Journal of Gastrointestinal Surgery (2019) 23:1095–1103
https://doi.org/10.1007/s11605-018-04088-7

2018 SSAT PLENARY PRESENTATION

Per-Oral Pyloromyotomy (POP) for Medically Refractory Post-Surgical Gastroparesis

Andrew T. Strong[1,2] · Joshua P. Landreneau[1,2] · Michael Cline[2,3] · Matthew D. Kroh[1,2,4] · John H. Rodriguez[1,2] · Jeffrey L. Ponsky[1,2] · Kevin El-Hayek[1,2]

Received: 1 June 2018 / Accepted: 16 December 2018 / Published online: 26 February 2019

Abstract

Background Post-surgical gastroparesis (psGP) is putatively related to vagal denervation from either therapeutic transection or inadvertent injury. Here, we present a series of patients undergoing endoscopic per-oral pyloromyotomy (POP) as a treatment for medically refractory psGP.

Methods Patients identified from a prospectively maintained database of patients undergoing POP procedures at our institution from January 2016 to January 2018 were included. Surgical history, symptom scores, and gastric emptying studies before and 3 months after POP were additionally recorded.

Results During the study period, 177 POP procedures were performed, of which 38 (21.5%) were for psGP. The study cohort was 84.2% female with a mean body mass index of 27.6 kg/m^2 and mean age of 55.2 years. Common comorbidities included hypertension (34.2%), depression (31.6%), and gastroesophageal reflux disease (28.9%). Hiatal/paraesophageal hernia repair (39.5%) or fundoplication (36.8%) preceded psGP diagnosis most often. The mean operative time was 30 ± 20 min. There were no intraoperative complications. Mean postoperative length of stay was 1.2 days. There were two readmissions within 30 days, one for melena and one for dehydration. The mean improvement in total Gastroparesis Symptom Index Score was 1.29 (p = 0.0002). The mean 4-h gastric retention improved from a pre-POP mean of 46.4 to 17.9% post-POP. Normal gastric emptying was noted in 50% of subjects with available follow-up imaging.

Conclusion POP is a safe and effective endoscopic therapy for patients with psGP. POP should be considered a reasonable first-line option for patients with medically refractory psGP and may allow stomach preservation.

Keywords Per-oral pyloromyotomy · Pyloromyotomy · Gastroparesis · Post-surgical · Endoscopy

Introduction

Several recent studies have shown convincing evidence that both the incidence and prevalence of gastroparesis have increased over the past decade.[1–3] While these trends have been chiefly driven by a concomitant rise in diabetes prevalence and increased identification of idiopathic gastroparesis, post-surgical gastroparesis continues to be an explanatory factor.[4,5] Historically, post-surgical gastroparesis (psGP) implied a prior vagotomy for the treatment of peptic ulcer disease.[5] With the success and popularity of proton pump inhibitor therapy, intentional vagal section became a less common etiologic factor for psGP. However, within a decade, the rise of laparoscopic fundoplication and other antireflux operations ushered in a new population of patients with potential for iatrogenic causes for sensorimotor gastric dysfunction.[6]

Diagnosis of gastroparesis is based on the presence of a spectrum of symptoms, a documented absence of mechanical

Prior presentation: Some of the data included in this manuscript has been previously presented at Digestive Disease Week June 2-5, 2018, Washington D.C., USA

✉ Kevin El-Hayek
elhayek@ccf.org

1 Department of General Surgery, Cleveland Clinic, Desk A-100, 9500 Euclid Avenue, Cleveland, OH 44195, USA

2 Cleveland Clinic Lerner College of Medicine of Case Western Reserve University, Cleveland, OH, USA

3 Department of Gastroenterology and Hepatology, Cleveland Clinic, Cleveland, OH, USA

4 Digestive Disease Institute, Cleveland Clinic Abu Dhabi, Abu Dhabi, United Arab Emirates

gastric outlet obstruction, and demonstrable delayed gastric emptying.[4] Symptoms include early satiety, post-prandial fullness, nausea, vomiting, bloating, and epigastric abdominal pain.[4] Classically, gastroparesis is divided into four major etiologic categories: medication-induced, diabetes-associated, idiopathic, and the aforementioned psGP. Initial treatment in each group centers around dietary modification, with prokinetic and/or anti-emetic medications offered as additional therapies. When symptomatic improvement falters, or medication side effects are intolerable, patients are considered medically refractory and referred for surgical consultation. Gastric electric stimulation has a conditional recommendation as a compassionate use device for patients with diabetic or idiopathic gastroparesis.[4] Because gastric electrical stimulation has not been effective in patients with psGP, there is currently no labeled indication for its use in this population. Recent work revealing the likelihood that symptomatic benefit is derived by a vagally mediated mechanism may explain the lack of efficacy in a population of patients with known or suspected vagal nerve injuries.[4,7] Thus, current treatment recommendations for psGP are less clear. Current evidence that does exist points toward a recommendation of total or subtotal gastrectomy, with each associated with significant potential complications and technical complexity.[8]

Temporary pyloric disruption accomplished by endoscopic stenting, balloon dilation, or pharmacologically using botulinum toxin have been shown to transiently reduce gastroparesis symptoms.[9–12] Surgically, this can be accomplished by pyloroplasty, performed with either open or laparoscopic approaches, with more durable response[13–15] While the exact mechanism is unknown, reduced restrictive function of the pylorus allows for antral myoelectric impulses to push food into the duodenum without the requirement for coordinated pyloric relaxation. In addition to achieving gastroparesis symptoms improvement, surgical pyloroplasty has been shown to also result in objective improvement of gastric emptying.[14–16] Thus, in a heterogeneous group of patients with gastroparesis, pyloric disruption appears to possibly play a role in organ preservation. Recent advances have introduced a less invasive corollary to pyloroplasty, namely endoscopic per-oral pyloromyotomy (POP).[17–19] This study sought to describe a single-center experience with POP among patients with post-surgical gastroparesis and evaluate short-term outcomes.

Methods

This was a retrospective study performed at a single academic referral center. All patients undergoing POP are prospectively tracked within a registry approved by the Institutional Review Board. Patients for this study were retrospectively identified from this registry. Inclusion criteria for this study were patients with medically refractory gastroparesis who had undergone a potentially causative surgical procedure prior to onset of gastroparesis symptoms, and who had at least 90 days follow-up. Medically refractory gastroparesis was defined as persistent or recurrent symptoms despite appropriate dietary modifications and maximal anti-emetic and pro-motility therapy, if medications were discontinued for severe side effects, or if other medical comorbidities were contraindications to recommended pharmacologic therapies, such as prolonged QT syndrome. Potentially causative operations were broadly defined but primarily included antireflux operations, paraesophageal hernia repair, and vagotomy. Patients who had not previously undergone surgical intervention were excluded, though patients with multiple possible explanatory etiologies (such as diabetes and a prior fundoplication that predated symptom onset) were included. The study period was from January 2016, when POP was introduced at our institution, to January 2018.

Pre-Procedural Evaluation and Patient Selection for POP

Patients with confirmed gastroparesis are managed by a multidisciplinary team that includes caregivers from gastroenterology, nutrition and dietetics, gastrointestinal psychology, chronic pain management, and surgeons with fellowship training in both flexible endoscopy and minimally invasive foregut surgery. Initial evaluation includes timeline of symptom onset in conjunction with a careful surgical history, as well as review of prior operative reports, gastrointestinal imaging studies, functional assessments, and endoscopies. All patients undergo biochemical testing to evaluate for autoimmune or connective tissue disorders as contributory factors for gastroparesis. If not performed recently, patients undergo diagnostic upper endoscopy to rule out mechanical obstruction or other gastric or duodenal pathologies, especially in the setting of prior antireflux or peptic ulcer surgery to rule out mechanical obstruction and assess anatomy.

Evaluation of gastroparesis symptoms is performed using the Gastroparesis Symptom Index (GCSI).[20,21] GCSI is a nine-item questionnaire used to generate 3 subscores: post-prandial fullness/early satiety (4 items), nausea/vomiting (3 items), and bloating (2 items). A balanced six-level scale is used to rate symptom severity from absent (0) to severe (5) symptoms over the 2 weeks prior to assessment. The overall GCSI is the arithmetic mean of the three subscores.[20,21] Objective evaluation of gastric emptying is preferably performed by 4-hour non-extrapolated solid-phase scintigraphic gastric emptying study (GES). Studies performed at our own institution are performed and interpreted according to established guidelines.[22] The percent retention at 4 hours is

used to define severity of delayed emptying: < 10% retention normal emptying, 10–20% mildly delayed, 20–35% moderately delayed, and > 35% as severely delayed gastric emptying, though this is often reported as gastroparesis severity. Wireless motility capsules may be used as an adjunct to GES [21]. Gastric emptying time of greater than 4 hours is diagnostic of delayed gastric emptying by wireless motility capsule.[23] Wireless motility capsules are typically utilized to determine if a concomitant colonic dysmotility or global dysmotility syndrome exists for patients with suggestive symptoms.

Patients with medically refractory gastroparesis are referred for surgical evaluation. For patients with psGP, enteral access in the form of endoscopic or laparoscopic jejunostomy tube is typically the first recommendation when significant malnutrition is present. Otherwise, patients were referred for either laparoscopic pyloroplasty or POP, based on patient preference. The POP procedure has been detailed previously.[18] Since that publication, two modifications have been made at our institution. In select patients, POP can be safely performed as an outpatient procedure, either in the endoscopy suite or operating room, provided general anesthesia is available in both locations. Fluoroscopic upper gastrointestinal series are no longer routinely obtained post-POP. Patients are recommended a liquid diet for 2 weeks after POP. All patients are prescribed four-times daily sucralfate and twice-daily proton pump inhibitor therapy for a minimum of 2 weeks after the procedure to prevent ulceration of the mucosa over the submucosal tunnel.

Data Collection

As is customary at our institution for any novel interventional technique, all patients undergoing POP are tracked prospectively in a registry approved by the Institutional Review Board. In addition to patient demographics and gastroparesis characteristics, procedure details and outcomes at 30 and 90 days are abstracted. Demographic information includes age, gender, body mass index (BMI), full medication list prior to the POP, gastroparesis etiology, prior interventions to treat gastroparesis, and a surgical history for patients with psGP. Baseline GCSI scores and objective gastric emptying studies are obtained and recorded prior to intervention. Procedural details include procedure location, procedure time, intraoperative complications, and length of stay. Thirty-day outcomes included operative intervention, or repeat endoscopy, delayed perforation of the duodenum or stomach, hemorrhage, gastric or duodenal ulcer, unplanned readmission, and mortality. Outcomes at 90 days included BMI, review of medications, need for new enteral access for supplemental nutrition, requirement of parenteral nutrition, and repeat gastric emptying studies and GCSI.

Statistical Analysis

Summary statistics for demographic variables, medications, and operative variables are expressed as mean and standard deviation for continuous variables or count and percent for categorical variables. Past operations are enumerated. Tests of significance comparing pre- and post-procedure outcomes of interest were performed using two-sample t tests for continuous variables. All tests were two-tailed and performed at a significance level of $\alpha = 0.05$. *R* (v3.3.1, 2016-06-21) software was used for all analyses.

Results

During the study period, 177 POP procedures were performed. Thirty-eight patients were diagnosed with post-surgical gastroparesis (21.5%) which comprised the study cohort. The psGP cohort was 84.2% female with a mean age of 55.2 ± 14 years (Table 1). At the time of POP, the mean BMI was 27.6 ± 5.2 kg/m^2. Frequent comorbidities included hypertension (34.2%), depression (31.6%), and gastroesophageal reflux disease (28.9%). Notably, 15.8% of the cohort also had diabetes, including two patients (5.3%) who were dependent on daily insulin for glucose control.

In terms of operations that preceded development of gastroparesis symptoms, hiatal or paraesophageal hernia repair with or without fundoplication was the most common (39.5%; Table 1). A similar proportion of patients had also undergone fundoplication alone (36.8%). Table 2 demonstrates the sometimes prolonged course patients took in terms of foregut surgery, which included as many as 4 operations prior to POP. Apart from the expected paraesophageal hernia repairs and fundoplications, other operations preceding gastroparesis symptoms included heart-lung transplant (n = 1), thoracotomy with excision of bronchial cyst (n = 1), transcatheter atrial ablation (n = 1), right hepatectomy with hepatico-jejunostomy for large hepatic adenoma (n = 1), and esophagectomy with gastric pull-up (n = 2). The mean time from most recent foregut operation to POP was 61 months (interquartile range 31–84 months). Several patients had previous interventions for gastroparesis, which included gastrostomy tube (including those with jejunal extension tubes) placement for either venting or enteral nutrition (n = 3, 7.9%), or jejunostomy tube (n = 2, 5.3%) for nutritional support. Possibly because botulinum toxin was used as a screening test early in our center's early experience with POP, 21.0% of the patients in this cohort had also undergone intrapyloric botulinum toxin injection.

POP procedures were primarily performed in the operating room (89.5%) as opposed to the endoscopy suite. The mean procedure time was 30 ± 20 min (interquartile range 21–36 min). In some cases, POP was performed in conjunction

Table 1 Demographics and comorbidities

Factor	$N = 38$
Female sex	84.2%
Mean age, years (±SD)	55.2 ± 14.0
Mean body mass index, kg/m^2 (±SD)	27.6 ± 5.2
Comorbidities	
Hypertension	34.2%
GERD	28.9%
Fibromyalgia	15.8%
COPD	18.4%
Dyslipidemia	21.1%
Diabetes	15.8%
Insulin dependent	5.3%
Non-insulin dependent	10.5%
Irritable bowel syndrome	5.3%
Depression	31.6%
Anxiety	15.8%
Bipolar disorder	2.7%
Frequency of contributing operations[a]	
Vagotomy	2.6%
Hiatal or paraesophageal hernia repair	39.5%
Fundoplication alone	36.8%
Heller myotomy	5.3%
Other	31.5%
Prior interventions for gastroparesis	
Gastrostomy tube	7.9%
Jejunostomy tube	5.3%
Gastric electric stimulator	0
Pyloric botulinum toxin injection	21.0%
Operative Characteristics	
Performed in operating room	89.5%
Mean operative time, min (±SD)	30 ± 20
Mean length of stay, days (±SD)	1.2 ± 1.1
Complications	
Gastrointestinal bleed	2.6%
Need for intravenous hydration	2.6%
Readmission with 30 days related to POP	2.6%

SD standard deviation, *GERD* gastroesophageal reflux disease, *COPD* chronic obstructive pulmonary disease, *POP* per-oral pyloromyotomy

[a] Some patients underwent multiple preceding operations, see Table 2

with another operation, including laparoscopic diverting loop ileostomy for concomitant slow transit constipation, laparoscopic removal of adjustable gastric band and port, removal of biliary stent, and nasojejunal enteral access tube placement, each performed in one patient. There were no intraoperative complications. The mean post-POP length of stay was 1.2 days (range 0–6 days). There were no reoperations within 30 days. One death occurred within 30 days; however, on autopsy, the cause of death was attributed to underlying cardiac disease and not specifically related to the POP procedure. There was one patient readmitted for melena, which was counted as a gastrointestinal bleed. The only other complication noted within 30 days was need for intravenous hydration ($n = 1$, 2.6%).

In terms of gastric emptying and symptoms, patients improved on average. Prior to POP the mean percent retention on solid-phase scintigraphic gastric emptying study was 46.4% at 4 h (interquartile range 21–67%; Table 3). At 90 days after POP, there was an absolute improvement of 28.5% emptying to a mean of 17.9% (interquartile range 1.5–26%; $p = 0.0012$ compared to baseline, based on 19 (50%) with comparable pre-post emptying data). Of patients with follow-up gastric emptying studies available, 50% had normal gastric emptying post-POP. In terms of gastroparesis symptoms, the mean overall GCSI was 3.72 ± 0.72. Given that gas-bloat syndrome is a known complication of fundoplication, it is not surprising that bloating was the most severe symptom subscore pre-POP (4.20 ± 1.23). POP had the greatest effect on nausea/vomiting symptoms (3.00 vs 1.55; delta of 1.45, $p = 0.003$). However, there was improvement noted overall in all subscores (Table 3). Over a median follow up of 8.4 months (interquartile range 6.3–14.6), there were three patients (7.9%) who had subsequent operations. One had a laparoscopic pyloroplasty, and the other two near-total gastrectomies with roux-en-y reconstruction.

Discussion

This is the first study to specifically investigate the role of POP for post-surgical gastroparesis. Overall, these results appear similar to studies that have demonstrated symptomatic improvement in patients with psGP following pyloroplasty.[14,17] The greatest observed effect was improvement in nausea and vomiting, though there was notable improvement in both early satiety and bloating symptoms as well. Moreover, a substantial proportion of the patients had normalized gastric emptying, indicating a restoration of at least that component of gastric function. The observed improvements following POP in both symptom scores and gastric emptying were similar to previous reports for both psGP and idiopathic gastroparesis.[24]

There are no currently accepted criteria to diagnose psGP. Most often, patients with symptoms consistent with gastroparesis, documented delay in gastric emptying, and a surgical history that includes a putatively contributory operation are classified as having post-surgical gastroparesis.[5,6,16] While it would seem most logical that symptoms consistent with gastroparesis beginning shortly after a possibly contributory surgery would clinch the diagnosis of post-surgical gastroparesis, many patients who experience nausea, vomiting, and bloating in the days or weeks after a foregut operation improve over time. In some cases, gastrointestinal

Table 2 Operations leading up to POP and subsequent operations after POP

Pt	Prior Operation 1	Prior operation 2	Prior operation 3	Prior operation 4	Operation after POP
1	HHR/PEHR, NF	Reduction of herniated fundoplication	HHR/PEHR, NF	HHR/PEHR, NF	Yes[a]
2	HHR/PEHR, ? fundoplication	HHR/PEHR, ? fundoplication	Takedown NF, esophageal diverticulectomy, longitudinal gastrectomy	–	No
3	Median arcuate ligament release	HHR/PEHR, fundoplication	–	–	No
4	Heart and double lung transplant	–	–	–	No
5	Heller myotomy, Belsey-Mark HHR/PEHR, ? pyloroplasty	Esophagectomy, gastric pull through	–	–	No
6	HHR/PEHR, NF	–	–	–	No
7	HHR/PEHR, NF	–	–	–	No
8	HHR/PEHR, NF	HHR/PEHR, with mesh, NF	Belsey-Mark HHR/PEHR	–	Yes[b]
9	NF	NF	–	–	No
10	HHR/PEHR	–	–	–	No
11	HHR/PEHR	–	–	–	No
12	Heller myotomy, Toupet Fundoplication	–	–	–	No
13	NF	HHR/PEHR, NF	–	–	No
14	HHR/PEHR	HHR/PEHR	–	–	No
15	NF	Takedown Fundoplication	–	–	No
16	NF	NF	–	–	No
17	HHR/PEHR, NF	HHR/PEHR, NF	HHR/PEHR, NF	HHR/PEHR, NF	No
18	Bronchial cyst excision	–	–	–	No
19	NF	Celiac artery bypass	–	–	No
20	HHR/PEHR	HHR/PEHR with mesh, NF	–	–	No
21	HHR/PEHR, NF	HHR/PEHR, NF	–	–	No
22	NF	–	–	–	No
23	Adjustable gastric band	–	–	–	No
24	Adjustable gastric band	HHR/PEHR	–	–	No
25	NF	NF	NF	–	No
26	NF	–	–	–	No
27	NF	–	–	–	Yes[c]
28	Transcatheter atrial ablation	Transcatheter atrial ablation	–	–	No
29	Partial hepatectomy	–	–	–	No
30	Paraesophageal hernia, NF	–	–	–	No
31	Esophagectomy, gastric pull through	–	–	–	No
32	NF	–	–	–	No
33	Heller myotomy, Toupet fundoplication	–	–	–	No
34	Belsey-Mark HHR/PEHR	NF	–	–	No
35	HHR/PEHR, NF	–	–	–	No
36	HHR/PEHR, NF	HHR/PEHR, wedge gastroplasty, NF, pyloromyotomy	–	–	No
37	HHR/PEHR, NF				No
38	HHR/PEHR, partial fundoplication	–	–	–	No

HHR/PEHR hiatal hernia repair/paraesophageal hernia repair, *NF* Nissen fundoplication

[a] Laparoscopic pyloroplasty, 602 days after POP procedure

[b] Paraesophageal hernia repair, near total gastrectomy with Roux-en-Y reconstruction, 203 days after POP procedure

[c] Paraesophageal hernia repair, takedown Nissen fundoplication, near total gastrectomy with Roux-en-Y reconstruction, 147 days after POP procedure

Table 3 Changes in gastric emptying and gastroparesis Cardinal Symptom Index

	Pre–POP	Post–POP (3 months)	*P* value
Solid-phase 4-hour scintigraphic retention	46.4 ± 26.8%	17.9 ± 24.0%	0.0012
Gastroparesis Cardinal Symptom Index			
Mean total (±SD)	3.72 ± 0.72	2.43 ± 1.17	0.0002
Mean post-prandial fullness score (±SD)	3.97 ± 0.92	2.70 ± 1.36	0.0015
Mean nausea/vomiting score (±SD)	3.00 ± 1.41	1.55 ± 1.30	0.0030
Mean bloating score (±SD)	4.20 ± 1.23	3.03 ± 1.69	0.0046

SD standard deviation

symptoms predate operations and worsen after surgery. In other cases, symptoms develop years after a possibly inciting operation. Moreover, symptoms may be associated with normal, rapid, or delayed gastric emptying, which may be impossible to distinguish clinically.[25]

From a historical standpoint, post-surgical gastroparesis was recognized as result of vagal nerve division in the setting of peptic ulcer surgery.[26] Intentional vagotomy has been demonstrated to impair receptive relaxation functions of the stomach, now understood to be a vagally mediated reflex.[6] The lack of fundic distension tends to accelerate liquid emptying, as the smaller relative gastric volume allows liquid to more quickly distribute through the stomach and then empty. The motor function of the stomach, while not controlled by the vagus nerve, is modulated by vagal input. Vagotomy also suppresses the pulsive antral component of the migrating motor complex, partially explaining the observed delay in solid food emptying.[6] Performing a concurrent gastric emptying procedure such as a pyloroplasty, antrectomy with Billroth I gastroduodenostomy, or Billroth II gastrojejunostomy mitigated some of these effects, such that over the long term, the rate of persistent gastroparesis symptoms following a vagotomy was relatively low.[27] The vagus nerve is also completely divided in most cases of esophagectomy, and the incidence of delayed gastric emptying may be as high as 50% in that patient population.[28] Intrapyloric botulinum toxin injection and pyloroplasty at the time of esophagectomy have each been attempted to improve gastric emptying of the intra-thoracic gastric conduit. While there have been effects noted in terms of decreased anastomotic leaks and pulmonary complications, the effect on gastric emptying is less clear in comparison to no pyloric intervention.[29] However, in the setting of documented delayed emptying of a gastric conduit, "rescue" pyloroplasty is associated with symptomatic improvement, weight gain, and decreased dependence on parenteral nutrition.[30]

The overlapping operations of fundoplication and hiatal/paraesophageal hernia repair are now the prototypical interventions that predate a diagnosis of psGP. In the open surgical era, an estimated 3–5% of foregut operations resulted in vagal nerve injury, and thus the physiology likely mirrors that of intentional vagal transection.[26] However, even in the absence of a vagal nerve injury, fundoplication alters gastric sensorimotor function, namely an impaired fundic relaxation in response to a food bolus.[6,31] Overall, gastric emptying tends to be more rapid following fundoplication, though it may be slowed in some cases.[6,26,32,33] Gas-bloat syndrome is a feared complication after fundoplication, though its correlation to gastric emptying has not been established.[34] In addition to antireflux operations, other operations have been implicated in the risk of partial or complete vagal nerve, including partial gastrectomy, bariatric operations, lung transplantation, and esophageal botulinum toxin injection.[6] Others, such as hepatectomy and pancreatectomy, have a less clear linkage to vagal nerve injury but have been associated with delays in gastric emptying in some patients.[6]

From a scientific standpoint, the proportion of patients who do not develop gastroparesis symptoms or delayed gastric emptying are as intriguing as those who do, as the physiology is incompletely understood. From a clinical standpoint, patients with psGP represent a challenging clinical dilemma. A whole body of literature was published detailing "post-gastrectomy syndromes," of which gastroparesis was a part, in the era where surgical treatment of peptic ulcer disease dominated foregut surgery.[35–38] In general, management of these patients often progressed to near-total or total gastrectomy, with no clear guidelines regarding when it became necessary.[8] That gastrectomy is an irreversible operation, with significant associated morbidity, should cause most surgeons to be reticent to offer this as an initial option. Much of the literature regarding quality of life following gastrectomy exists for patients with gastric cancer, but in general supports the conclusion that quality of life decreases.[39–41] For the patient's part, total gastrectomy obliges major alterations to diet content, eating patterns, frequency, vitamin supplementation, and even wardrobe.[42–44] Tellingly, even for patients with a genetic predisposition faced with almost certain future gastric cancer diagnosis, some may opt against prophylactic gastrectomy.[44] An increasing number of publications address gastrectomy for benign diseases, including gastroparesis.[45–50] In general, these publications support relief of some symptoms of gastroparesis in most, but not all patients.

Until recently, the only alternatives to offer in this patient population were venting gastrostomy and feeding jejunostomy tubes.[51,52] While POP introduces a potential

intermediate procedure, our study offers little guidance regarding when to purse pyloric disruption once psGP has developed. As discussed above, for several weeks after a foregut operation, patients may experience procedure-related bloating and nausea, but this generally improves. Medical therapy for psGP should always be first line prior to considering surgical intervention. As is noted in our series, patients may have medically responsive disease states for years prior to becoming refractory and warranting surgical intervention. Objective documentation of delayed gastric emptying must be established prior to considering surgical intervention, as symptoms of psGP can overlap with other conditions.

We propose that preservation of the stomach should be a guiding principle in the treatment of psGP. Conceptually, avoiding or delaying gastrectomy parallels the principle of limb-preservation in the setting of critical or threatened limb ischemia. Unfortunately, there has been little evidentiary precedent for surgeons to follow this approach with psGP until recently. Increasing understanding of gastric physiology that has outlined the endocrine or paracrine functions of the stomach further underscores the value of preserving the stomach. Pyloric disruption as a therapeutic option for gastroparesis has been previously reported using several modalities, including endoscopic pyloromyotomy.[16,53] Pyloroplasty in combination with fundoplication has been shown to be beneficial in terms of gastric emptying in some studies.[54,55] In a large series of laparoscopic pyloroplasty for gastroparesis, the majority of patients showed improvement in both symptoms and objective gastric emptying.[16] While the conclusion of that study asserts that pyloroplasty would be an appropriate first-line surgical option for gastroparesis, pyloroplasties in that series were performed concurrent with other foregut operations, making the effect of pyloroplasty alone difficult to evaluate. Our current study reports similar improvements in nausea, vomiting, and bloating that were noted following laparoscopic pyloroplasty.[16] In our study, POP also normalized solid-phase gastric emptying, an effect that should not be understated in this patient population. Moreover, a substantial proportion of patients included in our series were referred specifically for gastrectomy. That only 2 out of 38 (5.3%) patients progressed to gastrectomy after POP is similarly difficult to understate and is a significant deviation from what until now has been considered the best treatment option for psGP. When gastrectomy is necessary, we advocate that it be performed in high volume centers, since it implies re-operative foregut surgery.[56,57]

This study has several limitations. First, while patients were tracked prospectively in an institutional registry, pre-procedural therapies including medications were not standardized. The patients are heterogeneous in terms of type and number of foregut operations. However, this is reflective of the patients with post-surgical gastroparesis in many referral centers, so limits to generalizability should be minor. Follow up was not available for all patients, and it is impossible to conjecture as to the nature of the censored symptom scores or gastric emptying studies. While we communicate with patients that 4-hour solid-phase gastric emptying studies with retention or emptying percentage reported at 1, 2, and 4 hours are preferred, not all centers follow this protocol or reporting standard, and as such, some pre-post comparisons are impossible. Since the GCSI only asks patients to rate the prior 2 weeks, it is possible that assessment of GCSI at a different time would result in different GCSI scores. We have not routinely collected laboratory tests for nutritional parameters prior to, or post-POP, so it is not known when the improvements in symptom scores and emptying correspond to nutritional improvement.

Conclusion

Endoscopic per-oral pyloromyotomy results in significant improvement in all domains of the Gastroparesis Cardinal Symptom Index for most patients with medically refractory post-surgical gastroparesis. In addition, POP improves radiographic gastric emptying for most patients, potentially delaying or eliminating the need for gastrectomy in this patient population.

Author Contributions All the authors agree to be accountable to contents of manuscript.

Andrew Strong: study concept and design, data collection, statistical analysis, initial draft of abstract and manuscript, final approval of manuscript.

Joshua Landreneau: study concept and design, data collection and analysis, final approval of manuscript.

Michael Cline: study concept and design, data collection, critical appraisal of manuscript, final approval of manuscript.

Matthew Kroh: data collection, critical appraisal of manuscript, final approval of manuscript.

John Rodriguez: data collection, critical appraisal of manuscript, final approval of manuscript.

Jeffrey Ponsky: study concept and design, critical appraisal of manuscript, final approval of manuscript.

Kevin El-Hayek: study concept and design, data collection, data analysis and interpretation, critical appraisal of manuscript, final approval of manuscript.

Compliance of Ethical Standards

As is customary at our institution for any novel interventional technique, all patients undergoing POP are tracked prospectively in a registry approved by the Institutional Review Board.

References

1. Wang YR, Fisher RS, Parkman HP (2008) Gastroparesis-related hospitalizations in the United States: trends, characteristics, and outcomes, 1995-2004. Am J Gastroenterol 103:313–322
2. Hirsch W, Nee J, Ballou S, Petersen T, Friedlander D, Lee H-N, Cheng V, Lembo A (2017) Emergency Department Burden of Gastroparesis in the United States, 2006 to 2013. J Clin Gastroenterol. https://doi.org/10.1097/MCG.0000000000000972
3. Wadhwa V, Mehta D, Jobanputra Y, Lopez R, Thota PN, Sanaka MR (2017) Healthcare utilization and costs associated with gastroparesis. World Journal of Gastroenterology 23:4428
4. Camilleri M, Parkman HP, Shafi MA, Abell TL, Gerson L, American College of Gastroenterology (2013) Clinical guideline: management of gastroparesis. Am J Gastroenterol 108:18–37; quiz 38
5. Pasricha PJ, Parkman HP (2015) Gastroparesis: definitions and diagnosis. Gastroenterol Clin North Am 44:1–7
6. Quigley EMM (2015) Other forms of gastroparesis: postsurgical, Parkinson, other neurologic diseases, connective tissue disorders. Gastroenterol Clin North Am 44:69–81
7. Paulon E, Nastou D, Jaboli F, Marin J, Liebler E, Epstein O (2017) Proof of concept: short-term non-invasive cervical vagus nerve stimulation in patients with drug-refractory gastroparesis. Frontline Gastroenterol 8:325–330
8. Bhayani NH, Sharata AM, Dunst CM, Kurian AA, Reavis KM, Swanstrom LL (2015) End of the road for a dysfunctional end organ: laparoscopic gastrectomy for refractory gastroparesis. J Gastrointest Surg 19:411–417
9. Clarke JO, Sharaiha RZ, Kord Valeshabad A, Lee LA, Kalloo AN, Khashab MA (2013) Through-the-scope transpyloric stent placement improves symptoms and gastric emptying in patients with gastroparesis. Endoscopy 45 Suppl 2 UCTN:E189–190
10. Gourcerol G, Tissier F, Melchior C, Touchais JY, Huet E, Prevost G, Leroi AM, Ducrotte P (2015) Impaired fasting pyloric compliance in gastroparesis and the therapeutic response to pyloric dilatation. Aliment Pharmacol Ther 41:360–367
11. Wellington J, Scott B, Kundu S, Stuart P, Koch KL (2017) Effect of endoscopic pyloric therapies for patients with nausea and vomiting and functional obstructive gastroparesis. Auton Neurosci 202:56–61
12. Coleski R, Anderson MA, Hasler WL (2009) Factors associated with symptom response to pyloric injection of botulinum toxin in a large series of gastroparesis patients. Dig Dis Sci 54:2634–2642
13. Hibbard ML, Dunst CM, Swanström LL (2011) Laparoscopic and endoscopic pyloroplasty for gastroparesis results in sustained symptom improvement. J Gastrointest Surg 15:1513–1519
14. Gilsdorf D, Volckmann E, Brickley A, Taylor LJ, Glasgow RE, Fang J Pyloroplasty Offers Relief of Postfundoplication Gastroparesis in Patients Who Improved After Botulinum Toxin Injection. J Laparoendosc Adv Surg Tech A 27:1180–1184
15. Mancini SA, Angelo JL, Peckler Z, Philp FH, Farah KF (2015) Pyloroplasty for Refractory Gastroparesis. Am Surg 81:738–746
16. Shada AL, Dunst CM, Pescarus R, Speer EA, Cassera M, Reavis KM, Swanstrom LL (2016) Laparoscopic pyloroplasty is a safe and effective first-line surgical therapy for refractory gastroparesis. Surg Endosc 30:1326–1332
17. Shlomovitz E, Pescarus R, Cassera MA, Sharata AM, Reavis KM, Dunst CM, Swanström LL (2015) Early human experience with per-oral endoscopic pyloromyotomy (POP). Surg Endosc 29:543–551
18. Allemang MT, Strong AT, Haskins IN, Rodriguez J, Ponsky JL, Kroh M (2017) How I Do It: Per-Oral Pyloromyotomy (POP). J Gastrointest Surg 21:1963–1968
19. Rodriguez JH, Haskins IN, Strong AT, Plescia RL, Allemang MT, Butler RS, Cline MS, El-Hayek K, Ponsky JL, Kroh MD (2017) Per oral endoscopic pyloromyotomy for refractory gastroparesis: initial results from a single institution. Surg Endosc 31:5381–5388
20. Revicki DA, Rentz AM, Dubois D, Kahrilas P, Stanghellini V, Talley NJ, Tack J (2003) Development and validation of a patient-assessed gastroparesis symptom severity measure: the Gastroparesis Cardinal Symptom Index. Aliment Pharmacol Ther 18:141–150
21. Revicki DA, Rentz AM, Dubois D, Kahrilas P, Stanghellini V, Talley NJ, Tack J (2004) Gastroparesis Cardinal Symptom Index (GCSI): development and validation of a patient reported assessment of severity of gastroparesis symptoms. Qual Life Res 13:833–844
22. Abell TL, Camilleri M, Donohoe K, et al (2008) Consensus Recommendations for Gastric Emptying Scintigraphy: A Joint Report of the American Neurogastroenterology and Motility Society and the Society of Nuclear Medicine. The American Journal of Gastroenterology 103:753–763
23. Hasler WL, May KP, Wilson LA, et al (2018) Relating gastric scintigraphy and symptoms to motility capsule transit and pressure findings in suspected gastroparesis. Neurogastroenterol Motil. https://doi.org/10.1111/nmo.13196
24. Rodriguez J, Strong AT, Haskins IN, et al (2018) Per-oral Pyloromyotomy (POP) for Medically Refractory Gastroparesis: Short Term Results From the First 100 Patients at a High Volume Center. Ann Surg 268:421–430
25. Sarosiek I, Yates K, Abell TL, et al (2011) Interpreting Symptoms Suggesting Gastroparesis in Patients After Gastric and Esophageal Surgeries. Gastroenterology 140:S813
26. Shafi MA, Pasricha PJ (2007) Post-surgical and obstructive gastroparesis. Curr Gastroenterol Rep 9:280–285
27. Fich A, Neri M, Camilleri M, Kelly KA, Phillips SF (1990) Stasis syndromes following gastric surgery: clinical and motility features of 60 symptomatic patients. J Clin Gastroenterol 12:505–512
28. Lee H-S, Kim MS, Lee JM, Kim SK, Kang KW, Zo JI (2005) Intrathoracic gastric emptying of solid food after esophagectomy for esophageal cancer. Ann Thorac Surg 80:443–447
29. Arya S, Markar SR, Karthikesalingam A, Hanna GB (2015) The impact of pyloric drainage on clinical outcome following esophagectomy: a systematic review. Dis Esophagus 28:326–335
30. Datta J, Williams NN, Conway RG, Dempsey DT, Morris JB (2014) Rescue pyloroplasty for refractory delayed gastric emptying following esophagectomy. Surgery 156:290–297
31. Vu MK, Ringers J, Arndt JW, Lamers CB, Masclee AA (2000) Prospective study of the effect of laparoscopic hemifundoplication on motor and sensory function of the proximal stomach. Br J Surg 87:338–343
32. Bais JE, Samsom M, Boudesteijn EA, van Rijk PP, Akkermans LM, Gooszen HG (2001) Impact of delayed gastric emptying on the outcome of antireflux surgery. Ann Surg 234:139–146
33. Khajanchee YS, O'Rourke R, Cassera MA, Gatta P, Hansen PD, Swanström LL (2007) Laparoscopic reintervention for failed antireflux surgery: subjective and objective outcomes in 176 consecutive patients. Arch Surg 142:785–901; discussion 791-792
34. Pellegrini CA (2001) Delayed gastric emptying in patients with abnormal gastroesophageal reflux. Ann Surg 234:147–148
35. Sawyers JL (1990) Management of postgastrectomy syndromes. Am J Surg 159:8–14
36. Gustavsson S, Ilstrup DM, Morrison P, Kelly KA (1988) Roux-Y stasis syndrome after gastrectomy. Am J Surg 155:490–494
37. Vogel SB, Woodward ER (1989) The surgical treatment of chronic gastric atony following Roux-Y diversion for alkaline reflux gastritis. Ann Surg 209:756–761; discussion 761-763

38. Speicher JE, Thirlby RC, Burggraaf J, Kelly C, Levasseur S (2009) Results of completion gastrectomies in 44 patients with postsurgical gastric atony. J Gastrointest Surg 13:874–880
39. Nakada K, Takahashi M, Ikeda M, et al (2016) Factors affecting the quality of life of patients after gastrectomy as assessed using the newly developed PGSAS-45 scale: A nationwide multi-institutional study. World J Gastroenterol 22:8978–8990
40. Brenkman HJF, Tegels JJW, Ruurda JP, et al (2018) Factors influencing health-related quality of life after gastrectomy for cancer. Gastric Cancer 21:524–532
41. Shan B, Shan L, Morris D, Golani S, Saxena A (2015) Systematic review on quality of life outcomes after gastrectomy for gastric carcinoma. J Gastrointest Oncol 6:544–560
42. Lacy BE, Crowell MD, Mathis C, Bauer D, Heinberg LJ (2018) Gastroparesis: Quality of Life and Health Care Utilization. J Clin Gastroenterol 52:20–24
43. Yu D, Ramsey FV, Norton WF, Norton N, Schneck S, Gaetano T, Parkman HP (2017) The Burdens, Concerns, and Quality of Life of Patients with Gastroparesis. Dig Dis Sci 62:879–893
44. Garland SN, Lounsberry J, Pelletier G, Bathe OF (2011) "How do you live without a stomach?": a multiple case study examination of total gastrectomy for palliation or prophylaxis. Palliat Support Care 9:305–313
45. Clark CJ, Sarr MG, Arora AS, Nichols FC, Reid-Lombardo KM (2011) Does gastric resection have a role in the management of severe postfundoplication gastric dysfunction? World J Surg 35: 2045–2050
46. Gerritsen A, Furnée EJB, Gooszen HG, Wondergem M, Hazebroek EJ (2013) Evaluation of gastrectomy in patients with delayed gastric emptying after antireflux surgery or large hiatal hernia repair. World J Surg 37:1065–1071
47. Farahmand M, Sheppard BC, Deveney CW, Deveney KE, Crass RA (1997) Long-term outcome of completion gastrectomy for non-malignant disease. J Gastrointest Surg 1:182–187
48. Forstner-Barthell AW, Murr MM, Nitecki S, Camilleri M, Prather CM, Kelly KA, Sarr MG (1999) Near-total completion gastrectomy for severe postvagotomy gastric stasis: analysis of early and long-term results in 62 patients. J Gastrointest Surg 3:15–21, discussion 21-23
49. McCallum RW, Polepalle SC, Schirmer B (1991) Completion gastrectomy for refractory gastroparesis following surgery for peptic ulcer disease. Long-term follow-up with subjective and objective parameters. Dig Dis Sci 36:1556–1561
50. Takahashi H, Allemang MT, Strong AT, Boules M, Nor Hanipah Z, Guerron AD, El-Hayek K, Rodriguez JH, Kroh MD (2018) Completion Gastrectomy with Esophagojejunostomy for Management of Complications of Benign Foregut Surgery. J Laparoendosc Adv Surg Tech A 28:983–989
51. Jones MP, Maganti K (2003) A systematic review of surgical therapy for gastroparesis. Am J Gastroenterol 98:2122–2129
52. Borrazzo EC (2013) Surgical management of gastroparesis: gastrostomy/jejunostomy tubes, gastrectomy, pyloroplasty, gastric electrical stimulation. J Gastrointest Surg 17:1559–1561
53. Soares RV, Swanstrom LL (2015) Endoscopic approaches to gastroparesis. Curr Opin Gastroenterol 31:368–373
54. Farrell TM, Richardson WS, Halkar R, Lyon CP, Galloway KD, Waring JP, Smith CD, Hunter JG (2001) Nissen fundoplication improves gastric motility in patients with delayed gastric emptying. Surg Endosc 15:271–274
55. Masqusi S, Velanovich V (2007) Pyloroplasty with fundoplication in the treatment of combined gastroesophageal reflux disease and bloating. World J Surg 31:332–336
56. Luketich JD, Fernando HC, Christie NA, Buenaventura PO, Ikramuddin S, Schauer PR (2002) Outcomes after minimally invasive reoperation for gastroesophageal reflux disease. Ann Thorac Surg 74:328–331; discussion 331-332
57. Grover BT, Kothari SN (2015) Reoperative antireflux surgery. Surg Clin North Am 95:629–640