Gastric peroral endoscopic pyloromyotomy versus gastric electrical stimulation in the treatment of refractory gastroparesis: a propensity score-matched analysis of long term outcomes

Authors

Shanshan Shen[1,2,*], Hui Luo[1,3,*], Cicily Vachaparambil[1], Parit Mekaroonkamol[1,4], Mohamed M. Abdelfatah[1], Guifang Xu[1,2], Huimin Chen[1,5], Liang Xia[1,6], Hong Shi[1,7], Steve Keilin[1], Field Willingham[1], Jennifer Christie[1], Edward Lin[1], Qiang Cai[1]

Institutions

1 Division of Digestive Diseases, Emory University School of Medicine, Atlanta, Georgia, United States
2 Department of Gastroenterology, Nanjing Drum Tower Hospital, The Affiliated Hospital of Nanjing University Medical School, Nanjing, Jiangsu, China
3 State Key Laboratory of Cancer Biology, National Clinical Research Center for Digestive Diseases and Xijing Hospital of Digestive Diseases, Fourth Military Medical University, Xi'an, Shaanxi, China
4 Division of Gastroenterology, Faculty of Medicine, Chulalongkorn University and King Chulalongkorn Memorial Hospital, Thai Red Cross, Bangkok, Thailand
5 Division of Gastroenterology and Hepatology, Renji Hospital, School of Medicine, Shanghai Jiao Tong University, Shanghai, China
6 Department of Gastroenterology, The First Affiliated Hospital of Nanchang University, Nanchang, Jiangxi, China
7 Department of Gastrointestinal Endoscopy, Fujian Cancer Hospital, Fujian Medical University Cancer Hospital, Fuzhou, Fujian, China

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Corresponding author
Qiang Cai, MD, PhD, Division of Digestive Diseases, Emory University School of Medicine, 1365 Clifton Road, B1262, Atlanta, GA 30322, United States
Fax: +1-404-778-2578
qcai@emory.edu

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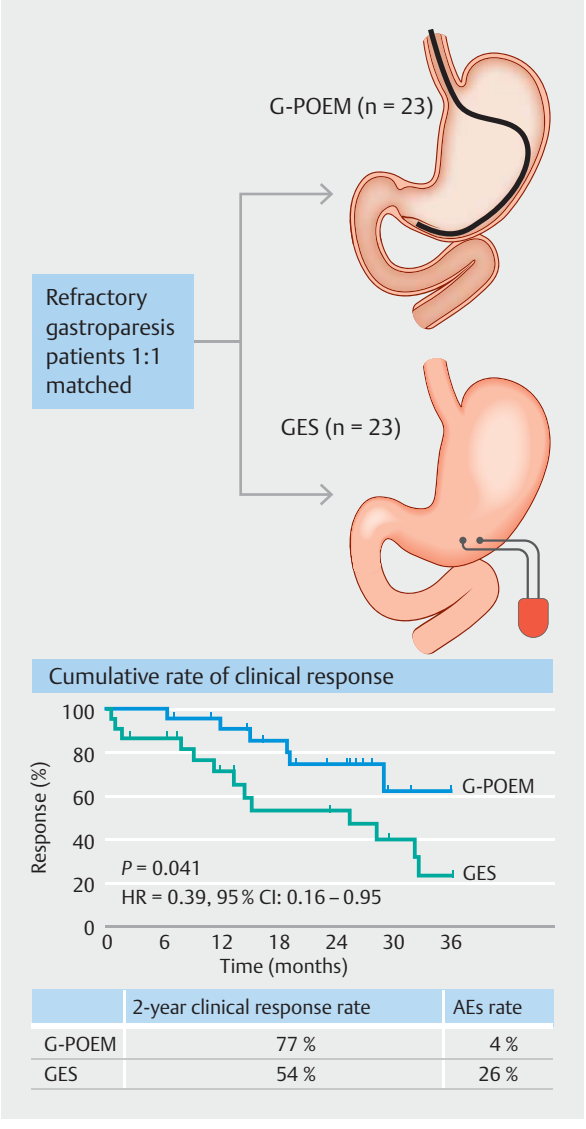
GRAPHICAL ABSTRACT



	2-year clinical response rate	AEs rate
G-POEM	77 %	4 %
GES	54 %	26 %

* These authors contributed equally to this work.

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ABSTRACT

Background Gastric peroral endoscopic pyloromyotomy (G-POEM) and gastric electrical stimulation (GES) have been reported as treatment options for refractory gastroparesis. In this study, we compared the long term clinical outcomes of G-POEM versus GES in the treatment of such patients.

Methods We retrospectively evaluated 111 consecutive patients with refractory gastroparesis between January 2009 and August 2018. To overcome selection bias, we used propensity score matching (1:1) between G-POEM and GES treatment. The primary outcome was the duration of clinical response.

Results After propensity score matching, 23 patients were included in each group. After a median follow-up of 27.7 months, G-POEM had a significantly better and longer clinical response than GES (hazard ratio [HR] for clinical recurrence 0.39, 95 % confidence interval [CI] 0.16 – 0.95; P = 0.04). The median duration of response was 25.4 months (95 %CI 8.7 – 42.0) in the GES group and was not reached in the G-POEM group. The Kaplan – Meier estimate of 24-month clinical response rate was 76.6 % with G-POEM vs. 53.7 % with GES. GES appeared to have little effect on idiopathic gastroparesis (HR for recurrence with G-POEM vs. GES 0.35, 95 %CI 0.13 – 0.95; P = 0.05). The incidence of adverse events was higher in the GES group (26.1 % vs. 4.3 %; P = 0.10).

Conclusion Among patients with refractory gastroparesis, clinical response was better and lasted longer with G-POEM than with GES. The positive outcomes with G-POEM are likely to derive from the superior clinical response in patients with idiopathic gastroparesis. Further studies are needed to confirm these findings.

Introduction

Gastroparesis is a chronic morbid motility disorder of the stomach, and is a syndrome characterized by delayed gastric emptying in the absence of any mechanical obstruction. Pharmacotherapy of patients with gastroparesis is often not very effective, with less than a third of patients showing clinical improvement after a year or longer on medical treatment [1]. Therefore, the treatment of gastroparesis remains quite challenging.

Gastric electrical stimulation (GES) has been introduced as a treatment option for medically refractory gastroparesis. Some open-label studies reported 1-year clinical response rates varying from 45 % to 74 % [2 – 5], with only a quarter of the initial patients maintaining a response at 3 years [6]. This invasive approach can be complicated by implantation site pain, infection, dislodgment, and skin erosion, and is associated with a removal rate of 6.3 % – 12.8 % [3, 6, 7].

As a pyloric-directed therapy and less invasive technique, gastric peroral endoscopic pyloromyotomy (G-POEM), also known as peroral pyloromyotomy, is becoming a promising treatment option for refractory gastroparesis. Several trials have shown that G-POEM led to a 1-year clinical response rate of 57 % – 85 % [8 – 10]. The effectiveness of G-POEM has also been observed for patients in whom GES failed [11]. Given the promising outcomes and less invasive nature of G-POEM, we hypothesized that G-POEM is superior to GES in the treatment of patients with refractory gastroparesis.

We conducted this study to compare the long term effectiveness of G-POEM with that of GES in patients with refractory gastroparesis.

Methods

Study design and patients

This was a single-center, retrospective, cohort study comparing the long term outcomes of G-POEM and GES in patients with refractory gastroparesis. The study was approved by the institutional review board. All patients provided written informed consent before the procedure.

Patients with gastroparesis in our center were managed according to clinical guidelines [12]. Refractory gastroparesis was defined as gastroparesis with evidence of delayed gastric emptying on scintigraphy, and not responding to a combination of dietary modifications, correction of electrolyte abnormalities, prokinetic, or antiemetic medication therapy for at least 6 months. Consecutive patients with refractory gastroparesis who underwent G-POEM or GES and had at least 6 months' follow-up in Emory Clinics from January 2009 to August 2018 were included.

Exclusion criteria consisted of patients younger than 18 years; patients with peptic ulcer disease or gastric outlet obstruction at endoscopy; patients with an average Gastroparesis Cardinal Symptom Index (GCSI) score of < 2; patients with narcotic-induced gastroparesis. Patients who had received previous treatments were not excluded from the study.

As G-POEM has only emerged recently, GES was the only available "less invasive" option for patients with refractory gastroparesis before 2013. The referral pattern at our institution has shifted since G-POEM became available. The choice of G-POEM or GES was individualized based on discussion between patient and referring physician. Some of the data have been published previously [8], in a paper unrelated to the aim of the current manuscript.

Data collection

The following data were extracted retrospectively from the medical records: demographic data, medical and endoscopic or surgical treatments, supplemental nutrition support, and gastric emptying scintigraphy before and after G-POEM or GES.

Gastric emptying studies were obtained 2 – 4 weeks before and 4 – 8 weeks after the intervention. The studies were performed according to guidelines established by the American Neurogastroenterology and Motility Society, and the Society of Nuclear Medicine [13]. The severity of gastric emptying was graded from 1 to 4 according to gastric retention at 2 or 4 hours as follows: grade 1 (mild), 61 % – 70 % retention at 2 hours or 11 % – 20 % retention at 4 hours; grade 2 (moderate), 71 % – 80 % retention at 2 hours or 21 % – 35 % retention at 4 hours; grade 3 (severe) 81 % – 90 % retention at 2 hours or 36 % – 50 % retention at 4 hours; grade 4 (very severe), 91 % – 100 % retention at 2 hours or > 50 % retention at 4 hours.

Baseline GCSI was collected on the day of the procedure. Follow-up data were obtained at 1, 6, 12, 18, 24, and 36 months after G-POEM or GES directly from the patients via a telephone call or clinic visit, or from the medical records. The data were collected at all time points to the furthest extent of follow-up period for each patient. If face-to-face time was possible during a clinic visit, an in-person interview would take place to obtain the data; otherwise, the data were extracted from the medical record of each designated clinic visit. The remaining required data that were not available from medical records were obtained via a telephone interview. A 2-week window period was allowed outside each time point to facilitate scheduling conflict and patient convenience.

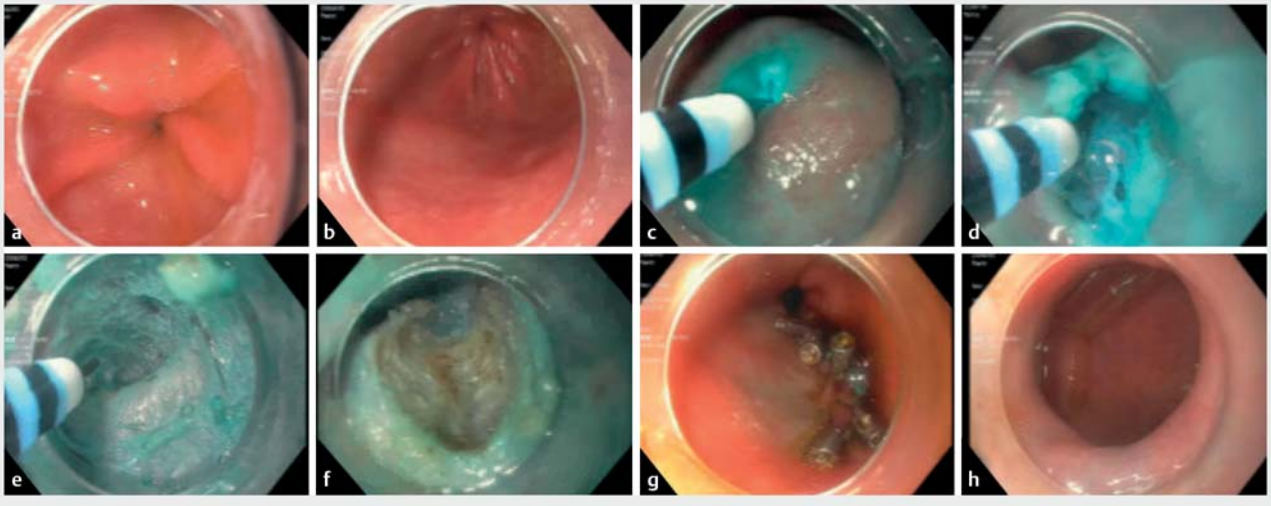
The GCSI score was calculated by averaging the mean score of 3 subscales: postprandial nausea/vomiting, fullness/early satiety, and bloating [8]. A significant improvement in gastroparesis symptoms was defined as at least 1-point decrease from the average baseline GCSI with more than a 25 % decrease in at least two subscales of cardinal symptoms, as reported in our previous study [8, 14].

Procedures

G-POEM

G-POEM was performed as described in our previous reports [14, 15]. Briefly, the procedure was performed using a gastroscope (GIF-H190; Olympus, Tokyo, Japan) with a transparent distal cap attachment (MH-588; Olympus) and Hybrid knife I-type (ERBE Elektromedizin GmbH, Tübingen, Germany) or a HookKnife (Olympus), and using only carbon dioxide for insufflation (UCR, Olympus). Submucosal tunneling was performed along the posterior wall of the greater curvature of the antrum (3 – 6 o'clock position) using spray coagulation mode 50 W at effect 2 (ERBE). A selective circular pyloromyotomy was performed after identification of the pyloric ring (▶ **Fig. 1**). All G-POEM procedures were performed by an interventional endoscopist (Q.C.) who was experienced in submucosal endoscopy. An advanced endoscopy fellow was involved in most cases with a varying degree of involvement at the endoscopist's discretion. Prophylactic antibiotics were administered shortly before or during the procedure.

After the procedure, patients were admitted to the hospital for observation. Patients were started on a clear liquid diet on the following morning and were subsequently discharged in the afternoon provided no complications were identified. Twice-daily proton pump inhibitors were prescribed routinely for 8 weeks. Oral antibiotics were given for a total of 5 days.



▶ **Fig. 1** Steps in the gastric peroral endoscopic pyloromyotomy (G-POEM) procedure. **a** Pylorus before G-POEM. **b** Antrum. **c** Antrum mucosal lifting and incision. **d** Submucosal tunneling. **e** Pyloric ring inside submucosal tunnel. **f** Myotomy. **g** Endoclips to close the incision. **h** Pylorus after G-POEM.

GES

Gastric electrical stimulators (Enterra; Medtronic, Minneapolis, Minnesota, USA) were all placed by an experienced surgeon (E. L.) using a standardized laparoscopic procedure, as previously described [16]. On the same day after surgery, the stimulator was turned on. Patients were discharged on the day of surgery if there were no issues. The neurostimulation settings were adjusted in the clinic according to a predefined algorithm and based on symptomatic outcomes.

Postprocedure

After the procedures, all patients were managed according to clinical guidelines [12]. Briefly, a low-fat, low-fiber diet of small portions and frequent feedings were recommended to patients. If a gastroparesis-suitable diet failed to manage symptoms, patients could be treated medically with pharmacological agents. If oral intake was insufficient, enteral or parenteral nutrition could be pursued at the discretion of the physician.

Outcome assessment

The primary end point was the duration of clinical response, which was defined as the time from the procedure to clinical recurrence. Clinical recurrence was defined as gastroparesis symptoms that were refractory to medical management and required at least one gastroparesis-related hospitalization, as well as a persistent GCSI score ≥ 3 for at least 6 months. The secondary end point was the incidence of adverse events. Postoperative moderate-to-severe pain requiring the use of controlled medication for at least 3 days, therapy-related (including bleeding, perforation, capnoperitoneum, and prepyloric ulcer, and infection, etc.) or device-related (including migration, erosion, shock, and dysfunction, etc.) adverse events were recorded.

Statistical analysis

To address the imbalance of potential confounders between the G-POEM and GES groups, we matched treatment groups using propensity score matching by using Stata statistical software (StataCorp LP, College Station, Texas, USA). The propensity score model included sex, age, body mass index, etiology, duration of disease, preoperative gastric emptying, and medical management. These variables were selected because they were considered to be relevant predictors of reduced symptoms of gastroparesis [1, 17]. We formed matched pairs between patients who underwent G-POEM or GES using a one-to-one nearest neighbor caliper of width 0.1 (maximum allowable difference in propensity scores). Only patients matched with propensity scores were included in analyses.

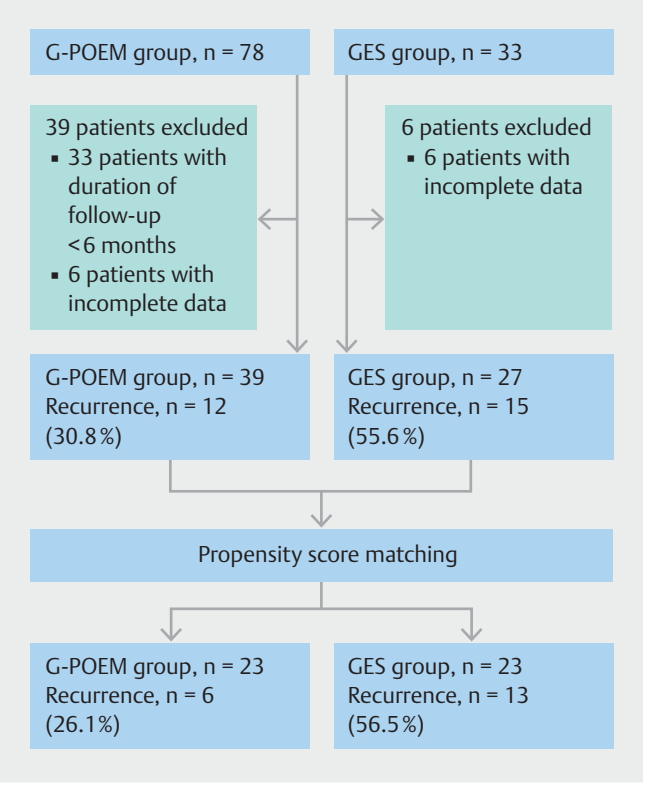
After propensity score matching, categorical data were expressed as numbers and percentages. Continuous data were expressed as a median and interquartile range or mean and standard deviation (SD). McNemar's tests were used to compare categorical variables, and Wilcoxon signed rank tests were used to compare continuous variables. Clinical response was described with the use of Kaplan – Meier estimates, and treatment groups were compared with the use of log-rank tests. The prognostic significance of factors was determined using univariate and multivariate Cox proportional hazards regression models. Variables that were significant ($P<0.05$) on univariate analysis were entered into the multivariate Cox regression model. A P value of <0.05 was considered statistically significant. Statistical analyses were performed using SPSS version 24.0 (IBM Corp., Armonk, New York, USA) and Stata version 15.1 (StataCorp LP).

Results

During the study period, 111 patients underwent G-POEM (n = 78) or GES (n = 33) treatment. The flow of patients through the study is shown in ▶ **Fig. 2**. A total of 33 patients were excluded because the duration of follow-up was less than 6 months, and 12 patients (6 in each group) were excluded due to incomplete data. Finally, 66 patients (39 G-POEM and 27 GES) were eligible for propensity score matching at a 1:1 ratio, resulting in 23 patients included in each group.

Baseline characteristics

Baseline characteristics of patients in both groups are shown in ▶ **Table 1**. There were no differences in the demographic characteristics, pharmacotherapy, or supplemental nutrition support between the two groups. Specifically, patients who underwent G-POEM were equally matched regarding etiology and duration of disease compared with patients who underwent GES ($P>0.99$ and $P=0.87$, respectively). Furthermore, the two groups had similar gastric emptying grade distributions and



▶ **Fig. 2** Flow chart of study participants. GES, gastric electrical stimulation; G-POEM, gastric peroral endoscopic pyloromyotomy.

▶ **Table 1** Perioperative baseline characteristics.

	G-POEM (n = 23)	GES (n = 23)	*P*
Female, n (%)	20 (87.0)	20 (87.0)	> 0.99
Age, median (IQR), years	41 (37 – 53)	43 (35 – 51)	0.13
BMI, median (IQR), kg/m^2	22.6 (18.7 – 34.1)	23.5 (17.1 – 35.7)	0.15
Etiology, n (%)			> 0.99
▪ Diabetes and others	12 (52.2)	10 (43.5)	
▪ Idiopathic	11 (47.8)	13 (56.5)	
Duration of disease, median (IQR), years	2 (1.5 – 5)	2.5 (1.5 – 4.6)	0.87
Current smoking, n (%)	4 (17.4)	5 (21.7)	> 0.99
Current drinking, n (%)	2 (8.7)	1 (4.3)	> 0.99
Surgery history, n (%)			
▪ Pelvic	9 (39.1)	11 (47.8)	0.55
▪ Abdominal	16 (69.6)	18 (78.3)	0.50
▪ Other	1 (4.3)	1 (4.3)	> 0.99
Comorbidity, n (%)			
▪ Type 1 diabetes	8 (34.8)	4 (17.4)	0.18
▪ Neurological disorders	6 (26.1)	4 (17.4)	0.48
▪ Hypertension	7 (30.4)	11 (47.8)	0.23
▪ Chronic renal diseases	5 (21.7)	3 (13.0)	0.70
▪ GERD	9 (39.1)	7 (30.4)	0.54
▪ Constipation	3 (13.0)	4 (17.4)	> 0.99
▪ Other diseases	1 (4.3)	2 (8.7)	> 0.99
Pharmacotherapy, n (%)			
▪ Erythromycin	14 (60.9)	17 (73.9)	0.35
▪ Metoclopramide	22 (95.7)	20 (87.0)	0.30
▪ Domperidone	11 (47.8)	13 (56.5)	0.56
▪ Other antiemetics	13 (56.5)	14 (60.9)	0.77
▪ Chronic analgesics	9 (39.1)	7 (30.4)	0.54
▪ Antidepressant	12 (52.2)	11 (47.8)	0.77
Nutritional support, n (%)	9 (39.1)	7 (30.4)	0.54
▪ PPN and TPN	4 (17.4)	3 (13.0)	> 0.99
▪ J-tube	4 (17.4)	1 (4.3)	0.35
▪ PEG	3 (13.0)	1 (4.3)	0.61
▪ PEG-J tube	2 (8.7)	3 (17.4)	> 0.99
Previous therapy, n (%)	3 (13.0)	9 (39.1)	**0.04**
▪ Pyloroplasty	0	2 (8.7)	0.49
▪ Botulinum injection	3 (13.0)	7 (30.4)	0.15
Gastric emptying, n (%)			0.52
▪ Grade 1	3 (13.0)	3 (13.0)	
▪ Grade 2	4 (17.4)	7 (30.4)	
▪ Grade 3	3 (13.0)	2 (8.7)	
▪ Grade 4	12 (52.2)	10 (43.5)	
GCSI, mean (SD)	3.7 (0.6)	3.8 (0.9)	0.66

G-POEM, gastric peroral endoscopic pyloromyotomy; GES, gastric electrical stimulation; IQR, interquartile range; BMI, body mass index; GERD, gastroesophageal reflux disease; PPN, peripheral parenteral nutrition; TPN, total parenteral nutrition; J-tube, jejunostomy tube; PEG, percutaneous endoscopic gastrostomy; G-J tube, gastrostomy-jejunostomy tube; GCSI, Gastroparesis Cardinal Symptom Index; SD, standard deviation.
P values < 0.05 are in bold as statistically significant.

baseline GCSI scores ($P = 0.52$ and $P = 0.66$, respectively). However, a higher proportion of patients in the GES group had received previous therapy (39.1 % vs. 13.0 %; $P = 0.04$).

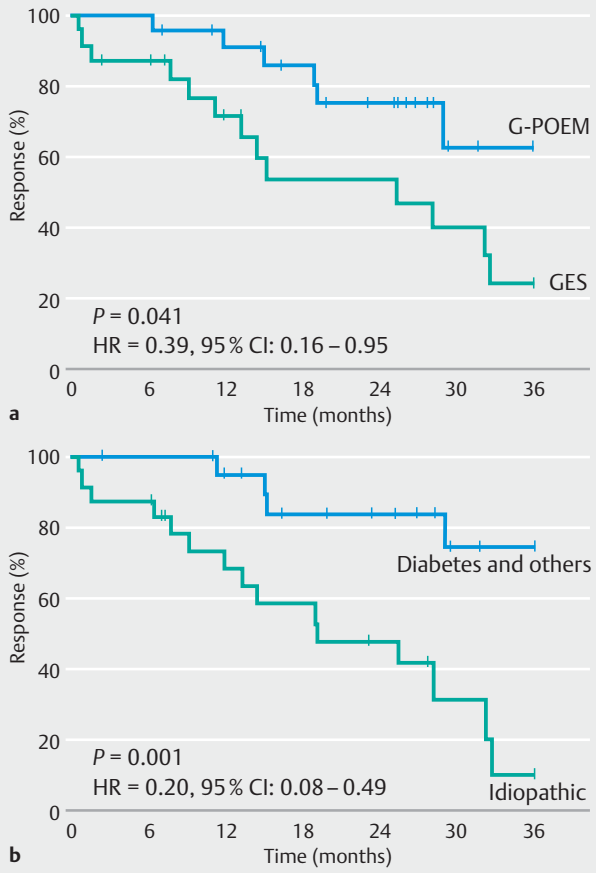
Primary end point and other time-to-event outcomes

G-POEM had a significantly better clinical response than GES (hazard ratio [HR] for recurrence 0.39, 95 % confidence interval [CI] 0.16 – 0.95; $P = 0.04$) (▶ **Fig. 3a**). Patients with idiopathic gastroparesis had a worse clinical response to treatments (HR for recurrence with non-idiopathic vs. idiopathic 0.20, 95 %CI 0.08 – 0.49; $P = 0.001$) (▶ **Fig. 3b**).

The median duration of response was 25.4 months (95 %CI 8.7 – 42.0) in the GES group and was not reached in the G-POEM group. At a median follow-up of 27.7 months (95 %CI 24.1 – 31.3), the Kaplan – Meier estimate of 12-month clinical response rate was 86.5 % (95 %CI 63.8 – 95.4) in the G-POEM group and 71.6 % (95 %CI 47.2 – 86.2) in the GES group. The 24-month clinical response rate was 76.6 % (95 %CI 52.5 – 89.6) in the G-POEM group vs. 53.7 % (95 %CI 29.2 – 73.1) in the GES group.

When stratified by etiology, clinical response was similar in the G-POEM and GES groups in patients with non-idiopathic gastroparesis (HR for recurrence with G-POEM vs. GES 0.68, 95 %CI 0.09 – 5.02; $P = 0.67$) (▶ **Fig. 4a**). However, GES had an inferior clinical response in patients with idiopathic gastroparesis (HR for recurrence with G-POEM vs. GES 0.35, 95 %CI 0.13 – 0.95; $P = 0.05$) (▶ **Fig. 4b**).

When stratified by treatment, patients with non-idiopathic and idiopathic gastroparesis had similar clinical response in the G-POEM group (HR for recurrence with non-idiopathic vs. idiopathic 0.32, 95 %CI 0.06 – 1.63; $P = 0.15$) (▶ **Fig. 4c**). However, patients with idiopathic gastroparesis had an inferior clinical response in the GES group (HR for recurrence with non-idiopathic vs. idiopathic 0.15, 95 %CI 0.05 – 0.45; $P = 0.004$) (▶ **Fig. 4d**).



▶ **Fig. 3** Cumulative rate of response among patients with refractory gastroparesis. **a** Response between gastric peroral endoscopic pyloromyotomy (G-POEM) and gastric electrical stimulation (GES) groups. **b** Response according to etiology. HR, hazard ratio.

Recurrence was observed in 6 patients (26.1%) in the G-POEM group and 13 patients (56.5%) in the GES group. After a median follow-up of 13.2 months from the day of GES treatment, seven patients (30.4%) required alternative therapies due to worsening or no improvement of symptoms (with a mean GCSI of 3.86): four patients underwent G-POEM, two patients underwent partial gastrectomy, and one patient underwent Roux-en-Y gastrojejunostomy. No patient in the G-POEM group underwent alternative therapies during follow-up.

Secondary end points and other postoperative outcomes

There was a trend toward more adverse events in the GES group than in the G-POEM group (26.1% vs. 4.3%; $P=0.10$) (▶ **Table 2**). Moreover, more patients in the GES group than in the G-POEM group received analgesics for at least 3 days for postoperative pain (56.5% vs. 13.0%; $P=0.002$).

The G-POEM group had a shorter procedure time (61 vs. 82 minutes; $P=0.001$) but longer mean postoperative hospital stay (2.0 vs. 0.5 days; $P<0.001$) compared with the GES group.

Improvements in symptoms were evident for each time point in both treatment groups, with at least a 1-point decrease from baseline in GCSI scores (▶ **Fig. 5a**). GCSI scores declined more over time in the G-POEM group than in the GES group, but this difference did not reach statistical significance (▶ **Fig. 5a**). The results for the nausea and vomiting scores were similar to those for the average GCSI (▶ **Fig. 5b**).

Additional analyses

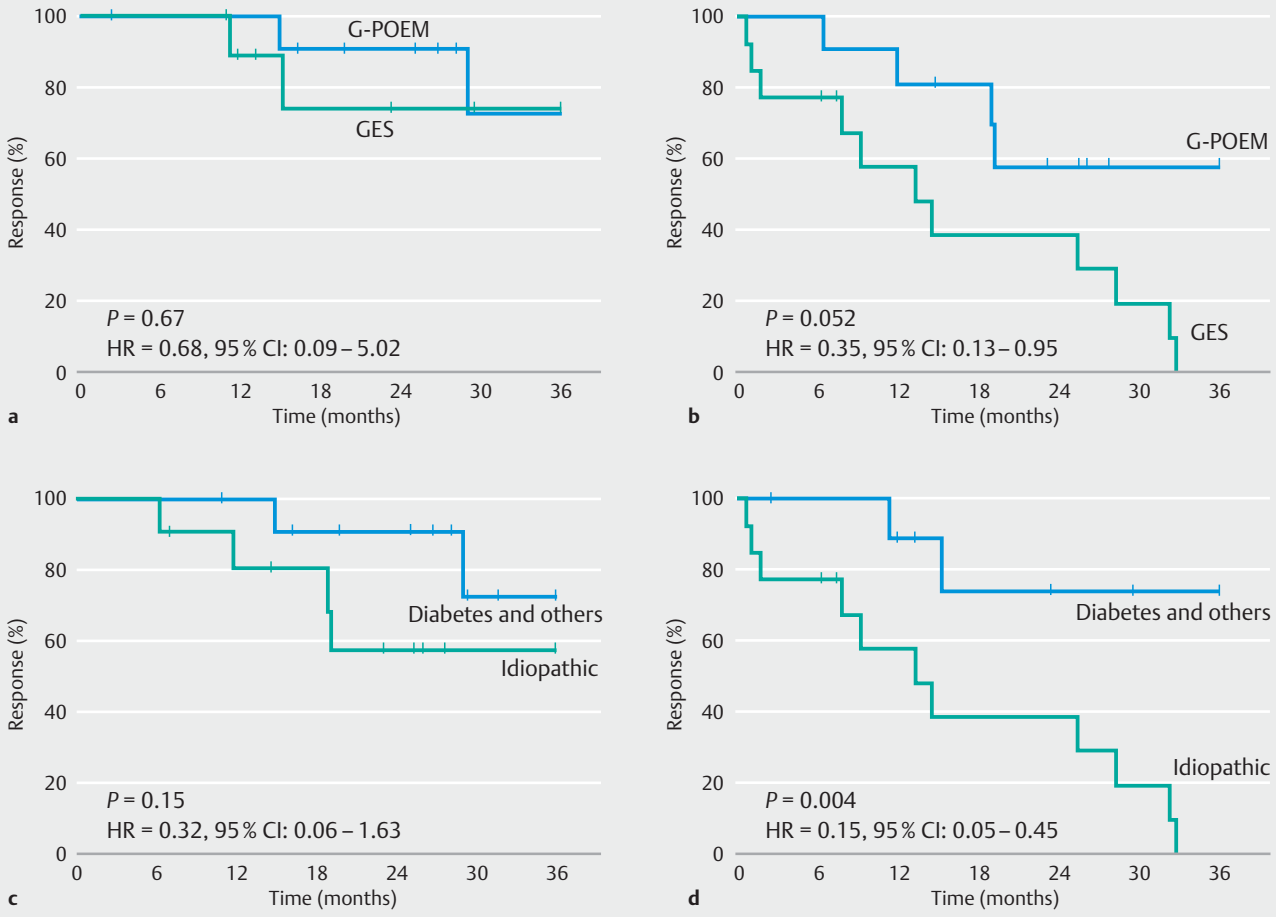
Factors affecting clinical response were assessed by Cox's proportional hazards regression models. G-POEM (HR 0.35, 95%CI 0.13 – 0.96; adjusted $P=0.04$) and non-idiopathic etiology (HR 0.11, 95%CI 0.06 – 0.68; adjusted $P=0.01$) were independently predictive of better long term clinical response (see **Table 1s** in the online-only supplementary material).

Discussion

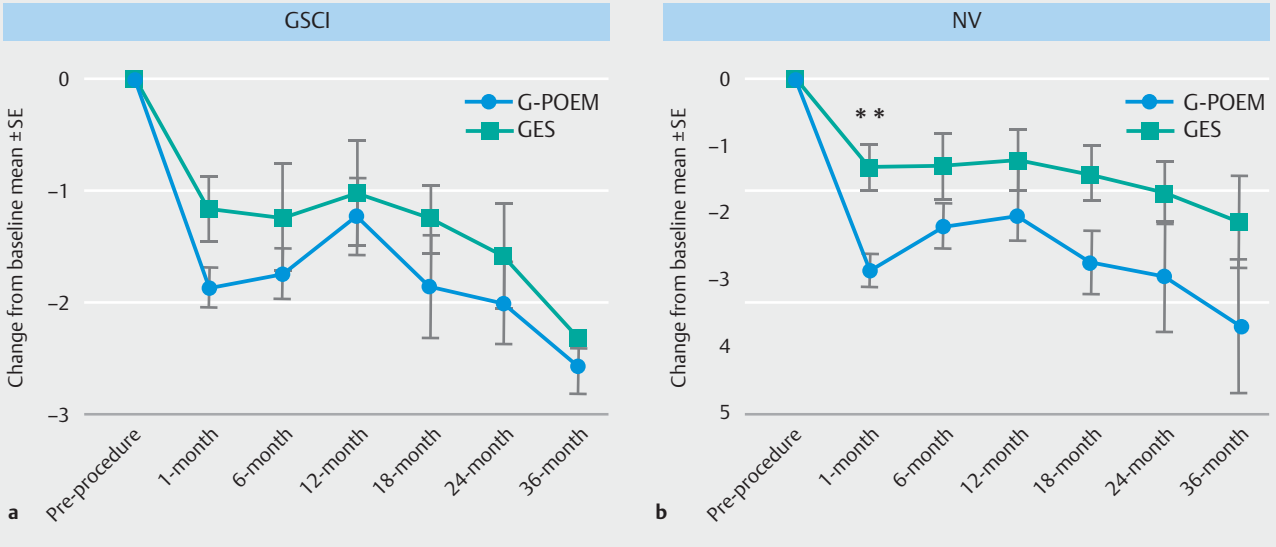
Gastroparesis remains one of the most challenging conditions seen in gastroenterology practice today. G-POEM and GES are available treatment options for medically refractory gastroparesis [12]. However, little is known regarding the long term clinical outcomes of patients who undergo G-POEM compared with those who undergo GES. In contrast to earlier studies on G-POEM, with follow-up limited to 3 – 15 months [8, 10, 14, 18 – 23], the current study evaluated patients with refractory gastroparesis with a median follow-up of 27.7 months, and showed that G-POEM was associated with better long term clinical response. G-POEM had a 60% lower risk of clinical recurrence compared with GES (HR for recurrence 0.39, 95%CI 0.16 – 0.95; $P=0.04$). G-POEM was effective for gastroparesis with various etiologies; however, GES had little effect on idiopathic gastroparesis.

There are several possible explanations for the favorable outcomes with G-POEM. First, delayed gastric emptying caused by pyloric sphincter dysfunction (or pylorospasm) is potentially a significant contributor to the symptoms of gastroparesis [24, 25]. The hypothesis that pylorus-directed therapy is superior to GES is mainly based on impressive results of laparoscopic and endoscopic pyloroplasty [9, 10, 14, 19, 26]. G-POEM is an endoscopic pylorus-directed therapy that is less invasive than laparoscopic pyloroplasty; G-POEM possibly also offers similar long-term relief for patients with refractory gastroparesis compared with surgery [27]. However, similar symptom and gastric emptying improvements were achieved in both treatment groups, although G-POEM maintained better long-term effectiveness in symptom improvement and had a lower recurrence rate (▶ **Fig. 3a**).

The mechanism of GES is not completely known. It may work through the enteric nervous system, the autonomic nervous system (vagally mediated), or via a direct central nervous system effect that could involve the stimulation of the nausea and vomiting center in the brain, leading to symptomatic improvement [28]. Theoretically, destruction of the extrinsic innervation to the stomach, loss of key neurotransmitters at the level of the enteric nervous system, loss of interstitial cells of Cajal, and fibrosis of the muscular layer of the pylorus in pa-



▶ **Fig. 4** Cumulative rate of response in subgroups stratified according to etiology and treatment. **a** Response between gastric peroral endoscopic pyloromyotomy (G-POEM) and gastric electrical stimulation (GES) in patients with non-idiopathic gastroparesis. **b** Response between G-POEM and GES in patients with idiopathic gastroparesis. **c** Response according to etiology in the G-POEM group. **d** Response according to etiology in the GES group.



▶ **Fig. 5** Changes from baseline to month 36 by treatment group. **a** Gastroparesis Cardinal Symptom Index. **b** Nausea and vomiting scores. GES, gastric electrical stimulation; G-POEM, gastric peroral endoscopic pyloromyotomy; SE, standard error. $^{**}P<0.01$.

▶ **Table 2** Postoperative clinical outcomes.

	G-POEM (n = 23)	GES (n = 23)	*P*
Clinical recurrence, n (%)	6 (26.1)	13 (56.5)	**0.04**
Operation time, mean (SD), minutes	60.9 (12.1)	81.7 (16.1)	**0.001**
Postoperative hospitalization, mean (SD), days	2.0 (1.3)	0.5 (0.8)	**< 0.001**
Moderate to severe acute pain, n (%)	3 (13.0)	13 (56.5)	**0.002**
Adverse events, n (%)	1 (4.3)	6 (26.1)	0.10
▪ Procedure related	1 (4.3)	3 (13.0)	0.61
	1 hematemesis	2 pocket infection 1 hematemesis	
▪ Device related	0	3 (13.0 %)	0.23
		2 pacemaker replacement due to device dysfunction; 1 lead replacement	
Gastric emptying, n (%)			0.58
▪ Normal	13/20 (65.0)	3/7 (42.9)	
▪ Grade 1	3/20 (15.0)	2/7 (28.5)	
▪ Grade 2	2/20 (10.0)	0	
▪ Grade 3	1/20 (5.0)	1/7 (14.3)	
▪ Grade 4	1/20 (5.0)	1/7 (14.3)	
Improved gastric emptying, n (%)	16/20 (80.0)	5/7 (71.4)	0.64
Pharmacotherapy, n (%)			
▪ Erythromycin	5 (21.7)	2 (8.7)	0.41
▪ Metoclopramide	10 (43.5)	9 (39.1)	0.76
▪ Domperidone	4 (17.4)	7 (30.4)	0.30
▪ Other antiemetics	18 (78.3)	20 (87.0)	0.44
▪ Chronic analgesics	8 (34.8)	12 (52.2)	0.23
▪ Antidepressant	10 (43.5)	10 (43.5)	1
Nutritional support, n (%)	7 (30.4)	8 (34.8)	0.75
▪ PPN and TPN	3 (13.0)	4 (17.4)	1
▪ J-tube	0	3 (13.0)	0.07
▪ PEG	2 (8.7)	1 (4.3)	1
▪ G-J tube	4 (17.4)	2 (8.7)	0.38
Postoperative therapy, n (%)	0	7 (30.4)	**0.01**
▪ Partial gastrectomy	0	2 (8.7)	
▪ Roux-en-Y gastrojejunostomy	0	1 (4.3)	
▪ G-POEM	N/A	4 (17.4)	N/A
No. of hospitalizations, mean (SD)	1.2 (1.4)	1.3 (1.2)	0.91
No. of emergency room visits, mean (SD)	1.1 (1.5)	1.5 (2.8)	0.56
No. adjustment of stimulator, mean (SD)	N/A	2.8 (2.1)	N/A

G-POEM, gastric peroral endoscopic pyloromyotomy; GES, gastric electrical stimulation; SD, standard deviation; PPN, peripheral parenteral nutrition; TPN, total parenteral nutrition; J-tube, jejunostomy tube; PEG, percutaneous endoscopic gastrostomy; G-J tube, gastrostomy-jejunostomy tube; N/A, not applicable.
P values of < 0.05 are in bold as statistically significant.

tients with gastroparesis may adversely affect the clinical response of GES [29, 30].

Second, etiology of gastroparesis was the strongest predictor of long-term clinical response in the current study (**Table 1s**), with significantly better clinical response in patients with non-idiopathic gastroparesis than in patients with idiopathic gastroparesis (▶ **Fig. 3b**). In particular, a failure to maintain a response ultimately negated the initial benefits of GES treatment over the follow-up period (> 16 months) in patients with idiopathic gastroparesis (▶ **Fig. 4b**), with an overall lack of clinical response compared with G-POEM treatment. Indeed, patients with idiopathic gastroparesis derived little benefit from GES treatment in other reports [3, 6, 31, 32]. Therefore, such patients are not ideal candidates for GES treatment (▶ **Fig. 4d**). Difficulty in maintaining long-term symptomatic improvement in patients with idiopathic gastroparesis led to an inferior overall response in the GES group. Although G-POEM and GES achieved similar symptomatic relief for patients with non-idiopathic gastroparesis (▶ **Fig. 4a**), G-POEM has the advantage of being a noninvasive procedure, which does not require surgical implantation or subsequent visits for pacemaker setting adjustment or battery replacement.

There is currently no consensus on the definition of clinical recurrence of refractory gastroparesis after interventional treatments. Adequate clinical response has been defined largely based on patients' reported gastroparesis-related symptoms in most studies [2, 3, 5, 10, 20, 21]. However, refractory gastroparesis is a chronic condition with recurrent symptoms and requires multiple hospitalizations. To systematically evaluate the efficacy of G-POEM in the current study, we defined clinical recurrence as gastroparesis symptoms that were refractory to medical management and required at least one gastroparesis-related hospitalization, as well as a persistent GCSI score ≥ 3 for at least 6 months.

In the medical literature, the proportion of patients with refractory gastroparesis who had a 1-year clinical response after GES treatment is reported to vary from 45 % to 74 % [2 – 5]. This variation might be a result of different surveillance intensity and definitions of clinical response. For example, one study reported a high 1-year response rate of 85 % in patients with refractory gastroparesis after GES treatment, based on improvement in overall quality of life score [33]. Our study reported 1-year response rate of 71.6 % with a median follow-up of 27.7 months. Long term data (> 12 months) for outcomes after G-POEM treatment are scarce [8 – 10]. Our 1-year response rate in patients receiving G-POEM treatment was 86.5 %. This finding aligns with two recent studies that reported a high 1-year response rate of 81 % – 85 % after G-POEM treatment [9, 10].

The safety profile of G-POEM in the current study was consistent with that of other studies [10, 20], and includes established safety as a salvage operation in patients with failed GES treatment [11, 15]. Device-related adverse events occurred in 13 % of patients who underwent GES treatment, which is similar to a GES system removal rate of 6.7 % – 13 % reported in other studies [3, 6]. As G-POEM is an emerging technique, patients undergoing the procedure require hospitalization in order to identify potential adverse events; the reported mean length of hospital stay ranges from 1 to 6 days [8 – 10, 14, 19, 20, 22, 23]. Our study showed a higher proportion of G-POEM patients requiring hospitalization and longer hospital stays compared with patients undergoing GES. However, a shorter procedure time and lower incidence of new-onset acute abdominal pain and adverse events were noted in the G-POEM group.

Despite the beneficial effects of G-POEM treatment, not all treated patients responded, and some patients' symptoms recurred. In the G-POEM group, patients with idiopathic gastroparesis had a higher recurrence rate than patients with non-idiopathic gastroparesis (4/11, 36.4 % vs. 2/12, 16.7 %; P = 0.37); this difference did not reach statistical significance (▶ **Fig. 4c**). These unfavorable results in patients with idiopathic gastroparesis should be interpreted with caution because of the small subgroup sample size.

There are a few limitations to this study. First, it was a retrospective study, and 50 % (39/78) of patients in the G-POEM group were excluded, mainly due to the duration of follow-up being less than 6 months. It is unclear whether the sample included in the analysis is representative of the overall G-POEM group. As a retrospective study, it was also susceptible to selection bias. Although the use of propensity score matching allowed us to balance the treatment groups, some confounders that were not incorporated into the propensity score, may still influence the results. There was a higher proportion of patients in the GES group who had received previous therapy (39.1 % vs. 13.0 %); among them, more patients had undergone previous botulinum toxin injection (30.4 % vs. 13.0 %). This difference is more likely to be indicative of the paradigm shift on the benefit of intrapyloric botulinum injection, rather than reflecting a more severe baseline condition in the GES group. Data from two randomized controlled trials have not suggested a benefit from botulinum toxin injection [34, 35]. However, despite these discouraging outcomes, there may be subgroups of patient that do benefit from the treatment, and it is important to recognize that both of the published randomized trials had small sample sizes. Finally, this was a single-center study and the sample size limits the power of the study. Future larger studies will be needed to confirm these findings.

In conclusion, these data suggest that patients with refractory gastroparesis who underwent G-POEM treatment had improved long-term clinical responses compared with patients who underwent GES treatment. The positive outcomes with G-POEM are likely to derive from the superior clinical response in patients with idiopathic gastroparesis. GES had a higher rate of adverse events than G-POEM. Further studies are clearly needed in this area.

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Competing interests

The authors declare that they have no conflict of interest.

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CORRECTION

Gastric peroral endoscopic pyloromyotomy versus gastric electrical stimulation in the treatment of refractory gastroparesis: a propensity score-matched analysis of long term outcomes

Shen S, Luo H, Vachaparambil C et al.

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In the above-mentioned article, the name of Mohamed M. Abdelfatah has been corrected.

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