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ASMBS Guidelines/Statements

Gastroparesis: an evidence-based review for the bariatric and foregut surgeon

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Abstract Gastroparesis is a gastric motility disorder characterized by delayed gastric emptying. It is a rare disease and difficult to treat effectively; management is a dilemma for gastroenterologists and surgeons alike. We conducted a systematic review of the literature to evaluate current diagnostic tools as well as treatment options. We describe key elements in the pathophysiology of the disease, in addition to current evidence on treatment alternatives, including nutritional considerations, medical and surgical options, and related outcomes. (Surg Obes Relat Dis 2023; ■:1–18.) Published by Elsevier Inc. on behalf of American Society for Metabolic and Bariatric Surgery.

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Gastroparesis comes from the Greek words *gaster* (stomach) and *paresis* (partial paralysis). It is a disease process defined by delayed or incomplete gastric emptying of the stomach in the absence of a mechanical obstruction. This is associated with many clinical symptoms such as early satiety, nausea and vomiting, and epigastric pain, among others.

Pioneering gastric emptying and motility studies are attributed to Beaumont, Marbiax, Salamanca, Carlson, and

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many others. They established the foundational knowledge to understand the normal mechanical physiology of the stomach [1]. Gastroparesis was first described by Rundles in 1945 [2], and the term *gastroparesis diabeticorum* was coined by Kassander in 1958 [2–4].

The incidence of gastroparesis has been reported in 9.8 women and 2.4 men per 100,000 persons, increasing to 10.5 per 100,000 in those aged 60 years and older [5]. Another study estimated that the incidence may be as high as 1.8%, but only a small number of patients completed the diagnostic work-up [6].

Symptomatic gastroparesis has been frequently associated with obesity. This may be related to coping behaviors used to control some of the symptoms of delayed gastric emptying. Because of this association, it is important to understand the pathophysiology and medical treatment of gastroparesis, and to be knowledgeable about surgical and endoscopic interventions with demonstrated efficacy to treat patients who fail medical treatment.

Gastroparesis may be idiopathic in origin or related to other disorders, such as metabolic diseases (diabetic gastroparesis), neuromuscular dysfunction, collagen vascular disease, viral infection, and iatrogenic disease (postsurgical, pharmacologic, etc.). It is essential to have a multidisciplinary approach to manage this disease.

Physiology and pathophysiology

The stomach produces pepsinogen and hydrochloric acid and is responsible for the first phase of food digestion. Normally, the stomach accommodates a large meal with different physical and chemical compositions over a short period, and it can expand 10–15 times greater than its empty state volume, without a significant increase in intraluminal pressure. This occurs because of receptive relaxation of the stomach musculature [7]. Water may empty from the stomach rapidly [7,8]. Digestible solids empty after they are minced to form chyme, which contains particles <2–3 mm in size [7,9]. Liquids and digestible solids are emptied in the digestive period that lasts 2–3 hours after a meal. However, the stomach retains large food particles (>5–7 mm) that escape mincing during the digestive period, and then forcefully dumps them into the small bowel during the interdigestive period [7,10]. Therefore, the stomach allows the delivery and storage of food (accommodation), proceeds with a second phase of grinding the food in small fragments (trituration), and, finally, the third phase is characterized by the propulsion of the chyme toward the duodenum (emptying).

Gastric emptying is facilitated by the vagus nerve that controls the fundic accommodation, antral contraction, and pyloric relaxation. Additionally, this regional gastric motility is mediated by the interstitial cells of Cajal and the enteric neurons, regulating the gastric pacemaker and smooth muscle activity, respectively [11,12]. The derangement in extrinsic neural control due to vagal dysfunction, as well as dysfunction of intrinsic nerves, cells of Cajal, and smooth muscle result in abnormal gastric emptying.

Finally, there are many components affecting gastric emptying including hormones. It is well known that many hormones, such as cholecystokinin, leptin, glucagon-like peptide (GLP)–1, glucagon, oxyntomodulin, peptide YY, gastrin-releasing peptide, enterostatin, pancreatic amylin, and pancreatic polypeptide, slow down gastric emptying, while ghrelin and motilin accelerate it. Some of these hormones, along with other mediators, act on other control centers to coordinate gastric motility with satiety, food intake, and energy balance. These hormones are released based on the characteristics of the food ingested and their metabolism [7].

Clinical presentation

Typical symptoms of gastroparesis include nausea, vomiting, abdominal pain, bloating, and early satiety [13,14]. Some patients also present with regurgitation, acid reflux, and frequent belching. These symptoms, usually present in clusters with pain, nausea, and bloating in the idiopathic type versus nausea, early satiety, and vomiting in the diabetic type. However, presentation may vary significantly from patient to patient, and symptoms may overlap greatly among different types of gastroparesis or with other dysfunctional disorders like dyspepsia. Other related symptoms may include those observed in dumping syndrome (sweating, hypotension, hypoglycemia, etc.). This may happen because of significant gastric distention that builds up intragastric pressure with subsequent gastric evacuation of a large nutrient load to the small bowel. This erratic gastric emptying may impair adequate glucose control in diabetic patients and may be associated with diarrhea. Dehydration, electrolyte imbalance, and mental status changes may appear due to frequent vomiting or even diarrhea. While patients with gastroparesis may have a myriad of clinical presentations, a poor quality of life is common.

Gastroparesis is often divided into subsets based on etiology or associated conditions, pathogenesis, pathophysiology, histopathology, or ultrastructure, and association with pain or bloating; however, the utility of these subsets in the diagnosis and treatment is still not well defined [15].

Causes

Major causes of gastroparesis are diabetes (29%), postsurgical (13%), and idiopathic (36%) [12,16]. Other causes may include metabolic diseases, neuromuscular dysfunction, collagen vascular disease, viral infection, and other iatrogenic (pharmacologic) (Table1). Diabetes is the most commonly recognized systemic disease associated with gastroparesis. The 10-year incidence of gastroparesis is 5.2% in type 1 diabetes and 1% in type 2 diabetes [12]. Postsurgical gastroparesis is most commonly associated with vagal nerve

Table 1
Causes of gastroparesis

Causes
Diabetes
Postsurgical
Idiopathic
Metabolic
Post–viral infection
Iatrogenic

Table 2
Diagnosis

Diagnosis
Gastroparesis Cardinal Symptoms Index
Esophagogastroduodenoscopy
Gastric emptying scintigraphy
Stable isotope breath test
Wireless motility capsule

injury during foregut surgery. A study based on the National Institute of Diabetes and Digestive and Kidney Diseases gastroparesis consortium showed that Nissen fundoplication is now the most common cause of postsurgical gastroparesis (52%), followed by partial gastric resection (22%), myotomy (9%), esophago-gastrectomy (9%), stomach stapling (4%), and vagotomy (4%) [17]. Idiopathic gastroparesis is the most common cause of gastroparesis with no apparent underlying abnormality (36%). Most patients with idiopathic gastroparesis are young or middle-aged women [12] and individuals with overweight or obesity [14]. The most common presenting symptoms were nausea (34%), vomiting (19%), and abdominal pain (23%) [14]. Medications causing delayed gastric emptying include those used to treat type 2 diabetes. Some amylin analogs or GLP-1 agonists that inhibit vagal function may cause iatrogenic pharmacologic gastroparesis [15,18,19]. Post–viral infection gastroparesis has been associated with Epstein-Barr virus, cytomegalovirus, and herpes virus [12,20]. Rare causes of gastroparesis include Parkinsonism, amyloidosis, scleroderma, paraneoplastic disease, and mesenteric ischemia [16].

Less frequent causes of gastroparesis

Other conditions associated with nonobstructive delayed gastric emptying include gastroesophageal reflux disease, achalasia, atrophic gastritis, celiac disease, functional dyspepsia, and hypertrophic pyloric stenosis, along with common medications including opioids, anticholinergics, proton pump inhibitors, alcohol, tobacco, and progesterone [21]. Multiple diagnostic tests are utilized in the diagnosis of gastroparesis as follows (Table 2).

Diagnostic testing for gastroparesis

Gastric emptying scintigraphy

Gastric emptying scintigraphy (nuclear medicine gastric emptying study) involves the ingestion of a solid meal containing a radioisotope with a short half-life, most commonly Technetium-99m (99mTc). Gastric emptying scintigraphy is considered the gold standard in the diagnostic work-up of gastroparesis. Solid state scintigraphy is most commonly performed and involves the radioisotope labeling of 120 g (4 ounces) of egg whites to be ingested with 2 slices of toasted white bread topped with 30 g (1 tablespoon) of strawberry jam with 120 mL (4 ounces) of water, and it is considered the gold standard [21,22]. Important time intervals in image acquisition include those at baseline and 60, 120, 180, and 240 minutes. Images at 240 minutes have demonstrated an ability to detect 30% more cases of gastroparesis [21]. Upper limit normal values include 90% retention at 60 minutes, 60% retention at 120 minutes, 30% at 180 minutes, and 10% retention at 240 minutes [23]. Patients who cannot tolerate solid meal ingestion have been studied with a liquid nutrient meal (Ensure Plus) which demonstrates a similar gastric emptying profile; however, these alternative test meals have not been validated. Patients must be free of prokinetic agents (48 hr), opioids (48 hr), anticholinergic agents (48 hr), and antidepressants, calcium channel blockers, and gastric acid suppressants for 72 hours prior to scintigraphy. Additional medications that need to be discontinued include laxatives, atropine, octreotide, nifedipine, progesterone, theophylline, benzodiazepine, and phenolamine. Blood glucose levels need to be controlled (<200 mg/dL) for accurate assessment. Contraindications include pregnancy, breastfeeding, egg allergy, hypoglycemia, hyperglycemia, and recent nuclear medicine study.

Stable isotope breath test

The isotope breath test incorporates a stable isotope, most commonly carbon 13 (^{13}C) in a substrate such as octanoic acid or Spirulina platensis (blue-green algae) to measure the rate of gastric emptying as reflected by the excretion of $^{13}CO_2$ in the breath. The test is conducted over 240 minutes after an 8-hour fast, collecting breath samples at 30-minute intervals, and has been validated as an alternative to gastric emptying scintigraphy [24]. Results can be affected by factors that change endogenous CO_2 excretion including physical activity, malabsorption, pancreatic exocrine insufficiency, significant lung or liver disease, and cardiac failure. The isotope breath test does not involve ionizing radiation and can be used safely in pregnancy, during breastfeeding, and in children.

Wireless motility capsule

The wireless motility capsule that is commonly used to measure colonic transit in suspected slow transit constipation has been additionally approved by the U.S. Food and Drug

Administration (FDA) for the evaluation of gastric emptying. The wireless motility capsule measures pH and passage into the duodenum is demonstrated by an abrupt rise in the measured pH. The correlation between the wireless motility capsule and gastric emptying scintigraphy is only 52.5%, suggesting that further validated studies in patients with gastroparesis are required [25,26].

Esophagogastroduodenoscopy

Esophagogastroduodenoscopy (EGD) is utilized to assess possible other causes that mimic the symptoms of gastroparesis including stigmata of gastroesophageal reflux disease, achalasia, atrophic gastritis, hypertrophic pyloric stenosis, and malignancy. If an EGD does not find a cause for symptoms, further investigations of gastric motility and the functional etiologies of symptoms should be pursued.

Gastroduodenal manometry

Gastroduodenal manometry is the fasting and postprandial intraluminal measurement of the pressure activity in the distal stomach and duodenum [24]. The test is only performed in a few specialized centers. In the postprandial period, a distal antral contraction of $<$40 mm Hg is suggestive of a myopathic disorder, such as gastroparesis [24].

Gastroparesis Cardinal Symptom Index

The Gastroparesis Cardinal Symptom Index (GCSI) is a reliable and valid instrument for measuring symptom severity and is based on 9 questions divided into 3 subscales: (1) postprandial fullness/early satiety (4 questions); (2) nausea/vomiting (3 questions); and (3) bloating (2 questions) [27]. It is most commonly used in clinical trials to assess the response after treatment of gastroparesis and is not currently used in clinical practice to determine which patient(s) should undergo confirmatory testing.

Treatment options for gastroparesis

The treatment of gastroparesis is multidisciplinary and should include medical, endoscopic, and surgical treatment options (Fig. 1).

Medical management of gastroparesis

Nonpharmacologic therapies.Smoking and alcohol cessation are recommended in patients with gastroparesis. Small frequent meals with a low-fat, low-fiber diet is desirable. Food with small particle size or even liquid meals may be indicated if the patient is not able to tolerate meals with regular consistency. A dietician may help tailor the diet for each patient's caloric and diet consistency requirements, while maintaining the low-fiber and low-fat diet. Weight loss of $>$5%–10% over a period of 3–6 months should prompt changes in the dietary plan, and appropriate pharmacologic and nonpharmacologic therapies may be added. In patients with no small or large bowel dysmotility, enteral nutrition via feeding tubes may help maintain nutritional requirements for weight goals. Parenteral nutrition should be considered in patients with bowel motility disorders and inability to tolerate enteral feeding. The risks and benefits of parenteral nutrition should be weighed and discussed with the patient before initiation. A long-term exit strategy should also be discussed.

Pharmacologic management

Options for pharmacologic management include prokinetic drugs, hormonal drugs, and drugs for symptomatic

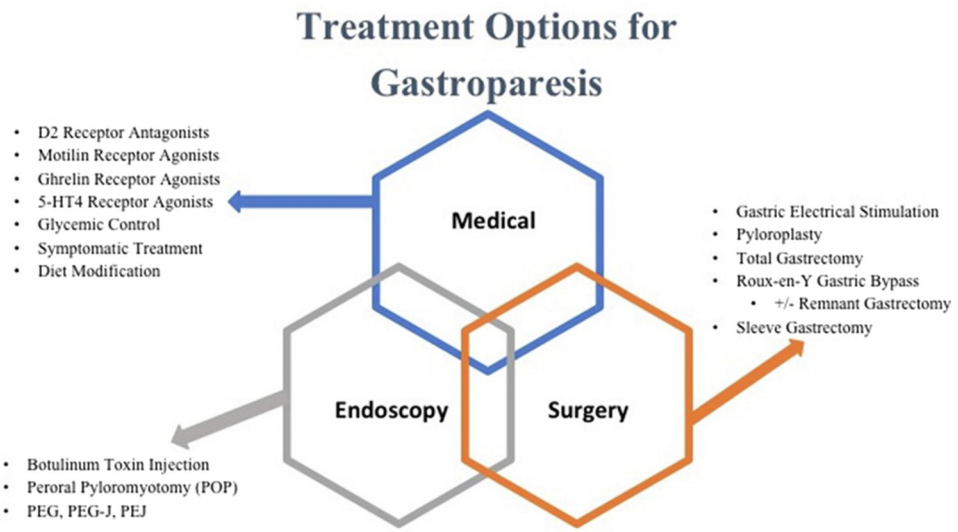

Fig. 1. Treatment options for gastroparesis. PEG = percutaneous endoscopic gastrostomy; PEG-J = percutaneous gastrostomy with jejunal extension; PEJ = percutaneous endoscopic jejunostomy.

control. Prokinetic drugs include dopamine 2 (D2) receptor antagonists, motilin receptor agonists, ghrelin receptor agonists, and 5-HT_4agonists.

D2 receptor antagonists

Drugs that exert prokinetic activity via interactions with the D2 receptor antagonist include metoclopramide and domperidone.

Motilin receptor agonists

Drugs that exert prokinetic activity via interactions with the motilin receptors include macrolides and camicinal [28,29].

Ghrelin receptor agonist

Ghrelin receptor agonists increase gastrointestinal motility through their actions on vagal, central, and enteric nervous system receptors [30]. Relamorelin is one such drug that has been studied in multiple studies [31,32].

5-HT_4 receptor agonists

Prucalopride is a highly selective 5-HT_4 receptor agonist that improves gut motility [33].

Glycemic control

In patients with diabetes, acute hyperglycemia is associated with delayed gastric emptying and other gastrointestinal symptoms in both type 1 and type 2 diabetes[34]. While earlier studies did not show any significant association between long-term glycemic control, that is, HbA1C levels and gastric emptying [35–37], more recent studies have shown that higher HbA1C is associated with delayed gastric emptying [38,39].

Symptomatic treatment

Given the antiemetic effects of ondansetron (5-HT_3 antagonist), prochlorperazine (phenothiazine), and promethazine (antihistamine), these agents have been used for symptomatic relief in patients with gastroparesis. A large cross-sectional study surveying patients with gastroparesis showed close to 43%–46% satisfaction rates, with antiemetics like ondansetron, promethazine, and prochlorperazine [40]. All 3 medications can lead to QTc prolongation and thus should be avoided in patients who are being treated with erythromycin or domperidone. In addition, promethazine is also associated with sedative effects.

There has been increased interest in the usage of cannabinoids in the symptomatic treatment of gastroparesis. In 2 cross-sectional studies, a subset of patients using marijuana reported improvement in nausea and abdominal pain associated with gastroparesis [41,42]. A small cohort study without a control group also showed that cannabinoids can improve overall symptoms of gastroparesis significantly, including abdominal pain [43]. This study included patients whose symptoms were refractory to standard gastroparesis therapies, including medical, endoscopic, and surgical therapies.

A small number of controlled trials have looked into the symptomatic treatment (i.e., treatment of nausea and vomiting) of gastroparesis, including neurokinin-1 (NK1) receptor antagonists and tricyclic antidepressants. Aprepitant is an NK1 receptor antagonist that acts centrally via vagal sensory and motor pathways in the brainstem [44]. It is thought to reduce nausea, regardless of its cause. It has also been shown to have significant benefit over traditional medications like ondansetron in treating chemotherapy-associated nausea and postoperative nausea and vomiting [45,46]. Although a few case reports were published demonstrating its benefits in treating nausea in patients with gastroparesis [47–49], it has not been shown to have significant benefits over placebo in a randomized controlled trial (RCT) [50]. Another drug in the same class, tradipitant, is currently under study. A full report of findings has not been published yet, but a placebo-controlled, double-blinded RCT presented in 2019 showed that it was associated with significant improvement in nausea scores and nausea-free days when compared with placebo in patients with gastroparesis [51]. Tricyclic antidepressants were assessed for symptomatic treatment of gastroparesis in RCTs and did not show any significant benefit [52,53]. Promethazine, prochlorperazine, and ondansetron can be used as an adjunct to prokinetics in the symptomatic treatment of nausea and vomiting associated with gastroparesis. These medications should be avoided when using prokinetics with QTc prolonging properties. Novel NK1 receptor antagonists, including aprepitant and tradipitant, may be used as a last resort to relieve symptoms of nausea in gastroparesis.

Endoscopic treatment

Several endoscopic interventions have been demonstrated to be very effective and less invasive to control the symptoms and delayed gastric emptying associated with medically refractory gastroparesis. However, the appropriate timing and type of procedure requires further research. There are several endoscopic interventions whose main focus is to improve the “pyloric dysfunction” and the gastric emptying. Endoscopic pyloric dilation and stenting have been described, but not widely used. We describe the 2 more widely used endoscopic procedures: botulinum toxin injection and peroral pyloromyotomy (POP). As newer endoscopic therapeutic options develop, these may appear more “attractive” due to the less invasive nature of these procedures when compared with surgery.

Botulinum toxin injection

Recently, the novel application of endoscopic functional luminal imaging probe (Endoflip; Medtronic Inc.) to study the pyloric sphincter has allowed for better characterization of its role in the pathophysiology of gastroparesis [54–56].

Moreover, current research has reported increased fasting pyloric pressure and decreased pyloric compliance in gastroparesis compared to healthy volunteers [56]. Thus, the focus of management strategies for refractory cases remains on the pylorus [12,57–63]. Among existing options, botulinum toxin A (BTA) injection is a readily available alternative for patients with persistent symptoms who prefer a nonoperative approach [57,59,64].

BTA is a bacterial neurotoxin that causes chemical denervation by irreversibly disrupting the release of acetylcholine from the presynaptic cholinergic terminals in the neuromuscular junction [57,59]. In gastroparesis, BTA disrupts pyloric myoelectrical activity and inhibits substance P signaling [65]. Hence, BTA can theoretically induce relaxation of the pyloric sphincter and improve gastric emptying [66,67]. Moreover, pyloric BTA injection has led to a significant reduction in nausea, fullness, and bloating in several case series and observational studies in patients with idiopathic and diabetic gastroparesis [68–75]. Generally speaking, pyloric BTA injection is associated with symptom amelioration in 40%–60% of patients, lasting 1–5 months after treatment, and with gastric emptying improvements of 30%–50% [68–75]. However, the validity of this evidence is curtailed by retrospective study designs, uncontrolled enrollment, and high risk of selection and recall bias.

In response to the initial studies, 2 randomized, double-blinded controlled trials evaluating BTA injection versus placebo were carried out [76,77]. The first one, by Arts et al. [76] enrolled 23 patients with gastroparesis in a cross-over design. Patients underwent 2 upper endoscopies at 4-week intervals. In each procedure, they were injected with either BTA (100 IU) or placebo (saline). Symptoms were evaluated through a validated questionnaire and gastric emptying was assessed before the start of the study and 4 weeks after each treatment. Interestingly, both the BTA and saline groups showed significant improvements after the first injection, with no changes noted thereafter. Notably, BTA caused significant improvement in gastric emptying. Similarly, Friedenberg et al. [77] failed to demonstrate a difference in outcomes at 1 month postendoscopy after randomizing 32 patients with gastroparesis to BTA injection (200 IU) or placebo (saline). Again, gastric emptying was accelerated by BTA therapy, although this time it did not reach statistical significance. The results of these trials have led to the decline of pyloric BTA injections as a treatment for gastroparesis [12,58,63]. It is important to mention, however, that both studies were underpowered, had small sample sizes, lacked proper patient selection (BTA should not be offered to patients without pyloric dysfunction), lacked objective measurement of the effects of BTA injection in pyloric physiology, and enrolled heterogeneous gastroparesis populations that may have confounded the results.

Even when accepting the findings of these trials in full, a subset of patients experienced improvement after pyloric BTA injection. The failure to find differences may be explained by suboptimal administration of BTA, or by incorrect selection of subjects. Rather than a unique disease, gastroparesis may be a diverse collection of gastric neuromuscular abnormalities that share the same clinical presentation but different mechanisms [57].

The conflicting evidence calls for further controlled prospective research with close attention to patient selection and should consider the addition of endoscopic ultrasound guidance to overcome technical difficulties as only high-quality investigations will provide definitive answers. Although consensus is still elusive, it is clear that pyloric BTA injections may not improve symptoms and may further complicate future definitive treatment. Until better evidence is available, endoscopic BTA pyloric injections to treat gastroparesis should be a last resort option in carefully selected patients who demonstrate normal gastric neuromuscular function and persistent bothersome symptoms.

Peroral pyloromyotomy

The first POP was described by Khashab et al. [78] in a human patient in 2003. This novel procedure involves the creation of a submucosal tunnel to access and cut the muscular fibers of the pyloric sphincter [79], following the concept of peroral endoscopic myotomy (POEM) developed by Inoue et al. [80] in 2010 for the treatment of esophageal achalasia. This innovative technique of third space or submucosal surgery has favorable reports in patients with gastroparesis [81,82] and is a promising tool in the post–bariatric surgery population with concomitant or postsurgical gastroparesis.

Given the observed values of gastric emptying studies and the GCSI after the procedure, it is most recommended for patients who have delayed gastric emptying of $>$20% at 4 hours, and a GCSI score of $>$2.5, as they would benefit the most by this intervention, especially for patients whose predominant symptoms fall in the nausea/vomiting subsection of GCSI. Patients who might not be good candidates for a POP procedure are those who are unable to tolerate general anesthesia, have severe coagulopathy, have contraindications for endoscopy, or have undergone a previous partial gastrectomy including the antrum [83].

The rising number of patients with obesity and gastroparesis is alarming [84]. Gastroparesis can appear concomitantly with obesity [85] or in some instances after bariatric surgery [84]. There is no standardization of the evaluation process or confirmation of diagnosis, especially in patients who have undergone bariatric surgery. Few reports have documented success with POP after sleeve gastrectomy (SG) [86]. In the bariatric population, knowledge of endoscopic postsurgical anatomy is critical. In sleeve anatomy, ruling out stenosis and spiraling is paramount. Although imaging studies are useful to assess the anatomy, functional studies are not standardized. It is important to consider that weight loss surgery, such as laparoscopic SG, might alter the preoperative gastric motility, resulting in a

significantly accelerated gastric emptying for liquids and solids after the procedure [87,88]. While further studies are needed to confirm these findings, post–laparoscopic SG status should be taken into consideration when interpreting the results from gastric emptying studies in these patients.

POP is generally performed under general anesthesia in an operating room or endoscopic suite [83,89,90], with a 3-day clear liquid diet and 12 hours of nothing by mouth before the procedure [79]. Although at the beginning of this new approach, antibiotic prophylaxis was administered in every patient, new studies suggest that this decision must be tailored on a patient-to-patient basis. Intravenous antibiotic prophylaxis should be especially considered in patients at higher risk of infectious complications, such as those who are immunosuppressed or have cardiac conditions [90]. POP starts with a routine upper gastrointestinal exploration (EGD) with a standard front-viewing gastroscope, fitted with a transparent, silicon-based, beveled endoscopic cap secured with tape, permanent CO_2 insufflation, and warm irrigation. Once the pyloric ring is located, a submucosal bleb is formed with a sclerotherapy needle 3–5 cm proximal to the pylorus at the lesser curvature of the stomach [89]. Submucosal lifting agent in gel or a solution prepared with 20 mL 1% methylene blue with 500 mL .9% saline and 1 mL 1:1000 epinephrine can be used. In our center, we favor gel lifting agents. Once the bleb is formed, and mucosal elevation is maintained, a 1.5–2 cm transverse mucosotomy is performed with a triangular tip (TT) knife, on dry cut mode, at 50 W, effect 3 (ERBE settings). The initial portion of the submucosal tunnel is created by deflecting the inferior mucosal flap downward by hooking the knife on the mucosal edge. The scope is then inserted through the mucosotomy to access the submucosal plane by catching the inferior mucosal flap with the beveled edge of the cap, which should be placed at the 6 o'clock position. The tunnel is created with the TT knife, on spray coagulation mode, at 50 W, effect 2 (ERBE). Permanent injection of the solution mentioned previously and the CO_2 insufflation should facilitate dissection of the submucosal space until the pyloric ring is visible. A Coagrasper (Olympus) in soft coagulation mode, at 80 W, effect 5 (ERBE) may be used to ensure hemostasis when encountering larger vessels [81]. Dissection should not extend further than .5 cm into the postpyloric channel due to increased risk for duodenal perforation [83]. The duodenal mucosa will be visible as stained fibers perpendicular to the pylorus. Once the pyloric ring becomes noticeable, white fibers against the methylene blue–stained submucosa and serosa, pyloromyotomy is performed by selectively dividing the inner circular muscle bundle in a distal to proximal fashion with a TT or insulated tip knife, on spray coagulation mode, at 50 W, effect 2 (ERBE). Exerting constant pressure with the gastroscope and insufflating with CO_2 might help carefully divide the avascular fibers of the pyloric ring, layer by layer, to avoid full-thickness perforation. After the myotomy is complete, meticulous hemostasis is verified before withdrawing the scope from the tunnel. Finally, the mucosotomy is closed in a stepwise fashion with endoscopic clips as necessary. The gastroscope is then removed so the patient can be extubated and transferred to the postanesthesia recovery unit [89].

Postsurgical care for POP has changed in the past few years, from a more conservative approach initially to a more expedited postprocedure early-discharge enhanced recovery after surgery (ERAS) protocol proposed by Landreneau et al. [90]. This POP ERAS care pathway includes discharge after postanesthesia observation, starting a limited volume of clear liquids immediately after recovery, and no routine imaging before discharge, as opposed to inpatient management, nothing by mouth overnight, and upper gastrointestinal series on postoperative day 1 to rule out leaks before diet progression [83]. While Tao et al. suggest maintaining proton pump inhibitor therapy for 8 weeks after the procedure [83], it should be at least administered during the first 2 weeks in combination with a mucosal coating agent such as sucralfate to prevent ulceration over the mucosotomy site [90,91]. It is also recommended that patients maintain a full liquid diet for 2 weeks postoperatively [90]. It is essential to mention, however, that this same-day discharge protocol was adopted at a tertiary referral center after a certain number of successful procedures had been performed with the original postprocedure conservative care pathway, which could be the safest option for surgeons and centers that are just getting started with this technique. Patients should also be adequately educated to recognize early warning signs that might be related to rare but possible complications such as leakage [90].

Peroral pyloromyotomy appears to be a safe and effective option for the treatment of medically refractory gastroparesis, with a significant improvement both in subjective GCSI and objective gastric emptying study scores with minimal complications [81,92]. Another benefit of this technique is that it does not preclude another, more invasive, surgical procedure if symptoms persist, such as gastric electrical stimulator placement, gastrectomy, or bypass. It does not radically alter the anatomy or need an external incision, and does not affect the peritoneal space, so it is less likely to cause severe adhesions or scarring, preserving all surgical options for the future if the treatment fails. POP can be considered a first-line, organ-sparing intervention for refractory gastroparesis [92].

There is a paucity of data supporting the use of POP. Much of the early published evidence is limited to small series and is often retrospective in nature. POP has been shown to compare favorably with laparoscopic pyloroplasty. A recent comparative cohort study [92] showed that POP had a shorter length of stay (1.4 versus 4.6 d), shorter operative time (33.9 versus 99.3 min), and lower complication rate (3.3% versus 16.7%). Further, significant improvements were found in both GCSI scores and objective gastric

emptying in both procedures. Another small retrospective series looked at outcomes with a median follow-up of 14.5 months and showed clinical success in 13 of 16 (81.25%) patients [93]. Interestingly, univariate regression analysis demonstrated that GCSI and gastric emptying studies had significant associations with the future clinical outcomes of the patients, but this was not confirmed in multivariate analysis.

A recent meta-analysis evaluated the outcomes of POP in 11 studies and 332 patients [90,94]. This showed a success rate of 75.8% (GCSI score) and 85.1% based on 4-hour gastric emptying study results, which, in both cases, compared almost identically (77.3% and 84%) with surgical pyloroplasty. Based on regression analysis, idiopathic gastroparesis, prior treatment with botulinum toxin, and previous treatment with a gastric stimulator have positive predictive effects on the 4-hour gastric emptying study results after POP. Another recent meta-analysis looked specifically at postsurgical gastroparesis [95] and found that success rates by GCSI and 4-hour gastric emptying study results were 89.6% and 81.5%, respectively. While pre- versus postprocedure 4-hour gastric emptying study rates were compared and showed improvement (93.8% versus 44.5%), these results were not statistically significant.

Another study examined the results of POP with recurrent or persistent symptoms after gastric electrical stimulation was performed [96]. In this series, GCSI improved by an absolute reduction of 1.63 points, with significant improvements in all subscores. Operative time and length of stay were short in this series (40 min and 1.4 d, respectively). A recent small prospective trial evaluating POP [97] showed significant improvement in GCSI, quality of life, and gastric emptying studies at 3 months (assessed by T1/2).

Although more published studies showing medium- and long-term follow-up are needed, early results with small series of POP show promise. At a minimum, POP appears comparable to laparoscopic pyloroplasty and should be considered in patients that are refractory to the medical treatment of gastroparesis.

Percutaneous treatment in gastroparesis

Percutaneous endoscopic treatment options aim to manage symptoms and provide enteral nutrition. As care is escalated in patients with refractory gastroparesis, the percutaneous options available include the following:

- Percutaneous endoscopic gastrostomy (PEG)
- Percutaneous gastrostomy with jejunal extension (PEG-J)
- Percutaneous endoscopic jejunostomy (PEJ)

The PEG tube has been used in venting the dysfunctional organ. It is important that the gastrostomy tube used is a large enough diameter to vent effectively. It has been postulated that venting of gastric gas and secretions would aid in decreasing vomiting and the sensation of fullness. This approach may be of limited utility especially since much of the bloating experienced by patients is due to bacterial overgrowth of the small bowel [98]. Limited data exist for the sole use of a PEG in the management of gastroparesis, as this approach is primarily aimed at symptomatic relief in the short term. Nonetheless, Kim et al. described patients in whom venting PEG tubes were placed and vented 5–6 times per week [99]. With continued oral intake, this group experienced significant, sustained improvement in symptoms and a mean weight gain of 4.5 kg in the first year and 7.3 kg over the long term [99]. However, when patients are unable to meet their nutritional needs with limited oral intake, the added benefit of a PEG-J can be seen. The progressive gastric dysfunction limits the ability of PEG to provide nutrition, given the delayed gastric emptying. As such, placement of a PEG-J offers the potential added benefit of dual lumens that permit the patient to vent gastric secretions and limit emesis while providing for postpyloric enteral feeding. Strijbos et al. utilized a stepwise approach with PEG-J as the final path [100]. In a group of 86 patients, 19 progressed to require a PEG-J. Symptomatic relief was observed in 84% of patients with a mean weight gain of 5.1 kg with 6 months of PEG-J placement. These patients were also able to maintain some oral intake in addition to the enteral tube feeding. Sixteen percent of the patients treated with PEG-J were ultimately able to resume complete oral intake with removal of PEG-J in 11 months [100].

In addition to PEGs and PEG-Js, PEJs have been utilized in the management of gastroparesis [101–103]. The sole purpose of PEJ is to optimize enteral alimentation. This procedure, while technically challenging, can be accomplished without the need for a laparotomy. Toussaint et al. reported a success rate of 78.6% [101]. However, a complication rate of 36.4% was also noted. More recently, Lim et al. reported a 90% success rate with PEJ placement over a 10-year period with a 30-day complication rate of 13% [103]. When comparing PEG-J with PEJ, Fan et al. reported lower reintervention rates for PEJ when compared with PEG-J (9.0% versus 39.5%); reinterventions were primarily due to tube migration [104]. Lim et al. reported reintervention rates of 31% versus 75% favoring PEJ. Feeding tube patency was also noted to be better with PEJ [103].

Percutaneous options are considered safe, and when compared with surgery, can provide a less invasive alternative in the management of gastroparesis. Complications for PEGs include pain, hemorrhage, pneumoperitoneum, and gastrocolic fistula. Late complications include stoma site infections, aspiration, tube dysfunction, and skin site issues (i.e., buried bumper, excessive granulation). PEG-J adds the potential for luxation of the jejunal extension and potential complications of PEJ including jejunal volvulus as well as a jejuno-colic fistula. When comparing PEG-J with PEJ, Fan et al. found a reintervention rate of 39.5% versus 9%, respectively [104].

These percutaneous procedures aid in the management of patients with limited response to first-line medical management. Each procedure provides potential benefits as well as risks. Patient symptoms, nutritional, and physiologic status will ultimately dictate the optimal option for the individual patient.

Surgical treatment

There are many surgical options available for the treatment of gastroparesis when nonoperative management fails. Before surgical referral, patients with gastroparesis have commonly experienced years of ineffective treatment and often have broader gastrointestinal dysmotility disorders. Therefore, it is imperative to align the potential benefits of surgical recommendations with each patient's symptoms and therapeutic objectives. For patients experiencing malnutrition, especially in the setting of global gastrointestinal tract dysmotility, gastric or jejunal feeding tubes may be effective initial surgical interventions. Gastrostomy may also improve symptoms of nausea and vomiting by venting and drainage of the stomach.

Gastric electrical stimulation has now been used to treat gastroparesis for nearly 2 decades. A 2017 systematic review and meta-analysis found that in 5 randomized trials, improvement of symptoms was not superior to sham intervention. However, in 16 open-label studies, gastric electrical stimulation did significantly improve symptoms. Placebo responses in gastroparesis trials suggest that cognitive influences on symptoms may be significant [105].

Laparoscopic pyloroplasty was shown to be safe and effectively improved gastric emptying in 90% of patients with gastroparesis in a 2016 study. It also significantly improved nausea, vomiting, bloating, and abdominal pain; however, two thirds of the patients in this study underwent fundoplication concurrent with pyloroplasty [106].

Gastric bypass with or without gastric resection is another effective treatment for gastroparesis. Diabetes is frequently associated with both obesity and gastroparesis. Studies have shown both significant symptom reduction as well as decreased use of prokinetics after Roux-en-Y gastric bypass (RYGB). In patients with morbid obesity, the additive benefits of weight loss and diabetes remission favor this approach [84,107].

Several case reports and small series have concluded that SG is an effective treatment for primary gastroparesis in patients with severe obesity. Improved gastric emptying has been demonstrated in patients undergoing SG [108].

Patients who have no improvement in symptoms of refractory gastroparesis after gastric electrical stimulator implantation can undergo any of the other endoscopic or surgical treatment modalities. As the opportunities for endoscopic treatment of gastroparesis expand, these options should be considered before proceeding to surgical options.

Most importantly, surgical options should be aligned with patient goals. Gastroparesis is often associated with diabetes and in these patients, gastric bypass and perhaps SG can be an effective treatment for both conditions. However, in many patients, gastroparesis may only be 1 manifestation of broader gastrointestinal motility disorders. Motility should be thoroughly evaluated before recommending any surgical intervention and the potential impact of surgery on motility and symptoms throughout the gastrointestinal tract should be considered.

Gastric electrical stimulation

Gastric electrical stimulator implantation is a surgical procedure reserved for patients with intractable symptoms of gastroparesis who remain symptomatic despite conservative management [109]. The idea of using gastric electrical stimulation was predicated on the knowledge that the human gastrointestinal tract is made up of natural pacemakers, the interstitial cells of Cajal, and a depletion of such cells is thought to be present in gastroparesis [110].

In general, 3 patterns of electrical stimulation have been studied: (1) gastric neurostimulation with short stimulus pulses; (2) gastric pacing with synchronized long pulses to restore gastric slow waves; and (3) microprocessor-controlled induction of propagated antral contractions [111]. Gastric neurostimulation is the only gastric electrical stimulation modality that is clinically available and consists of low-energy stimulation applied in nonsynchronized, high-frequency cycles of short pulses with a stimulation cycle well above the normal 3 cycles per minute [111]. It has been commercially available (Enterra Therapy System; Medtronic Inc.) through the FDA human device exemption program since 1993.

Gastric electrical stimulation preoperative preparation

The main indication for gastric electrical stimulator placement is the presence of gastroparesis (diabetic or idiopathic) with concomitant severe nausea and vomiting ($\geq$1 episode daily) who are refractory to medical management for at least 1 year [112]. Other relative indications include recurrent severe dehydration and need for parenteral/enteral nutrition. The procedure is contraindicated in patients that are not fit for a surgical intervention due to physical or mental conditions.

The gastric electrical stimulation device is incompatible with magnetic resonance imaging (MRI) and explantation of the device is necessary prior to MRI [109]. As such, in patients with anticipated need of frequent MRI, serious consideration should be given to alternative strategies [109].

The device is implanted surgically under general anesthesia, commonly via laparotomy or minimally invasive surgical techniques [109]. Preoperative antibiotics and venous thromboembolism prophylaxis are given. The system consists of a neurostimulator and 2 leads [113]. The leads with the electrodes are fixed to the greater curvature gastric

wall, typically at the level of the distal body. It is paramount to place the leads in the seromuscular layer of the stomach and not to breach the mucosa. Placement of the leads through the mucosa, in fact, will lead to an infection of the leads, and subsequently of the subcutaneous generator. In order to assure that the mucosa is not breached, direct endoscopic surveillance is utilized. The 2 leads are then exteriorized to the left lower quadrant where they are attached to the neurostimulator placed in a subcutaneous pocket [114]. The impedance of the stimulator is checked intraoperatively. The battery life is approximately 5–10 years.

Gastric electrical stimulation postoperative care

Patients are often hospitalized with a recovery time of 1–3 days, based on the oral tolerance. The preoperative medical therapy for gastroparesis is usually resumed postoperatively, with a goal of weaning from the treatment over time once the settings of the pacemaker are tailored to the symptoms [109]. Patients are seen several weeks after discharge for assessment of the incision and toleration of the diet, and then they are followed every 3–12 months depending on their clinical condition [109].

At follow-up visits, medications are reviewed, and the gastric electrical stimulator is interrogated and adjusted as needed. The impedance between the electrodes should be $<800\Omega$ or electrode displacement may be present. For persistent symptoms, the stimulator parameters are typically increased, beginning with the current from 5 to 7.5 mA and then to 10 mA. Subsequently, the frequency can be increased from 14 to 28 Hz, and then to 55 Hz. Rarely, the ON duration is increased from .1 to 1 second. Increasing the ON time can worsen the symptoms, cause abdominal pain, and decrease the battery life [109].

Gastric electrical stimulation failure

Reported outcomes after gastric electrical stimulator implantation have been conflicting. Data from large samples of adult patients from unblinded cohort studies have suggested long-term efficacy, with improved results reported in patients with diabetic rather than idiopathic gastroparesis [111]. However, RCTs have failed to consistently prove the benefits of gastric electrical stimulation.

A meta-analysis that included 13 studies—only 1 was an RCT, and the others were observational—showed significant improvements in severity of vomiting, nausea, total symptoms, severity scores, and validated quality-of-life scores [115]. Similarly, another meta-analysis including 10 trials—only 2 were RCTs—revealed that gastric electrical stimulation not only showed significant improvement of symptoms but also improved 2- and 4-hour gastric emptying for patients with gastroparesis [116].

In contrast, a meta-analysis of 5 clinical trials that randomly allocated 185 patients with gastroparesis who had undergone implantation of a gastric electrical stimulator to either active or no stimulation did not demonstrate significant differences in global or several key symptom-specific severity ratings, arguing against a true clinical benefit of gastric electrical stimulation and suggesting that placebo effects contribute significantly to the benefits reported in uncontrolled trials [105].

Regarding patients that fail to improve after gastric electrical stimulator implantation, it is believed that these individuals may have such severe gastric inflammation from their gastroparesis that they may not benefit from gastric electrical stimulation because the pylorus has become so stenosed that food is unable to pass [110]. For these patients, the next step may be to open the pylorus with a pyloroplasty [110].

Pyloroplasty

Pyloric interventions are among the oldest and most effective surgical procedures for the treatment of gastric outlet obstruction. Surgical pyloroplasty was first performed by a German surgeon, Dr. Walter Hermann Von Heineke, in 1886 for the treatment of an obstructive pyloric mass. Shortly after, Polish-Austrian surgeon Dr. Jan Mikulicz-Radecki (1887) reported a similar operation applied to a bleeding duodenal ulcer. These 2 reports concurred on opening the pylorus longitudinally and closing it transversely, and in recognition of both reports, this became the Heineke–Mikulicz method [117,118]. Finney (1902) and Jaboulay (1892) described other types of pyloroplasties with an associated gastro-duodenostomy. Ramstedt performed the first pyloromyotomy for what is now called idiopathic hypertrophic stenosis in 1912, which can be summarized as an extramucosal longitudinal dividing of the pyloric muscle without sutures [118]. Despite new surgical techniques that were developed (linear stapler, circular stapler in different endoluminal and extraluminal versions), the Heineke–Mikulicz pyloroplasty was widely adopted [117]. More current technological advancements, such as gastric peroral endoscopic myotomy (GPOEM) and POP, seem to be less invasive options [117].

Endoscopic transpyloric stenting has been described by Clarke et al. [119] with symptom improvement but is associated with complications, such as stent migration [60]. This procedure as well as botulinum toxin injection have demonstrated nonpermanent solutions; however, both procedures may be important temporizing interventions and may be used to preoperatively assess the potential response to a pyloromyotomy [120]. Similar to botulinum toxin injection, an endoluminal functional lumen imaging probe (Endoflip; Medtronic Inc.) may guide patient selection for pyloric interventions [121].

Pyloroplasty aims to widen the pylorus and prevent spasm. Mearin et al. demonstrated pylorospasm in 14 of 24 patients with diabetes and gastroparesis [122], so

pyloroplasty should be a reasonable treatment for those patients. However, the results have not been consistent; therefore, other factors such as the presence of concomitant antral hypomotility, or differences in compliance or "elasticity" of the pyloric area (e.g., as a result of scarring) may impact the efficacy of pyloric interventions [24]. Despite these limitations, pyloroplasty has been shown to improve or even accelerate gastric emptying, providing significant reduction in symptom severity and improvement in quality of life in patients with refractory gastroparesis [123].

Toro et al. [124] reported data from 50 patients with refractory gastroparesis that underwent laparoscopic pyloroplasty between 2006 and 2013. They reported a subjective improvement in symptoms of 82% after the procedure, which was confirmed by objective comparison of gastric emptying times. The median reduction of gastric emptying half-time (T ½) after laparoscopic pyloroplasty was 120 minutes with improved times in virtually all patients. Normalization (T ½ <60 min) and mild delay of gastric emptying times (T ½ <80 min) were achieved in 54% and 18%, respectively. Only 10% of the patients with objective improvement of gastric emptying times and persistence of symptoms required an additional gastric drainage procedure. All were performed laparoscopically without any perioperative complications.

Hibbard et al. [117] performed a retrospective review of prospectively collected data from 28 patients that underwent a minimally invasive pyloroplasty alone as treatment for gastroparesis. They reported that prokinetic use was significantly reduced from 89% to 14%. The gastric emptying T ½ decreased from 320 to 112 min and normalized in 71% of patients. Significant improvements were observed in the symptom severity score at 1 month for nausea, vomiting, bloating, abdominal pain, and gastroesophageal reflux disease symptoms. Significant improvement persisted at 3 months for nausea, vomiting, bloating, abdominal pain, and gastroesophageal reflux disease symptoms. The average length of stay was 3.71 days. Overall, 83% of patients indicated symptom improvement at their 1-month follow-up visit.

Shada et al. [106] reported data from 177 patients with gastroparesis who underwent a laparoscopic pyloroplasty. A total of 105 patients had a concurrent fundoplication for objective reflux. There were no intraoperative complications or conversions to laparotomy. Overall morbidity rate was 6.8% with 4 reoperations and 2 confirmed leaks (1.1% leak rate). Average length of stay was 3.5 days, and readmission rate was 7%. Gastric emptying scintigraphy improved in 86%, with normalization in 77%. Gastric emptying T ½ decreased from 175 ± 94 to 91 ± 45 minutes. Nineteen patients (10.7%) had subsequent surgical interventions: gastric stimulator implantation (n = 12), feeding jejunostomy and/or gastrostomy tube (n = 6), or subtotal gastrectomy (n = 4). Symptom severity scores for nausea, vomiting, bloating, abdominal pain, and early satiety decreased significantly at 3 months.

Mancini et al. [123] reported a retrospective study performed on 46 patients undergoing pyloroplasty for refractory gastroparesis. The postoperative gastric emptying scintigraphy improved in 90% and normalized in 60% of patients. Postoperative T ½ was significantly reduced as was 4-hour retention. The GCSI showed statistically significant reduction in symptom severity for all 9 categories as well as total symptom score.

In patients with refractory gastroparesis, laparoscopic pyloroplasty is an effective treatment, with an average success rate >80% for improving gastric emptying and symptoms, with very low rates of complications and very rarely mortality. It could be considered a first-line treatment when GPOEM/POP is not available or significant gastric emptying delay is present. Finally, for patients with previous gastric electric stimulation devices with persistent severe delayed gastric emptying, laparoscopic pyloroplasty may improve outcomes considerably [125].

Total gastrectomy for management of gastroparesis

Generally, patients may undergo progressive procedures (venting gastrostomies, jejunostomies, gastric electrical stimulators, pyloroplasties) to address the symptoms of gastroparesis [126]. The ultimate escalation occurs in those patients deemed to have end-organ dysfunction requiring total gastrectomy. End-organ dysfunction in this setting would include those patients deemed to have refractory gastroparesis. With time, patients with uncontrolled symptoms experience profound weight loss, malnutrition, need for nutritional support, repeated interventions/hospitalizations, and a severely diminished quality of life.

Total gastrectomy, defined as distal esophageal transection (resection of the stomach including the pylorus) with a Roux-en-Y esophago-jejunal reconstruction, is the ultimate removal of the primary offending organ in gastroparesis. Data on total gastrectomy in the management of gastroparesis are limited. Rather, we have a variety of surgical procedures including total, near-total, subtotal, partial, and completion gastrectomy, which comprise the literature in this subset of patients [127–130].

Speicher et al. reported on 44 patients who underwent near-total or completion gastrectomies in patients diagnosed with postsurgical gastroparesis [128]. When comparing preoperative and postoperative symptoms, they noted significant improvements in abdominal pain (from 97% to 59%), vomiting (from 97% to 31%), nausea (from 86% to 45%), and severe dietary intake limitations (from 57% to 7%). Postoperative complications occurred in 36% of patients, and there was 1 postoperative mortality. In the end, the symptomatic improvement in this patient population cannot be underestimated given the severely depressed preoperative quality of life [128].

Earlier studies by Forstner-Barthell et al. included 62 patients with refractory postsurgical gastroparesis [130].

Using a modified Visick grading system, the authors reported objective success in 43% of patients (postop Visick I/II). In this complex patient group (initially Visick grade III/IV), with a mean of 4 gastric procedures before the final intervention, 67% of patients reported symptomatic improvement after undergoing a near-total completion gastrectomy with a cardio-jejunal anastomosis. Preoperative nausea, vomiting, and postprandial pain were improved in these patients. However, 25 (40%) patients developed a postoperative complication including prolonged hospitalization due to pain control and narcotic withdrawal; an often under-recognized/reported problem [130]. Of note, there was also a decreased use of prokinetic and psychotropic medications in this group with a mean follow-up of 5.4 ± 0.4 years.

In a systematic literature review by Zoll et al., there were 263 patients in the partial or total gastrectomy group [129]. Total gastrectomy provided some improvement in nausea, vomiting, and epigastric pain. In their weighted statistics, 71.5% and 78.3% patients felt improvement when comparing total versus partial gastrectomies, respectively. This difference was not statistically significant. Of note, all of these procedures were performed open and therefore lacked the potential benefits of laparoscopic surgery [129].

In the minimally invasive surgery era, Bhayani et al. reported performing a total gastrectomy with esophagojejunostomy on 6 patients and near-total gastrectomy on 29 patients. This population was mixed with respect to the etiology of gastroparesis: 12 diabetic (34%), 8 idiopathic (23%), and 15 postsurgical (43%). With a mean of 6 months' follow-up, they reported significant reduction in nausea (72%), belching (79%), and bloating (89%) but less change in abdominal pain after surgery (50%). This is not unexpected because pain is the symptom that is consistently more challenging to treat. Leaks occurred in 6 (17%) patients. Another 4 patients experienced wound infections/hematoma. Length of stay was 4.5 days with no mortalities. Patients with gastroparesis of varying etiologies did well with laparoscopic total or near-total gastrectomy [131].

Patients with diabetic, idiopathic, and postsurgical gastroparesis have all undergone surgical resection to manage the recalcitrant symptoms of the disease with symptomatic improvement. However, the frailty of this subset of patients, combined with the complexity of the surgical procedure, puts these patients at risks for significant postoperative morbidity. Complications after total, near-total, and completion gastrectomy included small bowel obstruction, strictures, leaks, and death [128]. In light of these significant postoperative complications, the preoperative discussion and optimization of these patients cannot be overemphasized. These procedures are technically challenging on their own, and these patients often have undergone previous operative procedures in the overall management of their disease, which only serves to increase the operative difficulty.

While removal of the offending organ may be the overall goal, in the setting of a more extensive gastrointestinal tract dysmotility, our surgical endpoints may be more nuanced. Without conclusive evidence, one would be hard-pressed to recommend total gastrectomy as a primary procedure in the management of gastroparesis. As such, the majority of authors propose a tailored approach when surgical tools are to be employed, with the definitive total gastrectomy reserved as a last resort. However, given the significant improvement experienced by some patients, some authors have suggested that the initial surgical therapy include a total or near-total gastrectomy [127]. This is particularly expressed in the setting of postsurgical gastroparesis [128,131,132].

The choice of procedure performed will most likely remain dependent on the patient and the available skillset and specialty of the multidisciplinary treatment team.

Sleeve gastrectomy

Sleeve gastrectomy has rapidly become the predominant bariatric procedure performed worldwide and now outpaces the "gold standard" RYGB. SG involves resection of the gastric fundus and greater curvature of the stomach to create a tubular "sleeve," which is significantly less distensible and has greater intraluminal pressure, both of which contribute to early satiety. Resection of the proximal stomach and fundus decreases the reservoir function and accommodation reflexes of the stomach, resulting in increased intragastric pressure that precipitates rapid gastric emptying [133]. Together, these alter the motility mechanism of the gastrointestinal tract.

Gastric motility is involved in regulation of hunger and satiety as well as food intake. The slow waves responsible for gastric motility originate from a pacemaker region in the upper corpus of the greater curve and propagation of this bioelectrical activity spreads through the gastric musculature along the myenteric plexus and within the interstitial cells of Cajal [134]. Resection of the gastric pacemaker on the greater curve [134,135] during creation of the sleeve may result in altered electrophysiology of the stomach.

Mechanisms of action

Decreased gastric volume

In an animal model, Chambers et al. demonstrated that both RYGB and SG resulted in emptying 100% of a liquid meal in 5 minutes as opposed to sham animals who only emptied 6.1% [136]. This effect appears to be both volume dependent, with greater emptying rates after delivery of larger volumes, and due to abolition of neural regulation demonstrated by a lack of response to atropine and loss of ileal brake response to GLP-1 release [136]. Furthermore, in response to increasing nutrient density, animals who underwent SG had loss of expected negative feedback on gastric emptying after nutrient delivery to distal intestine

[136]. Together, these findings suggest that the resection of the gastric musculature with its myenteric plexus and its neurohumoral signaling mechanisms [137] interrupt the main regulators that function to slow gastric emptying; in this way, SG may be a reasonable therapy for patients with refractory delayed gastric emptying.

Distance of resection from pylorus

In a prospective study, Fallatah et al. [138] demonstrated that the distance of resection from the pylorus can influence gastric emptying and motility. When resection was carried out closer to the pylorus (4 cm), patients had increased nausea and vomiting as a consequence of slower gastric emptying; this was presumed to be secondary to interruption of antral innervation. However, at 7 cm from the pylorus, contractility of the antrum was preserved with resultant rapid gastric emptying of the newly formed sleeve and accompanying dumping-like symptoms. In contrast, Vives et al. reported faster gastric emptying with resection of antrum at 3 cm compared with 8 cm [139]. Likewise, Michalsky et al. found that radical resection of the pyloric antrum at 2.5 cm away from the pylorus did not interfere with gastric emptying after laparoscopic SG [140].

Sista et al. evaluated the impact of laparoscopic SG on gastric emptying utilizing half-emptying time [87]. Along with multiple other groups, they found decreased half-emptying time of the stomach contents for both liquids and solids [88,141,142]. In multiple studies, Melissas et al. also found increased gastric emptying 9 months after SG constructed with a 34F bougie [135,143]. In a scintigraphic evaluation of gastric emptying after SG, Bernstine et al. found no difference between pre- and postoperative gastric emptying measured as time required to empty half of a meal from the stomach (62.39 versus 56.79 min, $P = .36$) [144]; however, it is important to note that function was evaluated at 3 months postoperatively, participants served as their own controls, and SG was created using a 48F bougie with resection 6 cm from the pylorus.

Studies supporting SG for gastroparesis

Based on these reported increased rates of gastric emptying after SG, there has been increased interest in utilizing SG for treatment of gastroparesis. A small series of SG for diabetic gastroparesis showed resolution of nausea and vomiting for 3 of 4 patients [145]. Similarly, in a case series of 9 patients, SG resulted in subjective symptomatic improvement in all patients [146]. Traditionally, gastrectomy has been reserved for patients with refractory postsurgical gastroparesis. In a study by Forstner-Barthell et al., subtotal or completion gastrectomy was shown to improve symptoms in 67% of patients (n = 62) with gastroparesis, including postprandial pain, nausea, and vomiting [130]. However, due to the structural and physiologic changes in response to SG, it may be a viable alternative for treating gastroparesis.

In a published cohort of patients with medically refractory gastroparesis and delayed gastric emptying demonstrated on imaging, 19 of 122 patients were selected for laparoscopic SG [147]. These included patients with delay in fundic motility and food retention consistent with idiopathic gastroparesis as well as those with gastroparesis due to postsurgical vagal lesions (after undergoing antireflux operations) that demonstrated isolated proximal gastric accommodation failure of the fundus. The majority of patients had significant improvement in quality of life postoperatively as well as improvement of most symptoms. Of the 15 that returned for postoperative follow-up at 2 years, 20% (3 of 15) required another operation due to persistent delayed gastric emptying. Nevertheless, symptomatic success was achieved in 80% of patients after 12–60 months. Despite a limited sample size and need for reoperation among 3 of the participants, these authors demonstrated that for appropriately selected patients with gastroparesis, laparoscopic SG is a safe surgical option for gastroparesis and results in significant improvements in both symptoms and quality of life in those with fundus tonus problems and delayed gastric emptying.

In a study by Baumann et al. that assessed gastric motility, the newly formed gastric sleeve was found to lack any evidence of coordinated peristalsis while the remaining antrum had increased peristaltic waves, suggesting that the antrum is responsible for gastric emptying after laparoscopic SG [148]. In a prospective study evaluating the effect of laparoscopic SG on gastric emptying half-time in patients with morbid obesity and type 2 diabetes, Shah et al. demonstrated that gastric emptying was significantly faster in patients after laparoscopic SG compared with both lean control individuals and control individuals with diabetes and obesity [149]. More recently, Sioka et al. also found increased gastric emptying after laparoscopic SG [150]. Functionally, they demonstrated that the sleeve remained passive while the antrum had accelerated motility with rapid gastroduodenal transit time.

In summary, based on published literature, it appears that there may be a role for SG as treatment for gastroparesis. Technical details include some preservation of the antropyloric pump as well as total sleeve volume to preserve proximal peristalsis and avoid atony.

Gastric bypass with or without remnant gastrectomy

A number of surgical options are available for patients with gastroparesis that is refractory to medical therapies. Laparoscopic SG has been established as a safe therapeutic procedure in the treatment for obesity over many years [151]. SG, along with RYGB, may be of added benefit in patients with gastroparesis who have a body mass index >35 kg/m^2 [152].

Another proposed surgical therapy for gastroparesis is RYGB with or without near total gastrectomy. Gastrectomy has historically been reserved as a last resort therapy for refractory gastroparesis [12]. The literature addressing the use of RYGB with or without gastrectomy in the treatment of gastroparesis is limited to a number of case series. Most of these studies demonstrated an improvement in the symptoms of gastroparesis following RYGB. In a study of 18 patients, Watkins et al. reported an 85.7% rate of relief of nausea and vomiting symptoms following near total gastrectomy with Roux-en-Y reconstruction [153]. Wakamatsu et al. similarly reported a significant improvement in patient-reported nausea and a trend toward improvement of vomiting and abdominal discomfort following RYGB in study of 15 patients [114]. In a larger series of 44 patients undergoing total or subtotal gastrectomy for gastroparesis, Speicher et al. reported improvements in abdominal pain, nausea, vomiting, and dietary limitations [128]. Another case series from 2015 demonstrated significant improvement in nausea, abdominal pain, and bloating in 35 patients managed with total or near-total gastrectomy for gastroparesis [154]. Despite improvement in symptoms of gastroparesis, RYGB was associated with a significant morbidity of up to 37% in some of these series [131,154].

When performing a RYGB for gastroparesis, 2 main variations have been described where either a total or near total gastrectomy is performed or the stomach is left in situ. Both of these techniques have shown benefit in symptom relief in reported case series [107,114,153,154]. In a single-institution study, Landreneau et al. compared these 2 techniques in a retrospective review of 26 patients [154]. The authors reported that gastrectomy was associated with greater perioperative morbidity compared with leaving the stomach in situ with equivalent symptomatic improvement. However, patients undergoing RYGB without gastrectomy were more likely to require subsequent surgical intervention [154].

Much like SG, RYGB may have added advantages in patients with obesity and gastroparesis. In a case series examining the treatment of gastroparesis with RYGB in patients with obesity, Papasavas et al. reported marked symptom improvement as well as decreased prokinetic medication requirements following RYGB [107]. Sun et al. similarly reported a significant improvement in symptoms of gastroparesis following RYGB in a cohort with morbid obesity [84]. The safety of RYGB in populations with obesity has been well-established [155].

Therefore, when considering surgical options for medically refractory gastroparesis it is important to consider the etiology of the patient's gastroparesis, the response to previous therapies, as well as the mechanism of failure leading to gastroparesis. Both SG and RYGB have been proposed as safe surgical options for medically refractory gastroparesis with improvement in symptoms following intervention. However, data supporting the use of these surgical options in treating gastroparesis are limited. Sleeve gastrectomy and RYGB may offer added benefit in patients with obesity and gastroparesis.

Conclusions

Although multiple conditions have been associated with gastroparesis, the majority of cases are idiopathic (36%), diabetic (29%), or postsurgical (13%). Rare causes can include medication-induced, infiltrative processes such as scleroderma or amyloidosis, spinal cord injury, or central nervous system disorder [13]. Although symptoms of gastroparesis may be ameliorated with lifestyle, dietary, and pharmacologic interventions, a subset of patients may require endoscopic or surgical intervention and the etiology of gastroparesis plays an important role in determining which surgical procedure would be most beneficial. Finally, bariatric surgical procedures have shown promising results when gastroparesis is associated with morbid obesity.

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Disclosures

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Supplementary materials

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