery, history of psychiatric disease or use of psychoactive medication, opioid dependency, anticoagulant therapy, neurostimulation, normal gastric emptying test, compensated GP, having not undergone gastric rest, severe antral hypomotility (antral amplitudes <10 mmHg) [23], and unwillingness to undergo G-POEM.

Baseline assessment included Gastroparesis Cardinal Symptom Index (GCSI), C13-octanoic gastric emptying breath test, and antro-duodenal manometry.

Patients in the study underwent G-POEM according to the previously described procedure [3,6]. Immediately before G-POEM, pyloric function was evaluated using the EndoFlip device. Technical success was defined as successful completion of all steps of the G-POEM procedure, including mucosal incision, submucosal tunneling, pyloromyotomy, and closure. Clinical success was defined by at least a 1-point decrease in the mean overall GCSI score [6].

At 3 months after G-POEM, gastroduodenoscopy with EndoFlip measurement, GCSI and a C13-octanoic gastric emptying breath test were performed. GCSI was also measured at 6 and 12 months after G-POEM. The primary time point for clinical success was defined at 6 months.

The study was approved by the local ethics committee (METC 16-4-130) and was conducted in accordance with the Declaration of Helsinki. All patients gave informed consent.

Antro-duodenal manometry

Patients underwent antro-duodenal manometry (ADM) after an overnight fast of at least 8 hours, following standard procedures [24]. Medication affecting gastrointestinal motility was stopped 3 days prior to the study. A solid-state high-resolution catheter consisting of 36 transducers spaced at 1-cm intervals (Unisensor AG, Attikon, Switzerland) was introduced transnasally into the stomach. The catheter was advanced across the pylorus into the duodenum under fluoroscopic control, so that half of sensors were located distal to the pylorus and the other half in the distal stomach.

After 30 minutes of recording in fasting conditions, patients were given a standardized meal consisting of one scrambled egg, two slices of white bread with 5 mg of margarine, and 150 mL of water (283 kcal, 41.2% fat, 17.1% carbohydrates, 41.6% proteins). After the ingestion of the meal, data were recorded for 6 hours, during which patients were not allowed to eat or drink.

During the first 2 hours after meal ingestion, we determined antral and duodenal contraction frequency (contractions/min), contraction amplitude (mmHg) and motility index of antral and duodenal pressure waves (MMS Solar GI system, software version 9.5). Motility index (MI) was calculated using the formula: $MI = \ln([\text{number of waves} \times \text{amplitude}] + 1)$ both at the two pressure sensors located proximally and distally to the manometrically and fluoroscopically defined pylorus, as previously described [2]. Antral hypomotility was considered as a postprandial antral MI < 13.67 [25].

During the 6 hours after meal ingestion, fed period duration (min), number and duration of phase III contractions and migrating motor complexes (MMCs) were assessed. The following neuropathic patterns were scored: presence of bursts, retrograde peristalsis, clustered contractions, and absence of phase III contractions.

EndoFlip measurements

Intraluminal measurements of pyloric physiological characteristics were obtained using an EndoFlip device consisting of a 240-cm catheter with a bag mounted at its distal end (EF-325N, Medtronic), as previously described [19–21]. The EndoFlip device was introduced trans-orally into the stomach, then positioned in the pylorus under endoscopic visualization. Correct positioning was ascertained by identifying the waist-like constriction of the pylorus on the real-time topographic display at a low fill volume. The balloon was filled with 40 mL distension volumes and measurements of cross-sectional area (CSA), bag pressure, and distensibility index (DI) were recorded for a minimum of 30 seconds. Pyloric DI was assessed using the median value over 10-second dynamic measurement of the narrowest CSA and the corresponding intra-bag pressure (narrowest CSA in $\text{mm}^2/\text{intra-bag pressure in mmHg}$) [20]. Pyloric DI improvement at 3 months was defined as at least 20% improvement of baseline DI.

G-POEM procedure

Technical details of the G-POEM procedure are described under **Supplementary Methods**.

After the procedure, patients stayed overnight at the hospital and on postoperative Day 1, they started on a liquid diet with transition to a soft diet if tolerated. Temporary enteral feeding was started when oral intake was inadequate. Patients were discharged when their intake was adequate.

Data and statistical analysis

Data are presented as frequencies for categorical variables, and as median (interquartile range; IQR) in case of skewed distributions, or as mean (SEM) in case of normal distributions for continuous variables. Non-parametric tests were used in case of

the absence of normal distribution. A chi-squared test or Fisher's exact test was used to assess differences between categorical variables, whereas the Mann-Whitney U test and Kruskal-Wallis test were used for continuous variables.

No formal sample size calculation was performed as this was an explorative study to assess parameters for prediction of clinical response. A linear mixed model was used to assess changes in clinical response over time.

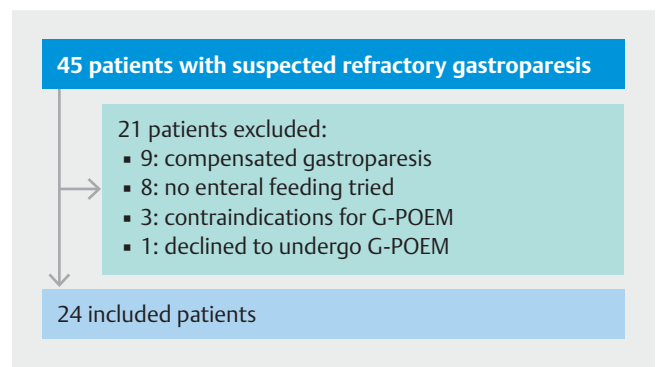
A binary logistic regression model was used to identify possible predictors of response at 6 months after G-POEM. Due to the number of included subjects per group of responders versus non-responders (dependent variable) in this study, only an explorative analysis was possible. Several parameters related to demographic and/or baseline characteristics (i. e. age, sex, GSCI score at baseline), EndoFlip measurements (i. e. DI pre and 3 months post G-POEM, and CSA 3 months post G-POEM) and antro-duodenal manometry parameters (antral MI, number of MMCs and absence of phase III contractions) were tested separately in different models. A two-sided $P < 0.05$ was considered statistically significant. Statistical analyses were performed using IBM SPSS Statistics version 26.0 (IBM Statistics for Macintosh, Chicago, Illinois, United States).

Results

Study population

Forty-five patients were screened for eligibility. Twenty-one were not eligible for G-POEM due to the following reasons: nine patients with compensated disease on current treatment: diet ($n = 4$), prokinetics ($n = 2$), botulinum toxin injection ($n = 2$), enteral feeding ($n = 1$); eight patients had not tried (long-term) enteral feeding; three patients with contraindication for G-POEM: severe antral hypomotility ($n = 1$), dual anticoagulant therapy ($n = 1$), neurostimulator ($n = 1$); one patient declined to undergo G-POEM (► **Fig. 1**).

Twenty-four patients (21 women, mean age 55.3 ± 3 yrs.) with decompensated GP (11 idiopathic, 7 postsurgical, 6 diabetes mellitus [DM]) fulfilled the inclusion criteria and underwent G-POEM under propofol deep sedation. Mean disease duration was 44 ± 7 months and mean GCSI score at baseline was 3.1 ± 0.1 (► **Table 1**).



► **Fig. 1** Patient flow through the study.

► Table 1 Baseline characteristics, procedural data and baseline EndoFlip measurements in all patients and by clinical response groups (at 6 months after G-POEM).

	Total (n=24)	Clinical success (n=14)	Clinical failure (n=10)	P value
Age	55.3 ± 2.9	52.6 ± 4.2	59.0 ± 3.7	0.412
Gender				0.754
Male	3 (12.5%)	2 (14.3%)	1 (10.0%)	
Female	21 (87.5%)	12 (85.7%)	9 (90.0%)	
Weight (kg)	67.0 ± 2.8	71.5 ± 4.0	60.7 ± 3.3	0.079
Disease duration (mos.)	43.7 ± 6.7	38.4 ± 6.9	51.1 ± 12.8	0.703
Etiology				0.317
Idiopathic	11 (45.8%)	5 (35.7%)	6 (60.0%)	
Postsurgical	7 (29.2%)	4 (28.6%)	3 (30.0%)	
Diabetes	6 (25%)	5 (35.7%)	1 (10.0%)	
GCSI baseline	3.1 ± 0.1	3.2 ± 0.2	3.1 ± 0.2	0.463
Gastric emptying T _{1/2} (min)	240 ± 28	239 ± 43	242 ± 34	0.382
G-POEM procedural data				
Procedure duration (min)	53.8 ± 5.4	60.1 ± 7.3	44.6 ± 7.1	0.102
No of clips	4.4 ± 0.9	4.2 ± 0.2	4.7 ± 0.3	0.260
In-hospital stay (days)	2.8 ± 0.3	2.7 ± 0.5	2.8 ± 0.3	0.218
EndoFlip measurements				
40-mL volume distension				
Pylorus CSA (mm ²)	142.1 [94.5;155.2]	149.8 [103.7;165.5]	135.9 [91.3;146.4]	0.143
Bag pressure (mmHg)	26.2 [17.6;33.2]	26.2 [19.8;31.7]	24.2 [16.4;41.0]	0.939
Pylorus DI (mm ² /mmHg)	5.3 [3.1;8.1]	5.3 [4.0;8.9]	4.6 [2.4;8.1]	0.589

Values expressed as mean ± SEM or median [Q1;Q3]

GCSI, Gastroparesis Cardinal Symptom Index; CSA, cross-sectional area; DI, distensibility index; G-POEM, gastric peroral endoscopic pyloromyotomy.

G-POEM procedure

The technical success rate was 100% (24/24). Mean duration of the procedure was 54 ± 5 minutes and mean length of hospital stay was 2.8 ± 0.3 days. Three adverse events were observed: two patients with pneumoperitoneum, both conservatively treated with endoclip during procedure and antibiotics, and one patient with melena several days after the procedure but without signs of active bleeding at gastroscopy.

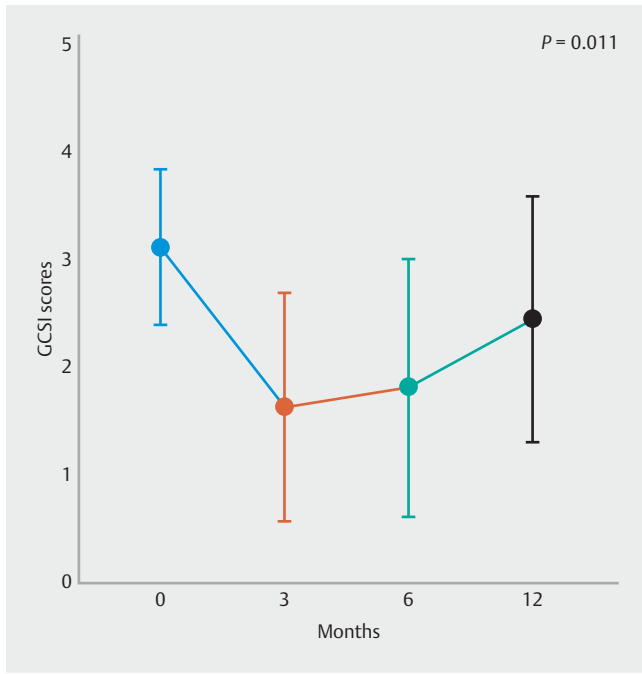
The clinical success rate was 70.8% (17/24) at 3 months, 58.3% (14/24) at 6 months and 33.3% (8/24) at 12 months after G-POEM. Mean GCSI improved significantly at 3 months (GCSI: 1.6 ± 0.2 vs. 3.1 ± 0.1, $P < 0.001$), at 6 months (GCSI: 1.8 ± 0.2 vs. 3.1 ± 0.1, $P < 0.001$) and at 12 months after G-POEM compared to baseline (GCSI: 2.4 ± 0.2 vs. 3.1 ± 0.1, $P = 0.03$) (► Fig. 2). This decrease was statistically significant ($P = 0.01$) when taking into account random intercept and considering all measurements over time using linear mixed models.

Baseline and postprocedural C13-octanoic gastric emptying breath test results were obtained from 18 patients (75%). At 3-month follow-up, mean gastric emptying T_{1/2} did not significantly decrease compared to baseline values (228 ± 23 vs. 249 ± 30 min, $P = 0.550$). Enteral feeding could be stopped in 60% of patients (9/15) shortly after the procedure.

Antro-duodenal motility

Antro-duodenal manometry was performed in 23 patients. In two of 23 patients, it was not possible to pass the pylorus with the ADM catheter. In those cases, only antral activity was measured.

At baseline, 78.3% of patients (18/23) showed antral hypomotility (Motility Index < 13.67) on antro-duodenal manometry: 100% of diabetic patients, 86% of postsurgical patients and 60% of idiopathic GP patients. Thirteen of 21 patients (61.9%) showed at least one neuropathic motor pattern: 28.6% of patients showed bursts, 19% retrograde peristalsis, 19% clus-



► **Fig. 2** Mean (SD) GCSI scores per measurement moment, i. e. Month 0, 3, 6 or 12. This decrease in the slope is statistically significant ($P=0.011$) when taking into account random intercept and considering all measurements over time using linear mixed models.

tered contractions and 19% absence of phase III contractions (► **Table 2**).

Fed period duration (min) and mean number of interdigestive migrating motor complex (MMC) during 6-hour measurements were significantly different between GP subtypes: fed period time idiopathic vs. postsurgical vs. DM: 220 ± 30 min vs. 124 ± 21 min vs. 321 ± 2 min, $P=0.02$, respectively; mean MMC number in idiopathic vs. postsurgical vs. DM: 0.8 ± 0.5 vs. 2.6 ± 0.8 vs. 0 ± 0 , $P=0.03$, respectively. A significant correlation was found between idiopathic GP and presence of neuropathic patterns during ADM ($\chi^2=6.4$, $P=0.01$).

No differences were found when comparing baseline ADM parameters between clinical success and clinical failure groups at either 6 or 12 months.

Pyloric distensibility

At 3 months after G-POEM, median [Q1;Q3] distensibility index (DI, mm^2/mmHg) at 40-mL distension volume improved significantly as compared with baseline (7.5 [6.9;11.7] vs. 5.3 [3.1;8.1], $P=0.004$) (► **Fig. 3**). Both median cross-sectional area (CSA, mm^2) and median bag pressure (mmHg) at 40-mL distension volume improved significantly at 3 months after G-POEM (CSA: 159.2 [121.0;187.6] vs. 142.1 [94.5;155.2], $P=0.020$; pressure: 19.0 [12.1;22.5] vs. 26.2 [17.6;33.2], $P=0.043$) (► **Table 3**).

A comparison of postoperative EndoFlip parameters between clinical response groups at 6 months after G-POEM is shown in **Supplementary Table 2**. A significant correlation was found between clinical response at 6 months and pyloric DI im-

► **Table 2** Antro-duodenal manometry parameters during 6-hour measurement.

Antral amplitudes (mmHg)	27.5 ± 1.6
Antrum motility index	12.1 ± 0.4
Duodenal amplitudes (mmHg)	27.4 ± 1.9
Duodenal motility index	13.8 ± 0.3
Fed period duration (min)	249 ± 22
Number of phase III contractions	2.3 ± 0.5
Duration phase III contractions (min)	7.7 ± 0.7
Number of MMCs	1.2 ± 0.4
Duration MMCs (min)	78 ± 9
Antral hypomotility	78.3% (18/23)
Neuropathic motor pattern (any)	61.9% (13/21)
Bursts	28.6% (6/21)
Retrograde peristalsis	19.0% (4/21)
Absence of phase III contractions	19.0% (4/21)
Clustered contractions	19.0% (4/21)

Values expressed as mean \pm SEM
MMC, migrating motor complex.

provement ($\chi^2=8.6$, $P=0.003$). This correlation was borderline significant at 12 months ($\chi^2=3.5$, $P=0.06$).

No correlation was found between baseline distensibility parameters and GP subtypes or gastric emptying. No predictors based on ADM were identified for distensibility improvement (data not shown).

Potential predictors of response

The explorative regression analysis identified no statistically significant potential candidate parameters for predictors of response at 6 or 12 months after G-POEM as shown in ► **Table 4** and **Supplementary Table 3**, respectively.

Discussion

This is the first study to examine antro-duodenal motility and pyloric distensibility patterns as potential predictive factors for the outcome of G-POEM in patients with decompensated GP. The main findings are: 1) pyloric distensibility patterns (cross sectional area [CSA], pressure and distensibility index [DI]) improved significantly after G-POEM; 2) the clinical response at 6 months after G-POEM was associated with pyloric distensibility improvement; and 3) no potential predictors of clinical response after G-POEM could be identified among antro-duodenal motility and pyloric distensibility parameters.

The improvement in pyloric distensibility patterns after G-POEM reflects an appropriate response of the pyloric sphincter to pyloromyotomy and these results are in line with the outcomes of two recent studies. Jacques et al. reported a significant increase in both pyloric diameter and DI after G-POEM,

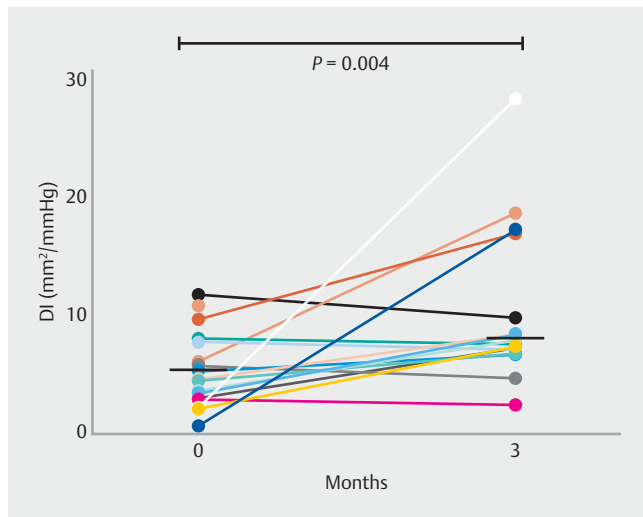


Fig. 3 Individual pyloric distensibility index (DI) values before and 3 months after G-POEM. Each line represents a unique patient at baseline and at 3 months. The black lines represent median DI at baseline and at 3 months.

especially in patients with diabetes [12]. In a multicenter study of 37 patients (including 19 from Jacques' study), Vosoughi et al. showed that both CSA and DI increased significantly after G-POEM [22].

The clinical response at 6 months after G-POEM was associated with pyloric distensibility improvement, indicating that pyloric function tests have the potential to be used as a predictive tool for clinical outcome after G-POEM. However, regression analysis did not reveal potential predictors of clinical response after G-POEM among pyloric function parameters. Due to a relatively low number of included subjects per group of responders versus non-responders in this study, only an explorative analysis was possible. Vosoughi et al reported that post G-POEM CSA was associated with clinical success at 12 months and improvement in gastric emptying after G-POEM [22]. However, the odds ratio (OR) value for pylorus CSA at 40-mL volume was only 1.02, raising the question about the clinical relevance of this outcome. Preliminary data from a prospective trial with 80 patients showed that the increase in pylorus DI following G-POEM was associated with clinical success with an OR of 1.23 [26]. Therefore, it appears that clinical response is primarily

Table 3 Comparison of EndoFlip measurements at baseline and 3 months after G-POEM.

	Baseline	3 months	P value
Pylorus CSA (mm ²)	142.1 [94.5;155.2]	159.2 [121.0;187.6]	0.020
Bag pressure (mmHg)	26.2 [17.6;33.2]	19.0 [12.1;22.5]	0.043
Pylorus DI (mm ² /mmHg)	5.3 [3.1;8.1]	7.5 [6.9;11.7]	0.004

Values measured at 40-mL distension volume, median [Q1;Q3]
CSA, cross-sectional area; DI, distensibility index; G-POEM, gastric peroral endoscopic pyloromyotomy

Table 4 Predictors of clinical response at 6 months.

Parameter	Odds ratio	95% CI	P value
I. Demographical / baseline characteristics			
Age (years)	0.97	0.91; 1.03	0.279
Sex (female reference)	0.67	0.05; 8.54	0.755
GCSI score pre-G-POEM	1.25	0.40; 3.84	0.706
II. EndoFlip parameters			
DI pre-G-POEM	1.08	0.81; 1.44	0.619
DI 3 months post-G-POEM	1.12	0.91; 1.36	0.281
CSA pre-G-POEM	1.01	0.99; 1.04	0.241
CSA 3 months post-G-POEM	1.02	0.99; 1.04	0.174
III. Antro-duodenal manometry pre-G-POEM			
Antral Motility Index	0.94	0.83; 1.06	0.314
Number MMCs	0.85	0.53; 1.36	0.500
No phase III contractions	0.29	0.04; 1.98	0.205

Odds ratios for having response in comparison to nonresponse.
95% CI: 95% confidence interval.
GCSI, Gastroparesis Cardinal Symptom Index; DI, distensibility index; G-POEM, gastric peroral endoscopic pyloromyotomy.

related to the extent to which the pylorus distensibility increases following pyloromyotomy but that this is not necessarily related to the distensibility prior to the intervention. Of note is that this increase in distensibility was not reflected by a significant improvement in gastric emptying as measured with an C13-octanoid breath test. This could be related to the shortcomings of the gastric emptying measurement technique and/or the fact that pyloric distensibility is not the sole factor contributing to gastric emptying [27].

In our department, we use the C13-octanoid breath test as a standard gastric emptying test for patient care. This test has shown a strong correlation with simultaneously obtained scintigraphy, is easy to perform, relatively cheap, and has no risk of radiation exposure [1]. In the present study, G-POEM did not correct significantly gastric emptying parameters. Although the C13-octanoid breath test has been validated as a gastric emptying test, several confounders that may influence the test results are changes in endogenous CO₂ excretion caused by physical activity, malabsorption, pancreatic exocrine insufficiency, and pronounced lung or liver disease or cardiac failure [28]. Furthermore, in literature, a weak correlation has been reported between symptoms and gastric emptying [1]. This is probably due to the fact that mere gastric emptying measurements are an imperfect way to capture gastric motor responses to their full extent.

A novelty in the present study was the assessment of antro-duodenal motility patterns in patients with GP before G-POEM. We found a high prevalence of antral hypomotility and duodenal dysmotility among our patients. Furthermore, differences between the different etiologies were identified regarding fed period duration and number of MMCs. Likewise, a significant correlation was found between idiopathic GP and presence of dysmotility patterns during ADM. More detailed analyses of antro-duodenal motility patterns in the different GP subgroups is needed in relation to their impact on the pathophysiology of GP and on clinical success after G-POEM.

Limited data are available on the role of antro-pyloro-duodenal dysmotility in GP. In the 1980s, abnormal intestinal manometric patterns were described in 12 of 14 patients with diabetes with a clinical diagnosis of GP [29]. In 1986, Mearin et al. defined pylorospasms as unusually prolonged, but intermittent contractions characterized by marked increases in baseline tone at the pylorus and these findings were reported in 14 of 24 diabetics with symptoms of GP [30]. Another study from the last century suggested that antral hypomotility is the major cause of delayed gastric emptying and abnormalities of pyloric and small intestinal motility were reported in patients with GP [17]. Recently, a high prevalence of enteric dysmotility during small bowel manometry was reported in 80% of patients with symptoms suggestive of GP and in 96% of patients with delayed gastric emptying. GP severity was associated with small bowel motor abnormalities but not with delayed gastric emptying [18].

The explorative regression analysis in the present study could not identify potential antro-duodenal parameters as predictors of response after G-POEM. This may be explained by the etiological heterogeneity of included patients. Furthermore,

exclusion of patients with severe motility patterns (i.e. severe antral hypomotility) could have influenced the outcomes. It appears, though, on the basis of our current findings, that motility patterns do not influence clinical response after G-POEM, in contrast to post-G-POEM pyloric distensibility. In other words, even a disturbed motility of the proximal duodenum does not negatively impact clinical response as long as the pylorus is able to pass gastric content. However, a larger cohort of patients is needed to corroborate findings on possible predictors of response after G-POEM among ADM parameters.

Given that the patients in our cohort suffered from severe decompensated GP and underwent a rigorous therapeutic regimen prior to inclusion, they potentially represent a different population compared to previous studies. Nevertheless, the technical and 6-month clinical success ratios in this particular group were 100% and 58%, respectively, indicating that G-POEM is technically feasible and effective with respect to symptomatic improvement in this patient category. However, we observed a low clinical success rate (33%) at 12 months. The reasons for this outcome remain unclear but we speculate that this is related to differences in patient characteristics. Preintervention symptom severity was not associated with clinical response either. In this regard, the position of G-POEM in the treatment spectrum of GP needs to be established. In our tertiary referral center, patients with GP are treated according to a stepwise approach, starting with dietary advice and prokinetics, followed by nasoduodenal tube feeding for 3 months (gastric rest). When oral reintroduction fails, PEG-J placement is offered for long-term nutritional support. In that setting, G-POEM is offered to patients with decompensated GP who have followed the different treatment steps. A trial period with gastric rest before considering G-POEM can lead to a significant symptom response in up to 47% of patients [2]. This phenomenon could theoretically also contribute to the lower clinical response to G-POEM compared to previous studies. Furthermore, gastric rest leads to an improvement in nutritional status and it identifies patients that cannot tolerate enteral feeding in the small bowel. Nevertheless, further research is needed to assess the position of G-POEM in the treatment spectrum for GP. A randomized trial could be considered comparing the effect of G-POEM and enteral nutrition by PEG-J on clinical symptoms, with particular emphasis on long-term follow-up.

The strength of the present study is the comprehensive motility analysis of patients with decompensated GP undergoing G-POEM, being the first study looking at antro-duodenal motility patterns in relation to treatment outcomes. Second, we studied a group of patients with decompensated GP who were homogeneous in terms of disease severity and had completed the same rigorous stepwise treatment approach, including enteral feeding.

A limitation of our study is the small sample size, taking into account that different etiological GP subgroups were included. This could have influenced the lack of outcome regarding the identification of predictors of response after G-POEM. Second, baseline and 3-month EndoFlip measurements were assessed using different methods of sedation modalities (propofol and

midazolam/fentanyl, respectively), which could be a possible confounder in pyloric distensibility test outcomes [27].

Conclusions

In summary, a comprehensive motility analysis is presented in patients with decompensated GP undergoing G-POEM in relation to treatment outcomes. A significant improvement in pyloric distensibility patterns was achieved after G-POEM. Furthermore, the clinical response at 6 months after G-POEM was associated with pyloric distensibility improvement. No potential predictors of clinical response after G-POEM could be identified among antro-duodenal motility and pyloric distensibility parameters. RCTs with larger sample sizes and follow-up duration are awaited to further assess predictors of clinical outcome with the G-POEM technique.

Competing interests

The authors declare that they have no conflict of interest.

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