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Endoscopic Therapies for Gastroparesis

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Abstract

Purpose of Review Gastroparesis remains a difficult-to-treat disease with limited therapeutic options. Though patients often have a common syndrome of stereotypic symptoms, the underlying pathophysiology is heterogeneous, often leading to variable treatment responses. Due to limitations in medical and surgical therapies, endoscopic options have been increasingly explored. These options can be broadly categorized into pyloric-directed therapy, non-pyloric-directed therapy, and nutritional support. In this review, we will highlight current and emerging endoscopic options, such as gastric per-oral endoscopic myotomy (G-POEM).

Recent Findings Early retrospective studies on G-POEM offer encouraging results up to one year out, with an acceptable safety profile. Other pyloric-directed therapies, such as pyloric dilation and stenting, have also been explored.

Summary While emerging endoscopic therapeutic options are encouraging, efficacy will likely depend on a better characterization of underlying pathophysiology and improved patient selection. Future prospective, controlled studies are needed.

Keywords Gastroparesis · Delayed gastric emptying · Endoscopic therapy · Gastric peroral endoscopic myotomy

Introduction

Gastroparesis, defined as a delay in gastric emptying, leads to prominent symptoms of nausea, vomiting, and early satiety. Over the past two decades, its prevalence has been on the rise, and its effect on quality of life and economic burden has been well-documented [1–3]. It has gained a notorious reputation for being a disease that is difficult to diagnose, harder to manage, and largely incurable.

Part of the difficulty lies in its heterogeneous pathogenesis, with loss of interstitial cells of Cajal (ICC), neuropathy, and myopathy being thought to play a pathogenic role in different patients [4]. These abnormalities all lead to various downstream dysfunctions, including impaired fundic accommodation, gastric dysrhythmias, antral hypomotility, antroduodenal discoordination, and pylorospasm [5, 6]. Complicating the picture further is research showing an overlap of gastroparesis with functional dyspepsia raising the possibility that factors other than delayed gastric emptying, especially visceral hypersensitivity, might contribute to a patient's symptoms [7–9]. This multiplicity of pathogenic mechanism highlights the importance of proper diagnosis, characterization of a patient's disease, and a potential need for sub-categorization of gastroparesis patients in the future.

Treatment outcomes for gastroparesis remain subpar at best. A large multicenter prospective study by the NIH-funded gastroparesis clinical research consortium found that only 28% of patients had a clinically significant reduction in symptoms at one year [10]. Existing pharmacologic and surgical options are often ineffective or limited by side effects. Recently, endoscopic options, such as G-POEM, have shown promising results. In this review, we aim to offer an update on endoscopic options available to gastroenterologists in the clinical management of gastroparesis.

Medical Therapy

The medical management starts with interventions like control of hyperglycemia and stopping medications known to delay gastric emptying. This is followed by dietary and lifestyle

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modifications [6]. Low-fat, low-residue, and small, frequent meals are usually recommended, but evidence of their efficacy was largely based on anecdotal evidence until recently [11–13]. Formal nutritional consultation remains underutilized in this population, with only a third of patients availing themselves of such services despite the fact that two-thirds are taking a calorie-deficient diet [14].

If a patient remains symptomatic, pharmacotherapy involves peripherally acting prokinetic and centrally acting antiemetic agents. Unfortunately, their long-term impact is limited by untoward side effects or tachyphylaxis.

Decades after its development, metoclopramide remains the recommended first-line therapy, followed by domperidone and macrolides [15]. Unfortunately, each of these agents has its limitations. Metoclopramide, primarily a dopamine D2 antagonist and weaker 5HT3 antagonist and 5HT4 agonist, is FDA-approved for up to 12 weeks for gastroparesis. Its chronic use is limited by a lack of long-term data [16], concerns with neurologic side effects, and an FDA black box warning for its risk of irreversible tardive dyskinesia (< 1%) [17]. While it is a good drug for treating nausea, there is little if any evidence that it is a prokinetic. Domperidone is a prokinetic, which does not suffer from neurological side effects because it does not cross the blood–brain barrier [18, 19]. However, it is only available through an investigational new drug application in the United States, and there have been concerns over its risk for QT prolongation [20, 21]. Macrolides act as motilin agonists to induce phase III of the migrating motor complex and promote gastric emptying [22]. However, they are limited by tachyphylaxis after four weeks, QT prolongation [23], and inherent risks of chronic antibiotic use [24]. Erythromycin is the most studied macrolide, but azithromycin is an alternative agent with a longer half-life and potentially less side effects [25].

Data supporting the use of centrally acting antiemetic agents as treatment for gastroparesis is lacking, but their efficacy as treatment for other etiologies of nausea was extrapolated to this population. The most widely used antiemetics are the central 5HT3 antagonists (ondasetron, granisetron), antihistamine agents (meclizine, diphenhydramine), and anticholinergic agents (scopolamine). Aprepitant, a neurokinin receptor-1 antagonist that is FDA-approved for chemotherapy-induced nausea and vomiting, recently completed a randomized clinical trial (RCT) specifically in gastroparesis patients [26]. While the primary outcome of decreased nausea and vomiting based on a visual analog scale was not met, multiple secondary outcomes showed improvement in these symptoms, so enthusiasm for its use remains.

Novel and promising medications are in development or use outside the US and could become commercially available in the near future. These include the non-antibiotic motilin agonist, camicinal [27], a selective 5HT4 agonist, velusetrag [28], and the ghrelin agonist, relamorelin [29]. Perhaps the most promising new prokinetic agent is the selective 5HT4 agonist, prucalopride, that was approved for chronic idiopathic constipation in Europe [30]. It retains the same prokinetic effects of 5HT4 agonism without the nonselective cardiotoxicity seen with cisapride and tegasorod [31]. Studies have shown that its prokinetic benefit extends to the stomach as well [32, 33]. Clinical trials in gastroparesis have shown encouraging unpublished preliminary results [34]. While it is not yet FDA-approved in the US for any use, it has gained increasing off-label usage for gastroparesis [35].

Surgical Therapy

Surgeons have long dealt with delayed gastric emptying as a complication of certain gastrointestinal operations. This was first seen in 1945 when truncal vagotomy used to treat peptic ulcer disease was complicated by delayed gastric emptying [36]. At the time, a concomitant preventative gastric drainage procedure became standard of care. More recently, prophylactic pyloroplasty has been performed to prevent delayed gastric emptying commonly seen after esophagectomy or pylorus-preserving pancreaticoduodenectomy [37].

Borrowing from the experience gained in treating postoperative gastroparesis, gastric drainage procedures are being studied as treatment for nonsurgical gastroparesis [38, 39]. Bhayani et al. performed a retrospective review of 35 patients with gastroparesis of various etiologies who were treated with palliative laparoscopic gastrectomy. At six months, symptomatic improvement in nausea and vomiting was seen in up to 70% of patients, but 17% had surgical leaks requiring repeat intervention [40]. Another review of 31 patients showed similar symptomatic benefit [41]. Regardless, gastrectomy remains a rare treatment of gastroparesis given its invasive nature.

Increasingly, less invasive surgical options, such as laparoscopic pyloroplasty, are being explored as minimally invasive, anatomy-preserving alternatives [42]. Results are encouraging, with reports of up to 80% symptom improvement [43–46]. The largest study to date was performed by Swanstrom et al. in 177 patients. They showed symptomatic improvement at one and six months post-operatively [47•]. While most of these studies have been done in an unblinded manner with unvalidated outcome measures, it is nonetheless a promising surgical approach that is less radical than a gastrectomy and might provide a salvage option for patients refractory to medical therapy.

Perhaps the most widely used minimally invasive surgical option is a laparoscopically placed gastric electrical stimulator (GES; Enterra®), which was approved for refractory gastroparesis by the FDA in 2000 under a humanitarian device exemption [48]. Its exact mechanism other than local neurostimulation remains unclear, but several open-labeled, prospective trials have shown symptom improvement without

clear shortening of gastric emptying times [49]. Three randomized, controlled, cross-over studies have shown mixed results. In only one of these studies was there symptomatic benefit during the blinded portion, but all three showed long-term improvement during the open-label period [50–52]. Due to the paucity of treatment options for gastroparesis, the American College of Gastroenterology (ACG) adopted this as a conditional recommendation for compassionate use. Especially in diabetic gastroparesis patients with predominant symptoms of nausea and vomiting for which it has demonstrated the greatest benefit [15, 53, 54]. Though minimally invasive, GES carries a 5–14% adverse event rate, mostly related to pocket infection or lead dislodgement. Unfortunately, these complications often require surgical reintervention [49]. The need for surgical placement, risks associated with GES, and a lack of convincing blinded RCT data demonstrating efficacy have restricted the role of GES to that of a humanitarian use device, and limited its widespread adoption.

Endoscopic Options

Due to the limitations of medical and surgical therapy, endoscopic options to palliate gastroparesis symptoms are increasingly being explored. These options can be broadly categorized into pyloric-directed therapy, non-pyloric-directed therapy, and nutritional support.

Evaluation of Feasibility of Pyloric-Directed Therapy

Until recently, most endoscopic therapies have been directed at the pylorus, which is the topic of a well-written review [55]. As discussed previously, surgeons are exploring pyloroplasty as a treatment for gastroparesis with encouraging results.

Prolonged post-prandial isolated pyloric pressure waves, also known as pylorospasm, have long been considered a potential mechanism of gastroparesis. In 1986, Mearin et al. used conventional manometry to evaluate post-prandial pyloric motor activity in 24 patients suspected of having diabetic gastroparesis. They found evidence of pylorospasm in over half of them [56].

Despite the belief that pylorospasm contributes to the pathogenesis of gastroparesis in a subset of patients, documenting it remains difficult. While the tools to perform high-resolution antroduodenal manometry are available, its use remains limited due to technical obstacles and a lack of standardized control data [57]. More recently, impedance planimetry, also known as the endoscopic functional luminal imaging probe (EndoFLIP), was developed to measure biomechanical properties of the gastrointestinal wall in real time. The device simultaneously measures intraluminal pressure and luminal cross-sectional area, which allows the calculation of compliance. To date, it has mostly been used to evaluate the biomechanical properties and motor function of the esophagus [58]. Only a few studies have evaluated its utility in assessing the pylorus. Gourcerol et al. were able to prove that the pylorus was identifiable as a relative high-pressure zone and showed that fasting pyloric compliance was significantly lower in gastroparesis patients compared to healthy controls [59•]. Snape et al. found a similar relationship between compliance and gastric emptying in patients with nausea [60•]. Lastly, Malik et al. showed that in gastroparesis other metrics (luminal diameter and cross-sectional area) can have an inverse correlation with early satiety [61•].

EndoFLIP is a promising new technology that potentially offers a more practical and expeditious way of evaluating the pylorus. However, it remains limited by the fact that it can only measure fasting pyloric metrics, whereas pylorospasm by definition is in the post-prandial state. There remains a need for further studies on this technology and its applicability in gastroparesis.

Intrapyloric Botox Injections

The first endoscopic pyloric-directed therapy to gain widespread use was intrapyloric botulinum toxin (BT) injection. Botulinum toxin is a potent neurotoxic protein that blocks the release of acetylcholine from axons at the neuromuscular junction, which causes a flaccid paralysis [62]. It was first used in the GI tract as a treatment for achalasia in the mid-1990s. Starting in 1997, multiple open-label studies of intrapyloric BT injections in patients with gastroparesis suggested symptomatic improvement lasting up to a mean duration of five months in gastroparesis [62–66]. One case report demonstrated its physiological effects with pre- and post-treatment antroduodenal manometry showing the presence and subsequent resolution of pylorospasm to accompany symptom improvement [67].

Momentum of its use was largely lost when two well-designed RCTs by Arts et al. [68] and Friedenberg et al. [69] showed no difference in symptoms or gastric emptying time after intrapyloric injections of placebo versus botulinum (100 or 200 units). This led to a strong recommendation by the ACG against the use of botulinum injections for gastroparesis in its most recent guidelines [15].

The story does not end there though. As noted by the guidelines and prior experts' opinion [55], there remains a need for further studies in patients with documented pylorospasm. In reality, a trial of intrapyloric botulinum toxin injections for a refractory gastroparesis patient remains widely used in clinical practice, largely due to a good safety profile and a lack of efficacious alternatives. Criticism of those two negative

clinical trials includes the small number of patients studied (54 total) and the likely heterogeneous gastroparesis population.

Subsequent studies have attempted to identify the subset of gastroparesis patients who are more likely to respond. Coleski et al. performed a retrospective analysis on 179 patients and identified factors that predicted a better response rate. Positive predictors included usage of a higher dose (200 units), females, younger patients (age < 50), and idiopathic gastroparesis [70]. More recently, Wellington et al. performed a prospective evaluation on a subset of 33 gastroparesis patients, all with proven normal gastromyoelectrical activity on electrogastrography. They hypothesized that these patients were likely to have pylorospasm as the underlying pathophysiology. There was symptom improvement in up to 78% of patients [71•]. These two studies offer encouragement that a subset of patients will respond to intrapyloric injections, and they emphasize the need for studies to evaluate factors that predict response.

Pyloric Stenting

Pyloric stenting is a standard treatment for malignant gastric outlet obstruction. Only recently was it studied in a small population of patients with gastroparesis. The first, by Clarke et al. in 2013, included only three refractory gastroparesis patients each of whom had marked symptom improvement after placement of a fully covered transpyloric stent [72]. They followed up their initial study with a larger retrospective analysis of 30 refractory patients (16 idiopathic, 8 diabetic, 6 postsurgical) using a Niti-S esophageal stent. Overall, 75% of patients had a positive clinical response. While the study had only a small group ($n = 5$) of patients with pain-predominant symptoms, they were less likely to respond to stent placement than were those with nausea-predominant symptoms (21% vs. 79%). Stents remained in place for a mean of 67 days, but migration was seen in 100% of patients if it was not anchored. Migration was only marginally improved (~ 50%) after fixation with clips or suturing [73].

Pyloric stent placement is largely limited by high stent migration risk whether fixed or not, making stenting a poor choice for permanent therapy. However, the original authors astutely highlight that stenting could be used to bridge severely symptomatic or refractory patients and facilitate discharge or as a therapeutic trial to identify patients who might benefit from a more definitive pylorus-directed therapy.

Pyloric Dilation

Pyloric dilation is another method commonly employed to treat mechanical gastric outlet obstruction, but its use as a treatment for gastroparesis remains limited. Similar to injections and stenting, it is not a permanent pyloric therapy for gastroparesis.

There is only one small study exploring dilation as a treatment for gastroparesis. In that study, Gourcerol et al. performed a prospective open-label trial with 27 gastroparesis patients. Ten patients with low fasting pyloric compliance identified by EndoFlip were treated with endoscopic balloon dilation to 20 mm (three times for a duration of 1 min each). Post-dilation pyloric compliance increased significantly along with improvement in symptoms and quality of life up to 10 days afterwards [59•]. The true significance of this study is probably the observations that pyloric compliance measurements can be used to categorize gastroparesis subtypes and that a well-defined subset of patients with gastroparesis might indeed respond to a pyloric-directed therapy.

Gastric Per-Oral Endoscopic Myotomy (G-POEM)

Potentially the most promising and exciting endoscopic therapy to emerge for gastroparesis is endoscopic myotomy (popularly termed G-POEM—gastric peroral endoscopic myotomy). Peroral endoscopic myotomy has already been pioneered for treatment of achalasia with promising short and medium term results. G-POEM uses similar techniques with minor changes to adapt the technique to the stomach. For the most part, technical success to date has been reported at 100%, with procedure times lasting between 1 and 2 h, and patients usually discharged within 1–2 days post-operatively.

The first published case report in a patient dates back to 2013 by Khashab et al. [74]. Since then, there have been a rapidly growing number of publications in the literature (see Table 1) [75–80, 81•, 82•, 83•, 84•]. The three most recent studies published in the past year by Khashab et al. (30 patients), Rodriguez et al. (47 patients), and Gonzalez et al. (29 patients), all include a larger number of patients [82•, 83•, 84•]. In a smaller study by Dacha et al. [81•], symptom improvement measured by various metrics occurred in over 80% of patients up to 12 months post-operatively. While the use of gastric emptying times as a marker of response to treatment is controversial [85], normalization or improvement is seen in upwards of 70% of patients.

So far, studies have included gastroparesis of all etiologies. While not statistically significant, Gonzales et al. did show a trend towards a better response in idiopathic and post-surgical patients as opposed to diabetic patients (92% and 80% vs. 57% respectively) [84•]. Overall, safety data are encouraging. Intraoperative capnoperitoneum has been reported in a minority of cases and managed with needle decompression. In these limited series, significant adverse events were rare but included one peri-procedural pneumonia, post-operative bleeding in

Table 1 G-POEM studies

Study	Date	Total[a]	I	D	S	Clinical symptoms	Gastric emptying	Adverse events
Khashab et al. [74]	2013	1	1	–	–	Symptom improvement	–	None
Chaves et al. [75]	2014	1	–	–	1	Symptom improvement	–	None
Chung et al. [76]	2014	1	–	–	1	Symptom improvement	–	None
Gonzalez et al. [77]	2015	1	–	1	–	Symptom improvement @ 1, 3 mo	Normalized	None
Shlomovitz et al. [78]	2015	7	5	–	2	86% Symptom improvement @ 3 mo	80% Improved	1 Bleeding ulcer (hemoclip) 1 Peri-procedural PNA
Mekaroonkamol et al. [79]	2016	3	2	–	1	100% GCSI improved @ 1 mo	66% Normalized 33% Improved	None
Gonzalez et al. [80]	2017	12	6	5	1	85% Symptom improvement @ 1, 3 mo Mean GCSI improved @ 1, 3 mo	75% Normalized	2 Intra-op capnoperitoneum
Dacha et al. [81•]	2017	16	6	9	1	81% Improved GCSI @ 1, 6, 12 mo Mean QOL improved @ 6 mo	75% Normalized	None
Khashab et al. [82•]	2017	30	7	11	12	86% Symptom improvement @ 6 mo	47% Normalized	1 Intra-op capnoperitoneum
Rodriguez et al. [83•][b]	2017	47	27	12	8	Improved GCSI @ 3 mo (4.6 vs. 3.3, $p < 0.001$)	Improved (pre 37% vs post 20%, $p < 0.03$)	One 30-day mortality secondary to underlying cardiac disease
Gonzalez et al. [84•]	2017	29[c]	15	7	5	79% Symptom improvement @ 3 mo 69% Symptom improvement @ 6 mo Improved GCSI @ 1, 3, 6 mo	70% Normalized	5 Intra-op capnoperitoneum 1 Bleed (hemoclip) 1 Bleed (self-limited) 1 peritoneal abscess[d] 1 delayed prepyloric fibrotic stenosis requiring tx by incision

[a] Total number of patients in the study

[b] First prospective study

[c] Two scleroderma patients included

[d] Authors noted this patient did not follow re-feeding protocol recommendations

I, idiopathic; D, diabetic; S, post-surgical; mo, months; GCSI, gastroparesis cardinal symptom index; QOL, quality of life; tx, treatment

three, and one postoperative peritoneal abscess in a patient who did not follow dietary recommendations.

Though these early results are promising, the procedure remains limited to highly specialized practitioners at only a few tertiary centers around the world in an investigative setting. Most studies to date have been retrospective in nature, so prospective, randomized-controlled studies are needed. Furthermore, as demonstrated previously, appropriate gastroparesis subtyping and patient selection are needed to maximize the benefit this procedure might provide.

Non-Pyloric-Directed Therapies

Aside from the pyloric-directed therapies reviewed above, a variety of non-pyloric-directed endoscopic techniques are also worth mentioning. The accepted practices mainly encompass endoscopic gastrostomy or enterostomy tubes, but certain investigational salvage techniques, such as endoscopic gastroenterostomy, or theoretical ones, such as endoscopic gastric electrical stimulators merit consideration.

Venting Gastrostomy Tube

Venting gastrostomy tubes (G-tube) are recommended conditionally in the most recent ACG guidelines. Evidence for palliative venting G-tubes in malignant obstructions was previously established [86–88]. Aside from a physiological basis and anecdotal experience, evidence for its use in gastroparesis patients is largely based on small studies in chronic intestinal pseudo-obstruction patients. They showed both symptom improvement and decreased hospitalization rates [89, 90]. Only one study in refractory idiopathic gastroparesis patients has been performed [91]. Endoscopic G-tubes were placed in eight patients with instructions to aspirate gastric contents with a 60 mL syringe to relieve symptoms as needed. Over a mean follow-up of 29 months, there was significant symptomatic improvement, in particular distension and nausea, along with weight gain and the ability to stop prokinetic agents.

Technically, G-tubes can be placed surgically, fluoroscopically, or endoscopically. In general, percutaneous endoscopic gastrostomy (PEG) is less invasive, takes less time, costs less, and has a lower complication rate compared to surgical placement [92, 93]. Endoscopic versus fluoroscopic placement tends to be comparable for these parameters [94].

At this time, a venting G-tube remains an option for refractory gastroparesis based on a low level of evidence. One must also be sure to review the inherent risks associated with G-tubes including a 0.5% procedure-related mortality and 16.7% complication rate [95]. Some of the common complications include infection (9%), perforation leading to peritonitis (2.3%), gastrointestinal bleeding (2.5%), or tube dislodgement (4%) [96].

Enteral Nutrition Delivery

If a patient is unable to maintain adequate oral intake, enteral nutrition should be recommended, and a variety of options can be considered [97]. Jejunal delivery of nutrients, rather than gastric, makes intuitive sense and comes with a conditional recommendation over gastric delivery by the ACG [15].

A study of 26 refractory diabetic gastroparesis after surgical jejunostomy tube (J-tube) placement showed improved overall health, improved nutrition, and fewer hospitalizations in more than half of patients [98]. The rate of complications after surgical J-tube placement varies and is likely dependent on the specific technique and institution. The range is from 1.5% to 21%, with the most common being catheter occlusion or dislodgement [99, 100].

Two types of J-tubes can be placed endoscopically. The first is a direct percutaneous endoscopic jejunostomy (DPEJ), and the second involves a PEG with a jejunal extension tube (PEG-J). The technical success rate for PEG-J is often higher (89% vs. 68% for DPEJ), but there is a significantly higher rate of tube dysfunction, mostly due to retrograde dislodgement [101–104]. One study showed the need for re-intervention over a 6-month period to be 75% for PEG-J versus only 31% for DPEJ [105]. Hemoclip placement may help prevent PEG-J tube migration, but the tubes still only lasted for a mean of 55 days [106]. For these reasons, DPEJ might be considered preferable if durable small bowel feeding is required and/or if there are frequent PEG-J dislodgements.

Fluoroscopic-guided placement of J-tubes is another less invasive alternative for providing enteral nutrition. The can be placed as a gastrojejunostomy (GJ) or direct J-tube. In general, GJ tube placement is considered comparable by both endoscopic and imaging-guided techniques, but there is no comparison for direct J-tube placement [107].

In the end, the best approach for J-tube type and placement should be decided case-by-case, and depend on a patient's anatomy, comorbidities, institutional expertise, and a multidisciplinary conversation. While a GJ tube may offer the ability for simultaneous gastric venting if needed, some would still advocate for a separate G-tube and J-tube if long-term use is expected. It is also important to assess a patient's tolerance to jejunal feeding prior to placement of percutaneous J-tube, especially if there is any concern for small bowel dysmotility. This is done by performing a 48–72 h trial of nasojejunal feeding [108].

Endoscopic Ultrasound (EUS)-Guided Gastroenterostomy

Palliative surgical bypass gastrojejunostomy without gastrectomy has been well-described for treating unresectable malignant gastric outlet obstruction (GOO) [109, 110]. Lumen-apposing metal stents (LAMS) are FDA-approved for drainage of pancreatic pseudocysts but have been evaluated for other investigational uses, including endoscopic gastrojejunostomy.

When compared to enteral stenting for malignant GOO, LAMS gastrojejunostomy showed a similar technical success, clinical success, and adverse event rate, but less need for re-intervention (4% vs. 28%) [111]. When compared to surgical gastrojejunostomy, it was found to be a non-inferior and less invasive alternative [112].

Only recently has it been investigated as a treatment of benign causes of GOO [113]. A multicenter study showed its feasibility (92% technical success, 85% clinical success, 11.5% adverse even rate) in both malignant and benign GOO, but most benign cases were from chronic pancreatitis or pyloric stenosis [114]. It has not yet been studied in refractory gastroparesis patients.

Endoscopic GES

While the Enterra GES must be placed laparoscopically, endoscopic techniques for placement of both temporary and permanent GES are being developed.

In 2005, Ayinala et al. were able to demonstrate the safety and feasibility of an endoscopically placed temporary GES in 20 patients [115]. Temporary leads were placed endoscopically with extension to an external generator through a pre-existent PEG tube or the esophagus. Stimulation led to rapid improvement in symptoms (vomiting and total symptom scores). Abell et al. performed a follow-up randomized cross-over study in hospitalized patients showing a trend towards improved vomiting after 72 h of treatment [116]. Long-term outcomes are not yet available, but temporary GES might provide a minimally invasive means of identifying patients most likely to benefit from more permanent surgical GES implantation.

More recently, a completely endoscopically implantable miniature GES that is wirelessly powered was developed and tested in a porcine model [117–119]. At the moment, the device can sustain charge for up to 3 months of operation. It remains to be seen if this can translate to use in humans with similar efficacy.

Conclusion

Gastroparesis remains a difficult-to-manage chronic illness with no cure. Though patients often have a common syndrome of stereotypic symptoms, the underlying mechanism and pathophysiology are heterogeneous. This heterogeneity partially stems from the different potential etiologies of delayed gastric emptying and is thought to contribute to the variable response rates seen in many available therapies, most notably gastric electrical stimulation and intrapyloric botulinum toxin injections.

Though there are developing treatment modalities on the horizon, efficacy will likely depend on a better understanding of pathophysiology and improved patient selection.

The challenge remains in identifying which patients will respond the best to which interventions, specifically to pyloric-directed endoscopic options. The ability to easily categorize gastroparesis patients into different groups based on not only etiology and predominant symptoms, but also underlying pathophysiology, is a key that we are still lacking. Being able to easily identify pylorospasm could potentially change the therapeutic landscape today. If we are able to solve these issues in the future, it will aide in maximizing any beneficial effect a particular patient might receive. Future studies should not only focus on prospective, controlled studies, but also an attempt at thorough classification of the underlying gastric neuromuscular dysfunction as well.

Compliance with Ethical Standards

Conflict of Interest Andrew Su, Jeffrey Conklin, and Alireza Sedarat declare that they have no conflict of interest.

Human and Animal Rights and Informed Consent This article does not contain any studies with human or animal subjects performed by any of the authors.

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