INTRODUCTION

Gastroparesis is a chronic debilitating disorder of gastric motility. This disorder is more commonly encountered in women than men, with an age-adjusted prevalence per 100,000 persons of 37.8 in women and 9.8 in men. Gastroparesis has put an increasing burden on the healthcare system over time with a 300% increase in gastroparesis related hospitalizations reported from 1997 to 2013 with an annual cost of $568 million annually. There are many etiologies of gastroparesis but the three most common are diabetic gastroparesis, post-surgical gastroparesis, and idiopathic gastroparesis. The pathophysiology of gastroparesis seems to be due to loss of antral contraction and abnormal pyloric movement. One study found abnormally prolonged, high amplitude pyloric contractions, deemed a “pylorospasm.” Other histologic studies have shown loss of the interstitial cells of Cajal which are the pacemaker cells controlling smooth muscle contraction.

Some common symptoms of gastroparesis include postprandial nausea, vomiting, bloating, early satiety, and abdominal pain. Treatment of gastroparesis generally begins with symptomatic management such as dietary changes and the administration of promotility medications. Metoclopramide is a widely used promotility agent but carries a risk of extrapyramidal effects such as tardive dyskinesia especially if used for longer than 12 weeks. Other commonly used drugs like domperidone and erythromycin have short term efficacy with the risk of tachyphylaxis. About 30% of patients do not respond to conservative management.

If conservative management fails, treatment options include the injection of botulinum toxin (Botox) around the pylorus, gastro-electrical stimulators (GES), and surgery. There have been mixed results to Botox injection with one case series showing only a 43% clinical response rate while another study showed a 77% response at a higher dose. GES has also had mixed results with 1-year clinical response rates reported anywhere from 45-74% with only about a quarter of patients having sustained response for 3 years. In addition, few centers have experience with placement and management of GES. Laparoscopic pyloromyotomy is the most invasive treatment but has shown the best results, improving symptoms in 83-86% of patients and normalizes gastric emptying in 60-90% of patients. It is limited by the fact that many surgeons are reluctant to operate on the stomach of...
patients with gastroparesis and the typical adverse effects of surgery such as leaks, bleeding, and wound infections.\textsuperscript{11}

**G-POEM TECHNIQUE**

**Background**

A recent development in the treatment of gastroparesis is the gastric peroral endoscopic myotomy procedure (G-POEM) which, as its name suggests, involves using an endoscope rather than surgery to perform a pyloromyotomy. G-POEM is a variation of the standard peroral endoscopic myotomy (POEM) procedure which is performed in the esophagus and used to treat achalasia.\textsuperscript{6} Challenges to G-POEM include the fact that the submucosal tunnel near the pylorus is curved compared to the straight esophageal tube, there is antral peristalsis causing movement which isn’t encountered in the aperistaltic esophagus, and that it is more difficult to identify the pyloric muscular ring (PMR) compared to the lower esophageal sphincter (LES).

This procedure was first described by Khashab et al. in 2013 who performed the procedure on a 27 year old woman with diabetic gastroparesis. Twelve weeks after the procedure, she continued to report improvement of symptoms and was able to tolerate a soft diet.\textsuperscript{12}

Prior to undergoing G-POEM, patients are often kept on a clear liquid diet for 2-3 days and nil per os (NPO) for 12 hours prior to the procedure to clear the stomach of retained food, improve visualization during the procedure, and to decrease the risk of procedure related infection.\textsuperscript{6} Prophylactic intravenous antibiotics are often administered. However, there is no high-quality data regarding the efficacy of these antibiotics nor is there any standardization on the type of antibiotics to be used.\textsuperscript{6} Common antibiotics that are used include 4.5g of piperacillin/tazobactam or 500mg of levofloxacin.\textsuperscript{13,14,15}

**Procedure Steps and Variations**

The general steps that are taken in a G-POEM procedure include mucosotomy to enter the submucosal plane, submucosal dissection to create a submucosal tunnel, myotomy, and closure of the mucosal defect.\textsuperscript{6} Each of these steps have a number of variations.

The initial mucosotomy was traditionally done on the greater curvature since the endoscope would be in a more neutral position with greater maneuverability.\textsuperscript{6} However, mucosotomy is sometimes performed on the lesser curvature. Advantages to a lesser curvature mucosotomy and approach include a “shorter” scope position and length, shorter length of the submucosal tunnel, less looping of the scope in the stomach, and a non-dependent position which avoids food residue, secretions, and pooling of blood.\textsuperscript{16}

There are also variations in how to identify the PMR. The conventional method is to inject a mixed solution of methylene blue and saline during submucosal tunneling causing the mucosa at and around the pylorus to appear blue. Xue et al., whose study involved mucosotomy on the greater curvature, carried out a variation of this procedure by placing an endoscopic clip at the 9 to 11 o’clock position of the pylorus and completing the procedure under fluoroscopy. In this study, the clip served as a reference point for the submucosal tunnel entry which occurred at the 6 o’clock position.\textsuperscript{17} One study found that the PMR was better identified under fluoroscopy and that G-POEM performed with the assistance of fluoroscopy had a shorter procedure time than the conventional method. However, there was no significant difference in outcomes between these two methods.\textsuperscript{17}

Although the length of the mucosal incision can be variable, one example of how this procedure is carried out is by making a mucosal incision 5cm proximal to the PMR and creating a submucosal tunnel to 1cm distal to the PMR. Then, a full thickness myotomy would be completed from a point 2-3cm proximal to the PMR to 0.5-1cm past the duodenal bulb.\textsuperscript{17,18} The mean myotomy length as reported by 6 studies was 2.7 ± 0.7 cm.\textsuperscript{19}

After completing the myotomy, the mucosa can be closed via endoscopic clips or sutures. One study of 25 patients found successful complete closure in all 15 patients with sutures and 9 of 10 patients with endoclips.\textsuperscript{20} However, a review of endoscopic techniques among patients undergoing G-POEM recommends that endoscopic clips should be used as first line therapy and sutures should be used if clip closure is unable to be completed.\textsuperscript{21} Overall, (continued on page 46)
endoscopic clips are widely used in practice. One pooled analysis found that clips were used in 266/285 cases while suturing was only used in 21/285 cases. A meta-analysis conducted by Meybodi et. al. that included 7 studies and 196 patients also found a technical success rate of 100%. There may be a component of publication or reporting bias. Although the technical success is around 100%, there is a large range in mean procedural time from 40-120 minutes which possibly can be due to the learning curve for this procedure. Notably, procedure time has dropped quite a bit from the 119 ± 23 minutes reported by an early study.

OUTCOMES
Technical Success
Even though G-POEM can be a challenging procedure, reported technical success rates are high. In a pooled analysis consisting of 10 studies and 292 patients, the technical success rate was 100%. A meta-analysis conducted by Meybodi et. al. that included 7 studies and 196 patients also found a technical success rate of 100%.

Symptoms Before and After G-POEM

One measure of clinical success is the Gastroparesis Cardinal Symptom Index (GCSI), which is based on three subscales which evaluate post-prandial fullness/early satiety, nausea/vomiting, and bloating. In a meta-analysis consisting of 10 studies and 281 patients conducted by Uemura et. al, the pooled mean difference in GCSI before and after the procedure was 1.76, which was a significant difference. These GCSI differences were durable. When using the longest follow up period for each study which ranged from 3-18 months, the mean difference in GCSI was 1.84 which was also statistically significant. Meybodi et. al. also reported a similar significant difference in GCSI before and after G-POEM of 1.57 in their meta-analysis. Of note, one symptom that is not asked about in the GCSI is abdominal pain, although many patients with gastroparesis complain of abdominal pain, especially in the post-prandial setting. Various studies have reported improvement of abdominal pain in 56-73% of patients following G-POEM.\(^6\)

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**Figure 5.** Good progress with the submucosal tunnel

**Figure 6.** Periodic inspection of the gastric lumen to assure that the tunnel is in the direction of the pylorus

**Figure 7.** First view of the pyloric muscle

**Figure 8.** Clearer view of the pylorus; duodenal submucosal vessels are seen below
Gastric Emptying Scans Before and After G-POEM
Another measure of clinical success that is often used is the Gastric Emptying Scan (GES). In the GES 4-h test, a patient will eat a liquid egg white meal with radiolabeled material, and the amount of food left in the stomach after 4 hours will be measured by scintigraphy. Uemura et al. found that there was a significant 26.28% decrease in retained food between the GES done before and 2-3 months after G-POEM.23 Meybodi et al found a similar significant decrease of 22.3%.22 When pooling the clinical success rates based on improvement of GCSI scores, Mohan et al. found a clinical success rate of 75.8% and when pooled by improvement in GES 4-h, the clinical success rate was 85.1%.24

Quality of Life Outcome Measures
Some studies examined improvement in quality of life as measured by the SF-36 form. The SF-36 form is a validated, patient reported survey which reports a patient’s health and quality of life in eight different subsections. One study examining long term outcomes of G-POEM found that at a mean follow up time of 16 months, there was a significant improvement in quality of life as measured by the SF-36.25 Improvement in SF-36 scores have been found in 70-78% of patients with significant improvements specifically in the domains of vitality, general health, mental health, and social functioning.6 Additionally, emergency room visits, gastroparesis-related hospitalizations, and anti-emetic medication use were found to be significantly lower post G-POEM as compared to controls.6

Changes in Pyloric Function
Endoscopic functional luminal imaging probe (Endo-FLIP, Medtronic, Minneapolis, USA) technology can give some useful information about patient outcomes following G-POEM. Endo-FLIP can assess pyloric function by measuring the length, pressure, cross sectional area (CSA), and distensibility of the pylorus. Malik et al. took Endo-FLIP measurements of the pylorus before and after G-POEM. They found that after G-POEM there was increased length, CSA, and distensibility of the pylorus. Along with this, there was decreased average pyloric pressure. However, only the increase in CSA had a statistically significant correlation with better clinical outcomes.3

Adverse Events
The three most common adverse events were GI bleeding (32%), abdominal pain (30%), and pneumoperitoneum (24%) with other adverse events like pulmonary embolism, abscess, and stricture occurring less than 5% of the time.23 GI bleeding is usually controlled with endoscopic intervention or medications like proton pump inhibitors. Mohan et al. found a pooled adverse event rate of 11% in a meta-analysis consisting of 332 patients in 11 studies.24 Meybodi et al. found only 12/196 (6.1%) had an adverse event in their meta-analysis.22 Several studies have reported pyloric ulcers at the incision site of the procedure. A causal relationship between the pyloric ulcer and bleeding has been established in some studies but not in others.6 Pneumoperitoneum, on the other hand, is often managed conservatively and resolves on its own. In severe cases, needle decompression can be used for treatment.6 No deaths have been reported due to G-POEM. Two studies of G-POEM have reported patient deaths. However, in both cases, autopsy revealed that the death was not due to the procedure.23

ANALYSIS
Predictors of Clinical Success
With G-POEM being one of many possible interventions for gastroparesis, it becomes useful to know which patients may benefit from the procedure prior to offering it to them. Unfortunately, predictive factors for clinical success are disputed. A 2017 study by Gonzalez et al. found efficacy rates after 3 months to be 93% for idiopathic gastroparesis, 57% for gastroparesis secondary to diabetes, 80% for post-operative gastroparesis, and 50% for scleroderma-induced gastroparesis. At 6 months, the rates were 92%, 43%, 50%, and 50% respectively. They found that diabetes as the etiology of gastroparesis and female gender were significantly associated with worse outcomes.26 Another study also showed patients with idiopathic and postoperative gastroparesis to have the best response to G-POEM with those with diabetes (continued on page 50)
any effect on G-POEM outcomes. There was no difference in outcome at the one or six month follow up. However, at the 12 month follow up, it was found that longer duration of disease was associated with worse outcomes as measured by GSCI score. Other predictive factors that have been associated with poorer outcomes include higher BMI, history of psychiatric medication use, and history of pain medication use. This may be due to the fact that both psychiatric medications and pain medications can often be anticholinergic.

Given the novelty of G-POEM, it has been hypothesized that there is a learning curve involved with the procedure and that operator experience could lead to better outcomes. One study found that complicated by advanced macrovascular disease having the worst outcomes.

On the other hand, Jacques et. al. found favorable outcomes when using Endo-FLIP to analyze diabetic patients after G-POEM. Mekaroonkamol et. al. conducted a single center, retrospective study with 25 diabetic and 15 non-diabetic patients and found no significant difference in GSCI scores or degree of improvement between the diabetic and non-diabetic groups. Additionally, within the diabetic group, baseline HbA1c level did not correlate with clinical response. This study also investigated whether the duration of the patient’s gastroparesis before G-POEM had

Figure 9. Pyloromyotomy is begun

Figure 10. Nearly complete pyloromyotomy

Figure 11. Endoscopic clips to close mucosotomy

Figure 12. Complete clip closure of mucosotomy
it took 18 procedures to reach procedural efficiency, defined as completing the procedure in less than 60 minutes. Other studies have investigated the association between provider experience with G-POEM outcomes, but have not shown a clear correlation. One study divided a provider’s first ten cases and the rest of their cases into two groups. Another study divided the first half and second half of cases performed by the same provider. Neither of these studies found any correlation between provider experience and outcomes.

**Comparison of G-POEM to other Treatments for Gastroparesis**

When compared to GES, G-POEM was associated with a better long term clinical response with a 60% lower risk of clinical recurrence at a median follow up time of 27.7 months. Additionally, G-POEM was more versatile; it is effective in patients with both idiopathic and non-idiopathic causes of gastroparesis while GES was not effective in patients with idiopathic gastroparesis. Landreaneau et. al. conducted a study which propensity matched patients undergoing G-POEM with those undergoing laparoscopic pyloroplasty (LP) and found similar clinical efficacy. G-POEM, however, performed better when it came to operative time, length of hospital stay, estimated blood loss and complication rate. Mohan et. al. also found similar clinical efficacy between the procedures. In their study, G-POEM was found to have a shorter procedure time, but hospital length of stay was not significantly different between the procedures.

**CONCLUSION**

Management of gastroparesis has been and remains a clinical challenge. A durable cure has long eluded medical providers as medications come with side effects and procedures such as Botox injection and GES placement have less than perfect success rates and do not always produce a sustained response. G-POEM have been introduced as another treatment to refractory gastroparesis which is less invasive than surgery and more effective than the methods listed above. The procedure has many variations but generally involves mucosotomy, submucosal dissection, myotomy, and mucosal closure. Technical success rates have been reported to be 100% across many studies. Patients undergoing G-POEM have also shown significantly improved GCSI, GES 4h, and quality of life scores along with trends towards improvement in Endo-FLIP scores. Adverse events have occurred in about 5-10% of patients but are often managed conservatively or with non-invasive interventions. G-POEM performs well when compared to GES and similarly to surgery. However, it does have the advantage of being less invasive and having a shorter procedure time than surgery. With these findings, G-POEM should be a consideration for patients with refractory gastroparesis at any facility with the capabilities to perform this procedure.

**References**

G-POEM: Review and Technical Update

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