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Review Article

Gastric per-oral endoscopic myotomy: Indications, technique, outcomes, and future directions

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A B S T R A C T

After the clinical success of per-oral endoscopic myotomy (POEM) for treatment of achalasia cardia, the principle of submucosal tunneling and mucosal flap valve has been used in several other areas of the gastrointestinal tract. Gastric per-oral endoscopic pyloromyotomy (G-POEM, POEP, POP) is a relatively new procedure described for the treatment of refractory gastroparesis. This review discusses the indications, patient selection, pre-procedure workup, and procedure details of G-POEM. It also reviews the current literature on this procedure and provides insights and future directions for research on this topic.

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Keywords: Gastric per-oral endoscopic myotomy; Gastroparesis; Per-oral endoscopic pyloromyotomy; Per-oral pyloromyotomy; Third space endoscopy

Introduction

Gastroparesis is defined as a clinical syndrome of objectively delayed gastric emptying in the absence of mechanical obstruction. The cardinal symptoms are early satiety, post prandial fullness, nausea, vomiting, bloating, and abdominal pain.^{1,2} The prevalence in the general population varies from 0.2% to 5%.¹ Gastroparesis significantly affects quality of life (QOL).³ Hospitalizations, emergency room visits, and doctor consultations for gastroparesis have shown a significant rise; and it has also been shown to be associated with increased morbidity and mortality.^{4,5}

The common etiological factors for gastroparesis include idiopathic, diabetes (types I and II), post-viral, infections or post-operative. Gastroparesis has also been reported in patients with thyroid disorders, Parkinson's disease, paraneoplastic syndrome, and early scleroderma.^{1,6}

Pharmacological therapy for gastroparesis is limited. Metoclopramide is the only drug that is U.S. Food and Drug Administration (FDA) approved; and it has a black box warning due to the risk of tardive dyskinesia; and a recommendation that it should not be used continuously for more than three months.⁷

Endoscopic and surgical interventions for gastroparesis have

revolved around relaxation, distension or destruction of the pyloric sphincter. Intra-pyloric injection of botulinum toxin, though initially thought effective, was later proved to have results similar to placebo in two controlled trials.^{8,9} Surgical pyloroplasty was shown to be effective to alleviate symptoms in patients with refractory gastroparesis.¹⁰ Similarly, trans-pyloric stent placement has shown good short-term clinical benefit, although stent migration is frequently noted and may necessitate re-interventions.^{11,12} Gastric electrical stimulation (GES) is a promising alternative; however, data is still evolving and the device is FDA-approved for only humanitarian use under research protocol settings.¹³ Also, the procedure is invasive; requiring surgical implantation of the device and necessitating hospitalization.

Based on the success of pylorus directed therapies like surgical pyloroplasty or stenting, gastric per-oral endoscopic pyloromyotomy (G-POEM) was described since it provides a minimally invasive and yet effective dehiscence of the pyloric sphincter.

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Patient Selection, Indications, and Technique of G-POEM

Indication and patient selection

The primary indication for G-POEM is refractory gastroparesis. Diagnosis of gastroparesis is mainly clinical and based on symptoms. The common symptoms reported include nausea, vomiting, and post-prandial bloating. Pain is less frequent although has been reported. Severe cases may present with malnutrition, weight loss and/or dehydration. The gastroparesis cardinal symptom index (GCSI) is a clinical score that is calculated to assess the severity of symptoms. GCSI is based on three sub-scales—post-prandial fullness/early satiety (4 items); nausea/vomiting (3 items), and bloating (2 items); each item being scored from 0 to 5. The total score is calculated and correlates with symptom severity (Table 1).¹⁴ Esophageogastroduodenoscopy (EGD) is important to rule out mechanical factors contributing to the gastric outlet obstruction, e.g., duodenal or pyloric ulcers, infiltrating malignancy or extrinsic compression from surrounding structures. EGD can also assess the amount of gastric food stasis, which must be cleared before performing G-POEM. Contrast enhancement computed tomography abdomen is often performed to rule out compression by extrinsic mass lesions and/or to also rule out proximal bowel obstruction which may sometimes mimic the symptoms of gastroparesis. The standard investigation for assessment of gastroparesis is gastric emptying scintigraphy (GES) which measures and reports percent gastric retention of a ^{99m}Tc sulfur colloid-labeled solid meal at 1, 2, and 4 hours.¹ More than 30% gastric retention is considered clinically significant. Stopping prokinetics or other medications that can interfere with gastric motility before they are subjected to GES is mandatory. Endoluminal functional luminal imaging probe (EndoFLIP) estimates the distensibility of the pylorus whereas pyloric manometry can estimate the extent of pylorospasm. Other less frequently performed tests include—wireless motility capsule (that measures pH, pressure, and temperature and assesses gastric emptying by the acidic gastric residence time) and breath testing (using ¹³C-octanoate or spirulina).¹ Patients must be evaluated for their diabetic status, presence of possible hypothyroidism, and other metabolic workup to identify the potential etiology of gastroparesis. Although not mandatory, most centers may offer a therapeutic trial of diet modulation, prokinetics or even a transpyloric stent placement to assess symptom relief before schedul-

ing G-POEM.

Technique of G-POEM

The technique of G-POEM is based on esophageal POEM. A detailed description of the procedure has been reported earlier.¹⁵ Since G-POEM is a relatively new and evolving procedure, the technique is evolving; and many operators are likely to have their own preferences when performing this procedure. After a mucosal incision over a submucosal bleb raised 4 to 5 cm proximal to the pylorus (Fig. 1), submucosal tunneling is performed to reach and identify the pyloric muscle ring and the duodenal mucosa beyond it (Fig. 2, 3). Taking care to avoid injury to the duodenal mucosa, a full-thickness short myotomy of 2 to 3 cm length is performed to divide the pyloric ring from the distal to proximal direction (Fig. 4). After confirming hemostasis, the mucosal incision is closed using several mucosal clips (Fig. 5).^{12,15} The technique of G-

Fig. 1. Mucosal elevation 4 to 5 cm proximal to pylorus by submucosal injection of saline mixed with indigo carmine solution.

Table 1 Gastric Cardinal Symptom Index

Symptom	None	Very mild	Mild	Moderate	Severe	Very severe
1. Nausea (feeling sick to your stomach as if you were going vomit or throw up)	0	1	2	3	4	5
2. Retching (heaving as if to vomit, but nothing comes up)	0	1	2	3	4	5
3. Vomiting	0	1	2	3	4	5
4. Stomach fullness	0	1	2	3	4	5
5. Not able to finish a normal-sized meal	0	1	2	3	4	5
6. Feeling excessively full after meals	0	1	2	3	4	5
7. Loss of appetite	0	1	2	3	4	5
8. Bloating (feeling like you need to loosen your clothes)	0	1	2	3	4	5
9. Stomach or belly visibly larger	0	1	2	3	4	5

Data from the article of Revicki et al (*Qual Life Res.* 2004;13:833–44).¹⁴

This questionnaire asks you about the severity of symptoms you may have related to your gastrointestinal problem. There are no right or wrong answers. Please answer each question as accurately as possible.

For each symptom, please circle the number that best describes how severe the symptom has been during the past 2 weeks. If you have not experienced this symptom, circle 0. If the symptom has been very mild, circle 1. If the symptom has been mild, circle 2. If it has been moderate, circle 3. If it has been severe, circle 4. If it has been very severe, circle 5. Please be sure to answer every question.

Fig. 2. Submucosal tunnelling in a direction perpendicular to the circular muscle fibers. Arrow denotes direction of tunneling perpendicular to the circular muscle layer.

Fig. 4. Full-thickness pyloromyotomy with duodenal mucosa prolapsing after the myotomy. Arrow indicates completed full-thickness pyloromyotomy.

Fig. 3. Pyloric ring and duodenal mucosa (arrow) rising vertically beyond the ring.

Fig. 5. Closure of mucosal incision using mucosal endoclips.

POEM has evolved over time. Most operators prefer to use an IT-2 Knife™ (Olympus, Tokyo, Japan) instead of a TT Knife™ (Olympus) or Hook Knife™ (Olympus) for pyloromyotomy to prevent inadvertent duodenal mucosal injury.¹⁵ Identification of the pylorus may be sometimes challenging, and fluoroscopy guided G-POEM has been reported to reduce operative times and improve outcomes.¹⁶

Clinical Outcomes of G-POEM

Several studies have demonstrated impressive short- and medium-term outcomes after G-POEM (Table 2).^{17–28} All have reported 100% technical success for the procedure with minimal adverse events (AEs). Clinical success rates were more variable and ranged from 66% to 100%, but most observations were based on subjective criteria like GCSI; and GES was less frequently reported.

The longest follow-up was 18 months, and results were sustained during this period in most patients. Two international multicenter studies demonstrated around 85% resolution of clinical symptoms during 5.5 to 11.5 months follow-up.^{18,24} GCSI showed significant reduction (3.3 to 0.8, $P < 0.001$) as did the GES (222.4 to 143.16 min, $P \leq 0.05$). A recent single center case-controlled study reported sustained symptom relief in 66.7% patients at 18-month follow-up. All parameters—GCSI, QOL by Short Form-36 scores, emergency department visits, and hospitalizations—demonstrated significant improvement after G-POEM as compared to controls.²³

During the last one year, two systematic reviews and meta-analysis on G-POEM have been published.^{29,30} Aghaie Meybodi et al²⁹ reported outcomes of 195 patients from 9 studies. The weighted pooled results demonstrated impressive clinical success in 82% patients; and mean GCSI and gastric emptying improved significantly (−1.57 [95% confidence interval, CI; −2.2 to −0.9], $I^2 = 80\%$; $P < 0.001$) and (−22.3 [95% CI, −32.9 to −11.6], $I^2 = 67\%$; $P < 0.05$), respectively. Another meta-analysis by Yan et al³⁰

Table 2 Clinical Outcomes of G-POEM

Study	No. of patients	Technical success (%)	Clinical success (%)	Parameters to assess clinical success	Functional outcomes (%)	Adverse events	Follow-up (mo)*
Shlomovitz et al (2015) ¹⁷	7	100	86 (6/7)	GCSI	80 (4/5)	1 Bleeding (clips)	6.5 ± 2.1
Khashab et al (2017) ¹⁸	30	100	87 (26/30)	GCSI, GES	47 (14/30)	1 Capnoperitoneum, 1 ulcer	5.5
Gonzalez et al (2017) ¹⁹	12	100	83 (10/12)	GCSI, GES	75 (9/12)	2 Capnoperitoneum	5
Mekaroonkamol et al (2016) ²⁰	3	100	100 (3/3)	GCSI, GES	100 (3/3)	Nil	3
Gonzalez et al (2017) ²¹	29	100	3 mo: 79 6 mo: 69	GCSI, GES	55 (16/29)	1 Bleeding (clips), 1 abscess (conservative)	10 ± 6.4
Dacha et al (2017) ²²	16	100	81 (13/16)	GCSI, GES	75 (12/16)	Nil	6
Rodriguez et al (2017) ²³	47	100	66 (31/47)	GCSI, GES	34 (16/47)	1 Death (cardiac disease, unrelated to procedure)	3
Kahaleh et al (2018) ²⁴	33	100	85 (28/33)	GCSI, GES	100	1 Bleeding (clips), 1 ulcer	11.5
Xu et al (2018) ²⁵	16	100	81 (13/16)	GCSI, GES	100	NR	14.5
Malik et al (2018) ²⁶	13	100	73 (8/11)	GES, PAGI-SYM	PAGI-SYM: 72.7 GES: 66.6	Nil	3
Mekaroonkamol et al (2019) ²⁷	30	100	76.7	GCSI, GES	GES: 78.3 GCSI 1 mo: 80 6 mo: 71 12 mo: 57 18 mo: 67	NR	18
Vosoughi et al (2020) ²⁸	37	100	70	EndoFLIP	EndoFLIP prediction: specificity 91; sensitivity 71	NR	3

G-POEM, gastric per-oral endoscopic pyloromyotomy; GCSI, gastric cardinal symptom index; GES, gastric emptying scintigraphy; PAGI-SYM, patient assessment of gastrointestinal symptoms; EndoFLIP, endoluminal functional luminal imaging probe; NR, not reported.

*Values are presented as mean ± standard deviation or median.

evaluated 235 patients from 9 studies. Results similarly demonstrated impressive results by way of GCSI reduction (8/9 studies, odds ratio, OR; 3.00 [CI, 2.24–4.03], $P < 0.001$), GES at four hours (8/9 studies, mean difference, 23.78 [CI, 19.88–27.68], $P < 0.001$), and gastric emptying time reduction (6/9 studies, OR, 3.50 [CI, 2.12–5.78], $P < 0.001$). AEs were reported in 5.1% cases. Both meta-analyses concluded that G-POEM was safe and effective for treatment of refractory gastroparesis.

Compared to esophageal POEM, outcomes of G-POEM are less consistent. In the multicenter study by Khashab et al,¹⁸ although response was observed in 86.7% (26/30 patients), 4 patients failed to respond and one patient had worsening of symptoms. Gastroparesis is a complex clinical disorder wherein impaired gastric dysmotility and pylorospasm, both play a variable role in its pathophysiology. Impaired gastric body motility is likely the primary cause for diabetic gastroparesis (autonomic neuropathy), whereas pylorospasm may be an important factor in post-operative gastroparesis (after vagal injury or vagotomy). It is, therefore, essential to identify which patients are most likely to benefit by G-POEM.^{31,32} Gonzalez et al²¹ have attempted to address this question. In a series of 29 patients, they reported inferior outcomes of G-POEM for diabetic gastroparesis as compared to post-surgical or idiopathic gastroparesis (57% vs 80% and 93% at 3 months; 43% vs 50% and 92% at 6 months). Diabetes and female sex were found to be predictors of failure in univariate analysis, although this was not confirmed on multivariate analysis. Mekaroonkamol et al³³ in an abstract form reported that duration of symptoms rather than etiology of gastroparesis was the predictive factor for clinical response after G-POEM, with prolonged disease being associated with a significantly poorer response ($P = 0.02$). A prospective single-arm study of 20 patients reported outcomes of G-

POEM using a combination of preoperative EndoFLIP, GCSI, QOL index, and scintigraphy. Outcomes were evaluated on the basis of clinical and radiological response at three months; and the study concluded that G-POEM was efficacious and safe for treating refractory gastroparesis, especially in patients with low pyloric distensibility.³⁴ EndoFLIP measurements of pylorus have the potential to be used as a predicting tool of the G-POEM clinical outcome. Vosoughi et al²⁸ evaluated the role of pre-procedure EndoFLIP to predict post-G-POEM outcomes. Pyloric cross-sectional area (CSA), balloon pressure, and distensibility index (DI) were measured using 40 and 50 mL balloon fills before and 3-months post-G-POEM in 37 patients. Clinical success was achieved in 70% patients. Post-G-POEM CSA and DI were significantly higher in the clinical success group with both 40 mL (CSA, 89.9 ± 64.8 mm² vs 172.5 ± 71.9 mm², $P = 0.003$; DI, 5.8 ± 4.4 mm²/mmHg vs 8.8 ± 6.1 mm²/mmHg, $P = 0.043$) and 50 mL volume distention (CSA, 140.1 ± 89.9 mm² vs 237.5 ± 80.3 mm², $P = 0.003$; DI, 5.6 ± 3.3 mm²/mmHg vs 9.9 ± 6.6 mm²/mmHg, $P = 0.049$). CSA using 40 mL volume distention, with an area under the curve of 0.83 yielded specificity of 91% and sensitivity of 71% at a cut-off point of 154 mm². The study concluded that post-G-POEM pyloric CSA correlated with clinical success and improvement of GES after G-POEM.

One of the hypotheses for failure of long-term response to G-POEM or any other sphincter dividing procedure has been incomplete myotomy. To address this issue, Abdelfatah et al³⁵ performed double myotomy of the pyloric ring and compared double vs single myotomy in a retrospective cohort of 90 patients (55 single and 35 double) and demonstrated superior clinical response for double pyloromyotomy (86% vs 67%) at mean 6 months follow-up. It would be interesting to evaluate these results over long-term.

Results of G-POEM have also been compared to surgical pyloromyotomy^{36,37} and to GEST.³⁸ Mohan et al³⁶ found comparable efficacy with surgical pyloroplasty of G-POEM in 332 patients in a pooled analysis. This analysis also identified idiopathic gastroparesis, prior botulinum toxin injection and GEST as predictors for response after G-POEM. Landreneau et al³⁷ reported that G-POEM reduced perioperative morbidity in terms of procedure time, AEs and hospital stay as compared to laparoscopic pyloromyotomy with comparable functional outcomes. Shen et al³⁸ compared GEST with G-POEM in a propensity score matched analysis. The study showed significantly superior performance for G-POEM over GEST in terms of sustenance of clinical response (76% vs 53%, $P = 0.05$) at longest 27-month follow-up and superior safety profile (AE rates for G-POEM and electrical stimulation being 4.3% vs 26.1%, respectively).

G-POEM has demonstrated a good safety profile in all clinical trials. AEs are few and are of minor severity. However, outcomes need cautious interpretation. Most studies are retrospective single-arm small patient cohorts and randomized controlled trials comparing G-POEM to other modalities are lacking. Also, these studies have different methods to diagnose gastroparesis and assess treatment response and therefore meaningful comparisons are difficult to establish. Patient selection is largely based on symptoms (GCSI) and objective parameters are lacking. EndoFLIP or other techniques to assess pyloric sphincter relaxation or distensibility have failed to provide consistent results except in one study.^{28,39,40} Another issue requiring consideration is the incidence and potential long-term consequences of duodeno-gastric biliary reflux that may occur after G-POEM. In absence of objective parameters, the true challenge is to identify the optimum patient likely to benefit from G-POEM.³²

Conclusions

In our opinion, G-POEM has established itself as an effective minimally invasive method to treat refractory gastroparesis with an acceptable safety profile. Future research should be aimed at identifying the right patients who are likely to benefit by G-POEM; and towards randomized studies comparing G-POEM to other treatment modalities for gastroparesis. Prediction of long-term outcomes and potential factors contributing to clinical failures should be identified. The future for G-POEM appears bright. With the advent of more compelling data, it is likely that the role of G-POEM could be further established within the treatment algorithms for refractory gastroparesis.

Conflicts of Interest

No potential conflict of interest relevant to this article was reported.

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