



# A long-term follow-up study of gastric peroral endoscopic myotomy (G-POEM) in a large cohort of patients with postsurgical gastroparesis

Jiacheng Tan<sup>1</sup> · Hailu Wu<sup>1</sup> · Xinyi Yang<sup>1</sup> · Yuling Yang<sup>1</sup> · Ling Zhang<sup>1</sup> · Panpan Wang<sup>1</sup> · Jinjun Shi<sup>2</sup> · Yanjia Lu<sup>2</sup> · Qi Gao<sup>2</sup> · Ruihua Shi<sup>1</sup>

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## Abstract

**Introduction** Postoperative gastroparesis occurs after surgeries which affect the upper digestive tract. Gastric peroral endoscopic myotomy (G-POEM) is a treatment for postoperative gastroparesis. The present study boasts the long-term efficacy and safety of G-POEM in a large cohort of patients.

**Patients and methods** Gastroparesis Cardinal Symptom Index (GCSI) and Gastroesophageal Reflux Disease Questionnaire (GERDQ) were utilized for the assessment of postsurgical gastroparesis symptoms. Gastroscopy was used to observe the anastomotic site. Three-dimensional ultrasound was used to measure the morphological structure of the gastric antrum and pylorus tube. Gastric emptying time was calculated by analyzing the volume change of gastric antrum.

**Results** Significant clinical effectiveness of G-POEM was observed. The GCSI score, including each subscale score, showed significant decrease after G-POEM. Before G-POEM, there was a negative correlation between GCSI score and the inner diameter of pylorus, as well as a positive correlation with the length of pyloric tube. The similar results were found in the scores of nausea/vomiting and postprandial fullness/early satiety subscales. No correlation was observed between GCSI score and the emptying time, nor between the emptying time and the parameters of antrum morphology. After G-POEM, no correlation was found between GCSI (including subscales) score, the emptying time, and the parameters of antrum morphology. Patients who exhibited as clinical non-responders often accompanied with GERD symptoms. After G-POEM, the score of GERDQ decreased significantly. Either before or after G-POEM, no correlation was noticed between GERDQ scores, the emptying time and the parameters of antrum morphology.

**Conclusion** The technique of G-POEM was demonstrated as a minimally invasive approach with the long-term efficacy and safety in therapy of postoperative gastroparesis.

**Keywords** Postoperative gastroparesis · Gastric peroral endoscopic myotomy (G-POEM) · Gastroparesis cardinal symptom index (GCSI) · Gastroesophageal reflux disease questionnaire (GERDQ) · Three-dimensional ultrasound

Gastroparesis is a gastrointestinal dysfunction syndrome characterized by the non-mechanical obstruction of the gastric outflow tract. Postoperative gastroparesis occurs after esophageal or gastrointestinal surgery, or other surgeries which affect the upper digestive tract. The manifestations of postoperative gastroparesis include nausea, vomiting, upper

abdominal bloating, belching, gastric retention, weight loss. Postoperative gastroparesis can lead to a poor quality of life. Conventional treatments included lifestyle modification, psychological stress regulation, traditional Chinese medicine, prokinetic drugs, acupuncture and gastric electrical pacing, but these were often ineffective in alleviating symptoms [1]. Surgical procedures such as laparoscopic pyloroplasty or pyloromyotomy were performed to treat postoperative gastroparesis [2, 3]. In order to make the procedure more minimally invasive, endoscopic procedures such as intrapyloric injections of botulinum toxin and transpyloric stenting emerged [4–6]. However, intrapyloric injections of botulinum toxin was poor in improving the symptoms of postoperative gastroparesis. It was not recommended to perform

✉ Ruihua Shi  
ruihuashi@126.com

<sup>1</sup> Department of Gastroenterology, Zhongda Hospital Southeast University, No. 87 Dingjiaqiao, Nanjing 210009, Jiangsu, China

<sup>2</sup> Department of Ultrasound, Zhongda Hospital Southeast University, Nanjing 210009, Jiangsu, China

intrapyloric injections of botulinum toxin in the treatment of gastroparesis [7, 8]. Few data was published regarding transpyloric stenting in the literature. In 2013, Professor Khashab established the procedure of gastric peroral endoscopic myotomy (G-POEM) based on the theory of peroral endoscopic myotomy (POEM). Since then, G-POEM was gradually performed in the treatment of refractory gastroparesis [9–12]. Nevertheless, there was few study about the long-term efficiency of G-POEM in the treatment of postoperative gastroparesis. Our center performed G-POEM since 2016 and accumulated lots of relevant experiences. In the present study, the long-term efficacy and safety of G-POEM in treating postoperative gastroparesis were analyzed.

## Methods

This was a single-center and retrospective study of a prospective database. The patients suffered from postoperative gastroparesis went to the GI outpatient and admitted to the ward. This study complied with the ethical requirements of the declaration of Helsinki and was approved by our institutional research ethics board (Approval Number: ZDYJLY(2016)65). Each patient signed the written informed consent prior to the study.

**Inclusion criteria:** 1. The patients aged 18 years or older, with a history of surgery which affect the upper digestive tract. 2. The patients had the clinical manifestations of gastroparesis, with the score of Gastroparesis Cardinal Symptom Index (GCSI) > 2.3 [13]. 3. No significant improvement was found in the clinical manifestations after 6-month conservative therapy. 4. There were objective evidences of delayed gastric emptying [12].

**Exclusion criteria:** 1. The patients suffered the mechanical obstruction of gastric outflow tract. 2. The patients suffered diabetes, hypothyroidism, connective tissue diseases, neuromuscular disease, or other diseases which could cause gastroparesis. 3. The patients had the history of total gastrectomy or distal gastric subtotal resection. 4. The patients had the other malignant tumors. 5. The patients had undergone pyloroplasty or pyloromyotomy previously. 6. The patients could not tolerate general anesthesia or endoscopic procedures. 7. Women who were pregnant or breastfeeding.

**G-POEM procedure:** After the preoperative examinations, the patients with the contraindications were ruled out. The patients fasted for 12 h prior to the procedure. Cefoperazone/sulbactam (2.0 g) was given intravenously 1 h prior to the procedure. Cardiac monitoring, tracheal intubation and general anesthesia were performed throughout the procedure. The patients were in left lateral position. Low-flow carbon dioxide air pump should be used throughout the procedure. The G-POEM procedure was performed by a single expert who had profound experience in endoscopic

submucosal dissection (ESD) and POEM. A high-definition gastroscope (GIF-HQ 290, Olympus, Tokyo, Japan) was used. The procedure was performed on the posterior wall of gastric antrum. A mucosal incision was created about 5 cm upstream from the pylorus. A premixed methylene blue / epinephrine / sodium hyaluronate /normal saline solution was injected into the identified mucosal entry site to raise a mucosal bleb with a sclerotherapy needle (23G, NM4004-042, Olympus, Japan). The premixed solution was composed of 500 ml saline mixed with 0.5 ml epinephrine/5 ml methylene blue/2.5 ml sodium hyaluronate. A triangular-tip knife (KD 640L, Olympus, Tokyo, Japan) was used to make a 2-cm oblique mucosal incision, then establish the submucosal tunnel and perform the full-thickness myotomy of the circular and longitudinal muscular layers of the pylorus. Close attention should be made to ensure the integrity of the mucosa and serosa. The tunnel should be rinsed with saline after myotomy. Prophylactic hemostasis should be performed. The submucosal tunnel was extended toward the pylorus and ended at 1 cm beneath the pylorus. The mucosal entry and the perforated mucosa should be securely closed with the endoclips. The G-POEM procedure is shown in Supplementary Fig. 1 [12].

**Preoperative management:** All the patients were asked to stop using drugs which affect gastrointestinal smooth muscle contraction one week prior to the study. GCSI and Gastroesophageal Reflux Disease Questionnaire (GERDQ) [14] were used to assess the symptoms of postsurgical gastroparesis. Gastroscope was used to observe the anastomotic site and the residual stomach, and measure the distance from the anastomotic site to the incisor. Upper gastrointestinal imaging was used to observe the morphological structure of the residual stomach and the emptying process of ioversol. Three-dimensional ultrasound was used to observe the morphological structure of gastric antrum and pylorus tube. The emptying time was calculated by analyzing the volume change of gastric antrum. It was reported that three-dimensional ultrasonography had good consistency with scintigraphy—the ‘gold standard’ technique to measure gastric emptying [15–19].

**Postoperative management:** Postoperative management included fasting, water restriction, acid suppression, anti-infection and fluid replenishment. Close attention was paid for the vital signs and the signs of fever/hematemesis/melena/peritonitis. If no adverse event occurred, liquid diet was given 48 h after G-POEM. Semi-liquid diet was given 3–5 days after G-POEM. Soft diet was given half a month after G-POEM. The patients were discharged if gastroparesis symptoms were improved and no adverse event occurred. The patients were followed up at 1-month, 6-month, 1-year, 2-year and 5-year post-G-POEM.

The primary outcomes included the improvement of gastroparesis symptoms and gastric emptying function. The

secondary outcomes included the improvement of gastroesophageal reflux symptom, the procedure-related complications, and the other outcomes (e.g., BMI, diet status, medication use, operation time, post-procedure hospital stay, and incision length)

## Statistical analysis

Statistical analyses were conducted using SPSS software (SPSS 26.0, Chicago, IL). *T* test was used to analyze continuous parametric. Two-way ANOVA was performed to analyze the influence of different factors on GCSI (including subscales of GCSI) score and GERDQ score during the follow-up. Spearman correlation analysis was performed to analyze the relationship between GCSI (including subscales of GCSI) score, the emptying time and the pyloric morphologic parameters. *P* value < 0.05 was considered statistically significant.

## Results

### Baseline information

None of the 115 patients suffered from pyloric stenosis or hypertrophy before G-POEM. The baseline information is shown in Supplementary Table 1. The patients were divided into two groups based on the onset time of postsurgical gastroparesis: gastroparesis occurred within two-year post-surgery and gastroparesis occurred after two-year post-surgery. There was no difference between this two groups (GCSI score:  $2.79 \pm 0.55$  vs  $2.76 \pm 0.51$ ,  $p = 0.954$ ). According to the duration of postoperative gastroparesis, the patients were divided into two groups: the duration  $\leq 1$  year, and the duration  $> 1$  year. There was no difference between these two groups (GCSI score:  $2.77 \pm 0.57$  vs.  $2.79 \pm 0.47$ ,  $p = 0.063$ ). The patients were divided into two groups based on whether they were accompanied with GERD. The severity of post-operative gastroparesis symptoms was not related to the accompany condition of GERD (GCSI score:  $2.78 \pm 0.53$  vs.  $2.77 \pm 0.53$ ,  $p = 0.805$ ).

### The primary outcomes

#### The improvement of symptom based on GCSI

To evaluate the clinical effectiveness of G-POEM, GCSI score was analyzed before and after G-POEM. The clinical effectiveness was separated as clinical responder and non-responder [20]. At 1-month post-G-POEM, there were 3 patients lost to follow-up. In the follow-up patients, 100 patients (89.3%, 100/112) exhibited as clinical responders and the GCSI score decreased from  $2.78 \pm 0.53$  to

$0.82 \pm 0.78$ . Among the 12 patients (10.7%, 12/112) exhibited as non-responders, 9 patients (75%, 9/12) accompanied with GERD. At 6-month post-G-POEM, there were 10 patients lost to follow-up and 4 patients followed up insufficient time. Eighty-nine patients (88.1%, 89/101) exhibited as clinical responders and the GCSI score was  $0.85 \pm 0.74$ . Among the 12 patients (11.9%, 12/101) exhibited as non-responders, 5 patients (41.7%, 5/12) accompanied with GERD. One year after G-POEM, there were 27 patients lost to follow-up and 7 patients followed up insufficient time. Seventy-six patients (93.8%, 76/81) exhibited as clinical responders and the GCSI score was  $0.72 \pm 0.65$ . Among the 5 patients (6.2%, 5/81) exhibited as non-responders, 3 patients (60%, 3/5) accompanied with GERD. Two years after G-POEM, there were 30 patients lost to follow-up and 9 patients followed up insufficient time. Seventy-two patients (94.7%, 72/76) exhibited as clinical responders and the GCSI score was  $0.73 \pm 0.61$ . Among the 4 patients (5.3%, 4/76) exhibited as non-responders, 3 patients (75%, 3/4) accompanied with GERD. Our study followed up a large number of patients to 5 years. Among these 47 patients, 41 patients (87.2%, 41/47) exhibited as clinical responders and the GCSI score was  $0.91 \pm 0.89$ . Among the 6 patients (12.8%, 6/47) exhibited as non-responders, 5 patients (5/6, 83.3%) accompanied with GERD. None of the patients occurred pyloric stenosis in the follow-up. Among all the patients with recurrent symptoms, repeatedly inserting the gastroscope into the distal duodenum during gastroscopy examination could alleviate the symptom of gastroparesis. The overall clinical effect of G-POEM is shown in Table 1.

GCSI score was evaluated in the patients with different disease duration before and after G-POEM (Fig. 1). Either in the patients whose disease duration  $\leq 1$  year or  $> 1$  year, GCSI score decreased significantly since 1 month after G-POEM. Nevertheless, GCSI score was significantly higher in the patients whose disease duration  $> 1$  year at 1-month, 6-month, and 5-year post-G-POEM ( $p = 0.0376$ ,  $p = 0.0095$ ,  $p = 0.0361$ , respectively). In the patients whose disease duration  $\leq 1$  year, GCSI score maintained a steady trend in the follow-up ( $F_{4,208} = 0.06617$ ,  $p = 0.9919$ ). In the patients whose disease duration  $> 1$  year, GCSI score showed a slightly fluctuating trend in the follow-up ( $F_{4,199} = 0.9488$ ,  $p = 0.4369$ ).

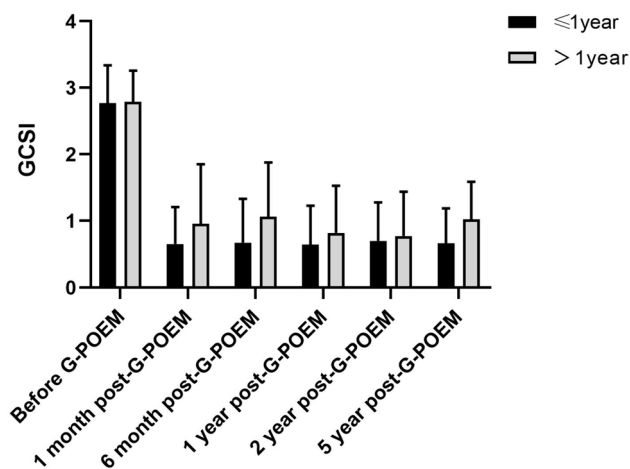
GCSI score was evaluated in the patients with different anastomotic sites before and after G-POEM. The score of GCSI was not significantly different between the patients with different anastomotic sites before G-POEM ( $p = 0.118$ ). For each anastomotic site, the score of GCSI decreased significantly after G-POEM ( $F_{5,502} = 98.28$ ,  $p < 0.0001$ ). No significant difference of GCSI score was found between the patients with different anastomotic sites in the follow-up ( $F_{4,392} = 0.5347$ ,  $p = 0.7103$ ) (Fig. 2A). The GCSI consists of three subscales, including nausea/vomiting scale,

**Table 1** Overall clinical effect of G-POEM

	Before	1 month	6 months	1 year	2 years	5 years
Total (n)	115	112	100	81	76	47
GCSI	2.78 ± 0.53	0.82 ± 0.78	0.85 ± 0.74	0.72 ± 0.65	0.73 ± 0.61	0.91 ± 0.89
<i>p</i> value		< 0.001	< 0.001	< 0.001	< 0.001	< 0.001
Clinical response (n)	–	100	89	76	72	41
Clinical failure (n)		12	12	0	0	0
GERD (n)		9	5	0	0	0
Recurrence (n)	–	0	0	5	4	6
GERD (n)		0	0	3	3	5

Clinical response: GCSI score decreased at least 1 point with more than a 25% decrease in at least 2 subscales. Clinical failure: no clinical response at initial follow-up or gastroparesis symptoms recurred within 6 months. Clinical recurrence: gastroparesis symptoms recurred and GCSI score returned to the baseline or GCSI score  $\geq 3$  lasted at least 2 months after initial complete response

*p* value: Compared with GCSI before G-POEM

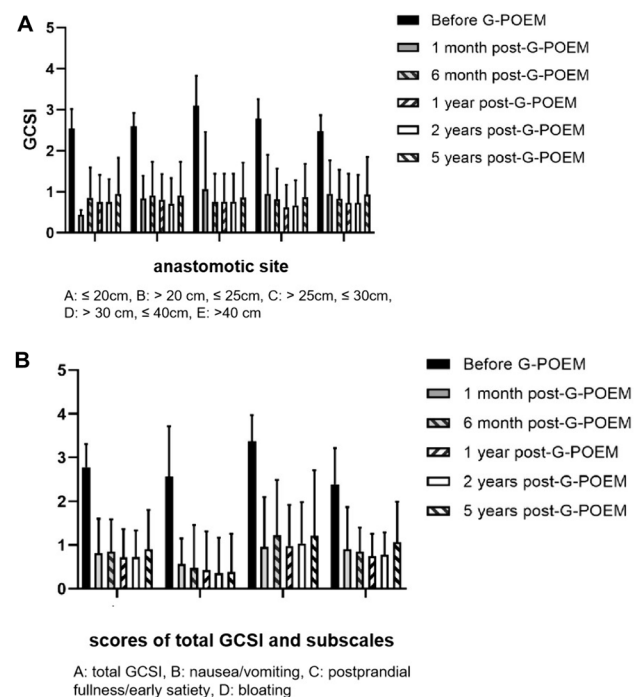


**Fig. 1** GCSI score of the patients with different disease durations before and after G-POEM. GCSI score decreased significantly since 1-month after G-POEM. GCSI score was significantly higher in the patients whose disease duration  $> 1$  year at 1-month, 6-month, and 5-year post G-POEM. In the patients whose disease duration  $\leq 1$  year, GCSI score maintained a steady trend in the follow-up. In the patients whose disease duration  $> 1$  year, GCSI score showed a slightly fluctuating trend in the follow-up

postprandial fullness/early satiety scale, and bloating scale. The score of each subscale decreased significantly after G-POEM, and the trend was similar as the score of total GCSI ( $p < 0.0001$ , respectively) (Fig. 2B). The effect of G-POEM was better in nausea/vomiting and postprandial fullness/early satiety than in bloating ( $p < 0.0001$ ) (Supplementary Fig. 2).

### The improvement of gastric emptying function

The volume of gastric antrum was measured using three-dimensional ultrasound examination. The emptying time was calculated by analyzing the volume alteration of gastric



**Fig. 2** GCSI score of the patients with different anastomotic sites and the scores of subscales. **A** GCSI score of the patients with different anastomotic sites before and after G-POEM. No significant difference of GCSI score was found between the patients with different anastomotic sites before G-POEM. For each anastomotic site, significant decrease of GCSI score was found after G-POEM. No significant difference of GCSI score was found between the patients with different anastomotic sites in the follow-up. **B** The scores of total GCSI and subscales after G-POEM. Significant decrease was found in each subscale score after G-POEM, and the trend was similar as GCSI score. No significant difference was found in each subscale score in the follow-up

antrum. The half-emptying time and whole-emptying time shortened significantly in the follow-up (Table 2).

**Table 2** The half-emptying time and whole-emptying time before and after G-POEM

	Before G-POEM	6-month post-G-POEM	1-year post-G-POEM	2-year post-G-POEM	5-year post-G-POEM
Half-emptying time (min)	49.15 ± 36.29	13.11 ± 8.92	12.18 ± 7.52	10.68 ± 8.14	11.42 ± 6.24
<i>p</i> value*	–	< 0.001	< 0.001	< 0.001	< 0.001
Whole-emptying time (min)	125.65 ± 70.20	39.81 ± 21.20	42.65 ± 24.15	40.71 ± 22.54	44.71 ± 26.29
<i>p</i> value**	–	< 0.001	< 0.001	< 0.001	< 0.001

The half-emptying time and whole-emptying time shortened significantly in the follow-up

\*Compared with the half-emptying time before G-POEM

\*\*Compared with the whole-emptying time before G-POEM

Before G-POEM, GCSI score was negatively correlated with the inner diameter of pylorus ( $r_s = -0.613$ ,  $p < 0.001$ ) and positively correlated with the length of pyloric tube ( $r_s = 0.520$ ,  $p < 0.001$ ). No correlation was noticed between GCSI score and the thickness of pyloric tube muscle/antral wall ( $p > 0.05$ , respectively). No correlation was noticed between GCSI score and the emptying time ( $p > 0.05$ , respectively). Among GCSI subscales, the scores of nausea/vomiting and postprandial fullness/early satiety were both negatively correlated with the inner diameter of pylorus (nausea/vomiting:  $r_s = -0.317$ ,  $p = 0.011$ , postprandial fullness/early satiety:  $r_s = -0.332$ ,  $p = 0.008$ ), and positively correlated with the length of pyloric tube (nausea/vomiting:  $r_s = 0.343$ ,  $p = 0.006$ , postprandial fullness/early satiety:  $r_s = 0.251$ ,  $p = 0.048$ ). No correlation was noticed between the score of bloating and the parameters of antral morphology ( $p > 0.05$ , respectively). The emptying time had no correlation with the parameters of antral morphology ( $p > 0.05$ , respectively). Data are shown in Table 3. After G-POEM, there was no correlation between GCSI score and

the emptying time ( $p > 0.05$ , respectively). No correlation was found between GCSI (including subscales) score and the parameters of antral morphology ( $p > 0.05$ , respectively). The emptying time had no correlation with the parameters of antral morphology ( $p > 0.05$ , respectively). Data are shown in Table 4. Gastric emptying imaging was performed before and after G-POEM. The emptying of ioversol was observed accelerated after G-POEM (data are not shown).

### The secondary outcomes

**The improvement of gastroesophageal reflux symptoms** Eighty patients (80/115, 69.6%) accompanied with the symptoms of gastroesophageal reflux before G-POEM (GERDQ:  $10.44 \pm 1.76$ ). GERDQ score was analyzed in these patients with different anastomotic sites before and after G-POEM (Fig. 3). Before G-POEM, GERDQ score was significantly higher in the patients with the low anastomotic site (distance between the anastomotic site and the incisors  $> 40$  cm) ( $p < 0.0001$ ). GERDQ score decreased

**Table 3** Correlation between GCSI (including subscales) score, GERDQ score, the emptying time, and the morphological parameters of antrum before G-POEM

	Half-emptying time		Whole-emptying time		Inner diameter of pylorus		Thickness of pyloric tube muscle		Length of pyloric tube		Thickness of antral wall	
	$r_s$	$p$	$r_s$	$p$	$r_s$	$p$	$r_s$	$p$	$r_s$	$p$	$r_s$	$p$
GCSI	0.018	0.885	0.113	0.370	-0.613*	< 0.001	0.092	0.468	0.520*	< 0.001	-0.068	0.65
nausea/vomiting	–	–	–	–	-0.317	0.011	0.185	0.148	0.343	0.006	0.004	0.979
postprandial fullness/early satiety	–	–	–	–	-0.332	0.008	0.177	0.164	0.251	0.048	0.041	0.787
bloating	–	–	–	–	-0.233	0.066	-0.101	0.433	0.178	0.164	-0.081	0.592
GERDQ	0.065	0.606	-0.072	0.565	-0.148	0.246	-0.072	0.575	0.164	0.198	-0.185	0.212
half-emptying time	–	–	–	–	-0.083	0.499	-0.114	0.350	-0.004	0.971	-0.233	0.115
whole-emptying time	–	–	–	–	-0.094	0.441	0.023	0.851	0.016	0.898	-0.131	0.382

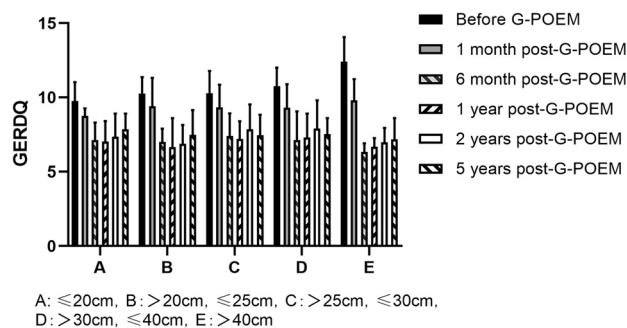
GCSI score was negatively correlated with the inner diameter of pylorus and positively correlated with the length of pyloric tube. No correlation was noticed between GCSI score and the thickness of pyloric tube muscle/antral wall. No correlation was noticed between GCSI score and the emptying time. Among GCSI subscales, the scores of nausea/vomiting and postprandial fullness/early satiety were both negatively correlated with the inner diameter of pylorus and positively correlated with the length of pyloric tube. No correlation was noticed between the score of bloating and the parameters of antral morphology. The emptying time had no correlation with the parameters of antral morphology. No correlation was noticed between GERDQ score, the emptying time, and the parameters of antral morphology.



**Table 4** Correlation between GCSI (including subscales) score, GERDQ score, the emptying time, and the morphological parameters of antrum after G-POEM

	Half-emptying time		Whole-emptying time		Inner diameter of pylorus		Thickness of pyloric tube muscle		Length of pyloric tube		Thickness of antral wall	
	$r_s$	$p$	$r_s$	$p$	$r_s$	$p$	$r_s$	$p$	$r_s$	$p$	$r_s$	$p$
GCSI	0.147	0.416	0.159	0.377	0.276	0.12	−0.029	0.873	0.129	0.475	0.114	0.624
Nausea/vomiting	–	–	–	–	0.269	0.130	−0.070	0.698	0.034	0.853	0.033	0.886
Postprandial Fullness/early satiety	–	–	–	–	0.075	0.680	−0.028	0.877	0.107	0.554	0.256	0.264
bloating	–	–	–	–	0.062	0.733	−0.035	0.847	0.102	0.571	0.373	0.096
GERDQ	−0.177	0.325	0.04	0.827	0.081	0.655	−0.034	0.851	0.159	0.376	0.142	0.540
Half-emptying time	–	–	–	–	−0.236	0.185	0.049	0.787	0.043	0.813	0.256	0.264
Whole-emptying time	–	–	–	4	0.032	0.858	0.206	0.25	−0.02	0.913	0.373	0.096

There was no correlation between GCSI score and the emptying time. No correlation was found between GCSI score and the parameters of antral morphology. No correlation was found between the scores of GCSI subscales and the parameters of antral morphology. The emptying time had no correlation with the parameters of antral morphology. No correlation was noticed between GERDQ score, the emptying time, and the parameters of antral morphology



**Fig. 3** GERDQ score before and after G-POEM. Before G-POEM, GERDQ score was significantly higher in the patients with the low anastomotic site. GERDQ score decreased significantly at 1 month after G-POEM. Compared with 1-month post-G-POEM, GERDQ score decreased significantly at 6-month post-G-POEM. For each anastomotic site, no significant difference of GERDQ score was found in the subsequent follow-up

significantly at 1 month after G-POEM ( $F_{4,147}=24.30$ ,  $p<0.0001$ ). Compared with 1-month post-G-POEM, GERDQ score decreased significantly at 6-month post-G-POEM ( $F_{1,138}=62.09$ ,  $p<0.0001$ ). For each anastomotic site, no significant difference of GERDQ score was found in the subsequent follow-up ( $F_{3,188}=1.238$ ,  $p=0.2973$ ). For different anastomotic sites, GERDQ score was not significantly different in the subsequent follow-up ( $F_{4,188}=1.333$ ,  $p=0.2594$ ). Neither before nor after G-POEM, no correlation was noticed between GERDQ score, the emptying time, and the parameters of antrum morphology ( $p>0.001$ , respectively). Data are shown in Tables 3 and 4.

**The procedures, adverse events, and complications of G-POEM** All the procedures of G-POEM were technically successful without serious adverse events, such as

bleeding, perforation, and pneumoperitoneum. The average length of antral myotomy was  $2.48 \pm 0.62$  cm. The average duration of G-POEM procedure was  $23.35 \pm 5.15$  min.

Eleven patients (9.6%) experienced upper abdominal pain (NRS score  $\leq 3$ ) on the first day after G-POEM. After ruling out perforation or peritonitis, analgesic therapy was given to these patients. During hospitalization, there were four cases (4/115, 3.5%) of bleeding and no case of perforation. After the therapy of endoscopic hemostasis, no one needed blood transfusion. No one required re-hospitalization for any complications or discomfort.

**Outcomes of diet status, BMI, and medications** After G-POEM procedure, all the patients were asked for hospitalization and fasting 48 h. Antibiotics (cefoperazone/sulbactam and levofloxacin) and PPI were administered intravenously. Liquid diet was given if the patients did not have any discomfort or complication after 48-h post-procedure. The patients were discharged if no complications or discomfort occurred. The average hospital stay was  $5.05 \pm 0.52$  days. One week after G-POEM procedure, semi-liquid diet was given to those patients who tolerated liquid diet. Half a month after G-POEM, soft and low-fiber diet was given. One month after G-POEM, normal diet was given. BMI was  $19.74 \pm 3.54$  kg/m<sup>2</sup> before G-POEM and did not change significantly during the follow-up period ( $p=0.962$ ). Compared to the daily use of PPI/prokinetic agents/mucosal protective agents before G-POEM, most patients tolerated discontinuation in the follow-up, while a few patients took these medications as need (Supplementary Table 2).

## Discussion

Esophageal or gastrointestinal surgery, or other surgeries that affect the upper digestive tract, can lead to postoperative gastroparesis [21–23]. Acute postoperative gastroparesis occurs when fasting is over or fluid food changes to semi-fluid food. Acute postoperative gastroparesis can be relieved by the conservative medical treatments. Chronic postoperative gastroparesis occurs weeks, months, or even years after surgery. The conservative treatments were often ineffective in alleviating the symptoms of chronic postoperative gastroparesis [1]. The side effects of prokinetic drugs limited the long-term usage of them in treating postoperative gastroparesis [24, 25]. Combining the effectiveness of pyloromyotomy and the benefits of minimally invasive endoscopic technique, the procedure of G-POEM was established on the theoretical basis of POEM [9, 26]. Many articles reported the outcomes of G-POEM [9, 10, 12, 27, 28]. Nevertheless, the long-term efficacy and safety of G-POEM are not currently available.

We noticed that the severity of gastroparesis symptom was neither related to the onset time of postsurgical gastroparesis, nor the disease duration. However, the clinical effect of G-POEM was related to the disease duration. After G-POEM, GCSI score of the patient with the short disease duration ( $\leq 1$  year) was significantly lower than the long disease duration ( $> 1$  year). This meant the early intervention of G-POEM could lead to both the short-term and long-term benefits. Several studies showed the similar viewpoint [29–32].

After G-POEM, the symptoms of postoperative gastroparesis were significantly improved. The score of each subscale decreased with the similar trend of the total GCSI score. Either before or after G-POEM, the most obvious symptom was postprandial fullness/early satiety, followed by nausea/vomiting. The reason might be that the mechanism of gastric receptive relaxation was disrupted after partial gastrectomy, leading to the increased postprandial intragastric pressure. The better effect of G-POEM was observed in nausea/vomiting and postprandial fullness/early satiety than in bloating. This was a subtle difference between this study and the others. In the other studies, nausea/vomiting responded better to G-POEM than postprandial fullness/early satiety and bloating [30, 31, 33]. In the patients without surgical history, postprandial fullness/early satiety was commonly related to gastric receptive relaxation, while bloating was commonly related to visceral sensitivity. In our study, each patient had underwent partial gastrectomy and the mechanism of gastric receptive relaxation was disrupted. Therefore, in the present research, the underlying mechanism that G-POEM improved postprandial fullness/early satiety was similar to nausea/vomiting.

Three-dimensional ultrasonography was confirmed as an accurate and valid measurement of gastric emptying, which had a good consistency with scintigraphy [15–17, 19]. Similar to the previous reports, the emptying time shortened significantly in the follow-up after G-POEM [12, 30]. Nevertheless, no correlation was noticed between GCSI and the emptying time neither before nor after G-POEM. Some articles considered that the symptoms of postoperative gastroparesis were not related to gastric emptying [1, 34–36]. The changes of gastric morphology could be observed by three-dimensional ultrasonography. Before G-POEM, the score of GCSI (including subscales) was negatively correlated with the inner diameter of pylorus and positively correlated with the length of pyloric tube. After G-POEM, no correlation was found between the score of GCSI and the parameters of antrum morphology. In the patients with postoperative gastroparesis, the symptoms of nausea/vomiting and postprandial fullness/early satiety maybe depended on the inner diameter of pylorus and the length of pyloric tube before G-POEM. The procedure of G-POEM disrupted the structure of the pyloric muscle and altered the pyloric compliance and pressure. However, the alteration of the pyloric compliance and pressure could not be reflected by the parameters of three-dimensional ultrasonography.

Eighty patients (69.6%) accompanied by the symptoms of GERD before G-POEM. Therefore, GERDQ score was analyzed as an observational indicator. Before G-POEM, GERDQ score was higher in the patients with the lower anastomotic site. After G-POEM, GERDQ score decreased significantly in the patients with different anastomotic sites. These results showed that GERDQ score could partly reflect the severity of postoperative gastroparesis and the effect of G-POEM.

As we know, there was no unanimous opinion on the optimal depth and the length of myotomy. Either the selective myotomy of the circular muscle or the full-thickness myotomy of the circular and longitudinal muscle was effective and safe [4, 9, 12]. According to the experience from POEM, the circular myotomy did not always lead to the satisfactory outcome, while the full-thickness myotomy could cover the shortage of the circular myotomy [37–40]. In the conventional surgical myotomy, the completeness of myotomy was considered as the prerequisite for the excellent long-term outcome [39, 41, 42]. Anatomically, the longitudinal muscle has a strong connection with the circular muscle, but has a weak connection with the serous membrane. The full-thickness myotomy could save the time consumed to carefully separate the longitudinal muscle and therefore decreased the adverse events related with the separating process and the procedure time [40]. In fact, the full-thickness myotomy in G-POEM did not increase the procedure-related adverse events [12, 29]. Some experts considered that the length of the myotomy should be between 2 cm and 3.5 cm [27, 43,

44]. The other considered that a long (> 2 cm) myotomy might worsen the antral motility [9]. In our study, the full-thickness myotomy was performed and the mean length of the myotomy was  $2.48 \pm 0.62$  cm. No serious adverse event such as bleeding, perforation, or pneumoperitoneum occurred in the G-POEM procedure.

The technical success rate of G-POEM in the present study was 100%. The clinical response rate was 89.3%, 88.1%, 93.8%, 94.7% and 87.2% at 1-month, 6-month, 1-year, 2-year and 5-year post-G-POEM, respectively. The data were higher than 69%–86% reported in the previous reports [20, 28, 45–48]. This may be because the full-thickness myotomy could disrupt the pyloric muscle completely. Among all the patients with the recurrent symptoms, no one suffered pyloric stenosis. Repeatedly inserting the gastro-scope into the distal duodenum could alleviate the recurrent gastroparesis symptoms. The effect may be due to the force generated from the torsion of the gastroscope when passing through the pylorus and duodenum. Redoing G-POEM was considered feasible and promising in alleviating the recurrent symptoms [29]. However, there were a lack of the long-term outcomes after redoing G-POEM.

G-POEM was a minimally invasive technique with good safety profile. G-POEM disrupted the pyloric muscle as similar as surgical pyloroplasty or pyloromyotomy [49]. However, the peritoneal space was not violated because G-POEM was based on the technique of submucosal tunneling. The complications of G-POEM were similar to the conventional endoscopic treatment. Bleeding was the most common complication, a few patients needed endoscopic hemostasis or even blood transfusion [10, 46, 47]. The other commonly complications included abdomen pain, perforation, pneumoperitoneum, ulcers, and pyloric stenosis [28, 30, 46, 47, 50–53]. In our center, there was no case of bleeding, perforation or pneumoperitoneum during the G-POEM procedure. Four cases occurred bleeding during hospitalization. After endoscopic hemostasis combined with powerful acid suppression, no one needed blood transfusion.

There were several limitations of the present study. Firstly, this was a single-center study. Although this study encompassed a large cohort of patients with postsurgical gastroparesis and followed up a long duration, not all the patients had completed the 5-year follow-up period yet. Some conclusions might change as more and more patients would complete the 5-year follow-up. Secondly, the G-POEM procedure was performed by one particular endoscopist with rich experience. The procedure might be not successfully performed by the general endoscopists. Considered this, the follow-up outcomes of G-POEM might be strictly dependent on the endoscopist's experience. Thirdly, there was no standardized protocol of G-POEM or standardized pre-/post-procedure management. Fourthly, normal diet was given to the patients till one month after G-POEM procedure. Though

the effect of diet on the outcomes was minimal from the perspective of long-term follow-up, the different characters of diet might cause a bias in the first month. Lastly, it was recommended to conduct additional evaluations both before and after G-POEM, such as antroduodenal/pyloric manometry and electrogastrography. The aforementioned data could be utilized in either predicting the success rate of G-POEM or further evaluating the efficacy of G-POEM.

The outcomes of this study were encouraging. G-POEM could be regarded as a minimally invasive technique with the long-term efficacy and safety in therapy postoperative gastroparesis. In future, further work should be conducted to explore the potential correlation between the amelioration of gastroparesis symptoms and changes in pyloric compliance and pressure.

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## Declarations

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