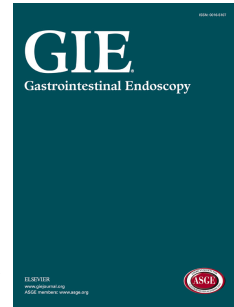


Journal Pre-proof



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PII: S0016-5107(19)32489-7

DOI: <https://doi.org/10.1016/j.gie.2019.11.039>

Reference: YMGE 11857

To appear in: *Gastrointestinal Endoscopy*

Received Date: 12 April 2019

Accepted Date: 19 November 2019

Please cite this article as: Spadaccini M, Maselli R, Chandrasekar VT, Anderloni A, Carrara S, Galtieri PA, Di Leo M, Fugazza A, Pellegatta G, Colombo M, Palma R, Hassan C, Sethi A, Khashab MA, Sharma P, Repici A, Gastric peroral endoscopic pyloromyotomy for refractory gastroparesis: a systematic review of early outcomes with pooled analysis, *Gastrointestinal Endoscopy* (2020), doi: <https://doi.org/10.1016/j.gie.2019.11.039>.

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Gastric peroral endoscopic pyloromyotomy for refractory gastroparesis: a systematic review of early outcomes with pooled analysis

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Key words: gastric peroral endoscopic pyloromyotomy, G-POEM, refractory gastroparesis

Marco Spadaccini: conception and design, analysis and interpretation of the data, drafting of the article.

Roberta Maselli: critical revision of the article for important intellectual content.

Viveksandeep Thoguluva Chandrasekar: analysis and interpretation of the data, critical revision of the article for important intellectual content.

Andrea Anderloni: critical revision of the article for important intellectual content.

Silvia Carrara: critical revision of the article for important intellectual content.

Piera Alessia Galtieri: critical revision of the article for important intellectual content.

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Gaia Pellegatta: critical revision of the article for important intellectual content.

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Alessandro Repici: critical revision of the article for important intellectual content; final approval of the article.

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ABSTRACT

Background and Aims: Gastroparesis (GP) is a chronic debilitating condition. Prior pyloric-targeted procedures are either invasive or have questionable efficacy. Gastric peroral pyloromyotomy(G-POEM) has been proposed as a minimally invasive approach. We performed a pooled-analysis to evaluate the efficacy and safety of G-POEM for GP.

Methods: Electronic databases(Medline, Scopus, EMBASE) were searched up to January 2019. Studies including patients who underwent G-POEM for GP were eligible. Procedural, clinical and safety outcomes were assessed pooling data by means of a random- or fixed-effect model according to the degree of heterogeneity to obtain a proportion with a 95% confidence interval(CI).

Results: Ten studies were eligible for inclusion (292 patients), 2/10 being prospective. Seven studies were performed in the United States, 2 in France and 1 in China. The endoscopic pyloromyotomy was feasible in all the patients. Significant symptomatic improvement was achieved after 83.9% of the procedures (mean follow-up period:7.8±5.5 months). When comparing the mean values of pre- and postprocedural scintigraphic evolution, there was a significant decreasing of the residual percentage at 2 and 4 hours. The overall adverse events rate was 6.8%.

Discussion G-POEM appears as a promising approach for GP in terms of safety and efficacy outcomes in the short term.

BACKGROUND

Gastroparesis (GP) is a chronic debilitating condition defined as a functional disorder with objective delayed gastric emptying in the absence of a mechanical obstruction. Clinical presentation includes postprandial fullness and epigastric discomfort, bloating, nausea, retching and vomiting. Moreover, the clinical burden of GP has been shown to be compounded by reduced quality of life and impaired nutritional status [1], causing an increasing incidence of GP-related hospitalization [2].

Several conditions have been correlated to GP, with approximately 90% of patients having diabetic [3], idiopathic or postsurgical GP. Other etiologies include neurological/muscular disorders and

collagen vascular diseases.

Dietary modification and prokinetics, such as Metoclopramide, are the initial treatments. However, these modestly address clinical needs due to the poor tolerability profile [4,5]. Further, several patients are refractory to these strategies, and no validated alternatives are available.

Aiming to assess a pathophysiological mechanism to be specifically targeted, Mearin et al [6] had manometrically described episodes of unusually intense and prolonged pyloric contractions, named as “pylorospasm”. This pyloric dysfunction has been recently correlated with GP symptoms by new and easier devices such as the endolumenal functional lumen imaging probe (EndoFLIP; Crospon Inc., Galway, Ireland) [7,8].

Therefore, interventional procedures on pyloric apparatus such as electrical stimulation, botulinum toxin intrapyloric injection, transpyloric stent placement and laparoscopic pyloromyotomy, have been proposed [9-11]. Unfortunately, none of them have confirmed yet their efficacy in well-designed prospective studies.

Gastric peroral endoscopic pyloromyotomy (G-POEM) is a minimally invasive endosurgical procedure recently introduced by Khashab et al [12]. G-POEM consists of creating a prepyloric submucosal tunnel extending to the pylorus, before dissecting circular and oblique muscle bundles, as per the endoscopic myotomy (POEM) previously described for treating achalasia [13].

Since its first report, several studies have followed. Thus, the aim of this article was to systematically review data on G-POEM and to pool the results of the different experiences, with a specific focus on efficacy and safety.

METHODS

The methods of our analysis and inclusion criteria were based on Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) recommendations [14]. Our systematic review protocol was registered with the International Prospective Register of Systematic Reviews (PROSPERO, www.crd.york.ac.uk/prospero/) on February 2019 (registration number:

CRD42019123323).

The following methods are reported in Appendix 1: data sources and search strategy, the selection process, data extraction and the quality assessment.

Inclusion and exclusion criteria

For the purpose of this systematic review, we considered all clinical studies including patients with refractory gastroparesis treated using gastric peroral endoscopic pyloromyotomy since 2013 (ie, when G-POEM was first reported). Only studies reporting data on technical success were considered. Authors of studies were contacted for accurate information if the data provided in the articles were insufficient. Prospective and retrospective studies, published as full text, including at least 5 patients were considered. Studies only published as abstracts were not considered. Studies not published in the English language were excluded.

Outcome assessment

The primary outcome was the technical success rate. Secondary outcomes were the mean procedural time, the rate of clinical success, and the rate of adverse events such as intra- and postprocedural bleeding, perforation and stricture. Pre- and postprocedural Gastroparesis Cardinal Symptom Index (GCSI) and gastric emptying scintigraphy (GES), if provided, were also assessed.

Statistical Analysis

For the purpose of statistical analyses, the measure of the effect of interest included pooled rates in form of percentages with number of events/success over the total number of patients (%) with 95% confidence limits. The I² test was used to denote the heterogeneity and p-value of <0.05 was considered significant. The corresponding forest plots were constructed with pooled estimates of these outcomes and individual studies were weighted according to the size. Meta-regression analysis was used for relating outcome estimates to study characteristics. All meta-analytic computations, including the estimates with 95% confidence intervals for pooled rates as well as heterogeneity (measured as I² statistics) were performed using statistical software Open Meta analyst (CEBM, Brown University, RI, USA). An I²-value of 0% to 30%, 30% to 60%, 60% to

75% and 75% to 100% were indicated as low, moderate, substantial, and considerable heterogeneity, respectively.

RESULTS

Study and patient characteristics

The literature search resulted in 439 articles (Figure 1). After preliminary screening of titles and abstracts, 17 articles were selected to be reviewed as full text. Of these, 10 articles, published between 2015 and 2019, matched the selection criteria and were included for quantitative syntheses. Seven studies were performed in the United States (227 patients), 2 in France (49 patients), and 1 study was from China (16 patients). All studies but 2 were single-center experiences. Eight studies had a retrospective design. Otherwise the studies by Rodriguez and Jacques were prospective. The average Newcastle Ottawa score was 5.5 (range 5-6). Studies characteristics are summarized in Table 1.

The 10 studies reported outcomes of 292 patients treated with G-POEM for refractory GP. Seventy-six out of 272 patients (27.9%) were males (provided by 9 studies) and the mean age was of 50.5 ± 6.0 years, ranging from 45.0 to 63.5 years (provided by 8 studies). In terms of etiology 76 out of 292 (26.7%) patients had a postsurgical GP, 78 of 292 (26.7%) patients had diabetes-associated GP, and 15 out of 292, 5.1% had other underlying conditions. The remained patients were classified as idiopathic (121/292, 41.5%).

All of the included patients had previously failed first line medical treatments with pro-kinetics. Nine studies (285 patients) reported any previous interventional approach: the most diffuse procedures were the botulinum toxin intrapyloric injection (28.1%) and gastric electrical stimulator (12.6%). Four and one patients underwent transpyloric stenting (1.4%) and dilation (0.3%), respectively. Laparoscopic pyloric surgery had been previously performed in 4 patients (1.4%). Preprocedural patients characteristic of each study are provided in Supplementary Tables 1 and 2.

Procedural outcomes

The endoscopic pyloromyotomy was feasible in all the 292 procedures, irrespective of the endoscopic approach. Most of the procedures were performed with a greater curvature approach (55.5%). Otherwise the lesser curvature was chosen for tunnelling in the 33.2% of cases. Finally, in 16 and 17 patients an anterior or posterior wall approach was preferred, respectively.

The mean myotomy length was 2.7 ± 0.7 cm, ranging from 2.0 to 3.5 cm (reported by 6 studies). Either clipping (266/285 cases) or suturing (21/285) were the 2 closure strategies to have the gastric mucosotomy sealed. Two patients were reported to undergo both endosuturing and clip placement in the series by Kahaleh et al.

Overall, a mean procedure duration of 62.4 ± 27.0 minutes (33.8-119.0) was reported by 8 studies. Procedural outcomes are summarized in Table 2 and a brief technical comment is provided in Appendix 2. Procedural characteristics of each study are provided in Supplementary Table 3

Clinical success

The mean follow up period was 7.8 ± 5.5 months in the 10 studies. Significant symptomatic improvement (provided by 8 studies) was achieved after 83.9% (95% CI, 78.5 – 89.3; $I^2 = 0\%$; $p = 0.928$) of the procedures (Figure 2). The result of meta-regression analysis showed no significant relationships between clinical success rate and patients characteristics such as gender, age, GP etiology, preprocedural GCSI score, and GES evaluation, and previous pylorus-directed treatment (Table 3).

Six studies reported the pre- and postprocedural Gastroparesis Cardinal Symptom Index score: the mean preprocedural GCSI score was 3.3 ± 0.6 and the mean postprocedural GCSI score dropped to 1.61 ± 0.61 ($p < 0.001$).

When comparing the mean values of pre- and postprocedural scintigraphic evolution, there was a significant decreasing of the residual percentage at 2 and 4 hours: 74.9 ± 5.2 % versus 52.5 ± 10.8 % (p value: <0.001), and 44.1 ± 13.0 % versus 20.6 ± 9.5 % ($p < 0.001$), respectively. Pre- and postprocedural GCSI and scintigraphic evolution of each study are provided in Supplementary Table 4.

Adverse events

Based on the data reported by all the studies, 26 procedures resulted in adverse events, yielding an overall pooled rate of 6.8% (95% CI, 2.4 – 11.2; I^2 – 60.8%; $p = 0.006$) (Figure 3). Immediate and postprocedural bleedings occurred in the 1.9% (95% CI, -0.1 to 3.9; I^2 – 27.8%; $p = 0.188$) (Supplementary Figure 1) and 2.6% (95% CI, 0.8 – 4.5; I^2 – 0%; $p = 0.969$) (Supplementary Figure 2) of procedures, respectively. Gastric ulcers were reported in 5 cases, with a pooled rate of 2.3% (95% CI, 0.6 – 4.0; I^2 – 0%; $p = 0.998$) (Supplementary Figure 3). Moreover, perforations and peritoneal abscess were reported in 3 and 1 cases, respectively. Late events such as pyloric strictures were reported after 1% (95% CI, -0.1% to 2.2%; I^2 – 0%; $p = 0.962$) of cases (Supplementary Figure 4).

Finally, the mean duration of hospital stay was 3.4 ± 1.6 days, ranging from 1.3 to 6.0.

Safety outcomes of each study are provided in Supplementary Table 5.

DISCUSSION

Gastroparesis remains a difficult clinical problem with few definitive, tolerable, and sustaining solutions. For refractory cases, pylorus-directed surgical options are too invasive, and endoscopic approaches seems to have conflicting results in term of both efficacy and safety. The technical feasibility and clinical success of esophageal POEM for achalasia has opened “third-space” doors for the treatment of other gastro intestinal motility disorders including gastroparesis, in which pylorospasm contributes to the underlying problem.

In our systematic review, the reported technical outcomes, clinical success, and adverse events were comprehensively evaluated. The efficacy data of G-POEM are relevant for the following reasons. A technical success rates of 100% coupled with a favourable safety profile, conclusively reassure on the technical feasibility of the procedure. This is not surprising given the procedural similarity with POEM. The esophageal procedure has already shown such high technical success rates [15],

although being slightly less feasible in patients undergone previous interventional treatment [16,17].

In our analysis, we could not categorize outcomes for G-POEM according to previous treatment, owing to limited available data, however considering the technical success rate recorded, prior treatment does not seem to result in inability to perform the procedure.

Secondly, although the definition of clinical success is still not standardized, G-POEM appears to be an effective options (83.9 %), with a significant improvement of both GCSI and scintigraphic studies. Our analysis supports the previous findings on pylorus-directed therapies, about improving nausea and vomiting, early satiety (both reported in GCSI score) and gastric emptying time at gastric scintigraphy [28, 29]. Currently, there are no reliable data to help in predicting which patients would benefit the most from G-POEM. In this setting GCSI score itself, aiming to capture symptoms related purely to pylorospasm, could be considered as an easy-to-use indicator of likelihood of responding to pyloromyotomy. Further, although not investigated in most of the included studies, objective parameters other than GES, such as pyloric manometry and impedance planimetry are being proposed as tools for outcomes prediction [30, 31]. Aiming to predict the patient benefit, we run a univariate metaregression investigating whether patient characteristics, GP etiology, preprocedural evaluation, and previous pylorus-directed treatment were related to G-POEM efficacy. No relations were founded; however, the limited sample size probably make our analysis underpowered to definitively rule out such relationships. Indeed, in our opinion only a better insight on the physiopathological mechanism of gastroparesis would permit a real breakthrough in better orienting within our therapeutic armamentarium.

Nevertheless, waiting for future evidences on these tools, considering the proposed mechanism that certain symptoms (ie, nausea/vomiting and early satiety) correlate with definite pathophysiological alteration (ie, pylorus dysfunction) [32-34], coupled with our data on GCSI score significantly improving after G-POEM, at the moment this symptomatic score could be considered a more feasible surrogate for preprocedural assessment in clinical practice.

However, it should be addressed that conclusions of our analysis are affected by several

shortcomings inherent to the included studies. First of all, being G-POEM a relatively new technique, long-term data on symptom relief are still lacking. Moreover, all the individual experiences but one [27], enrolled less than 50 patients, preventing any reliable estimate on G-POEM outcomes. Nevertheless, in our opinion a comprehensive sample size of almost 300 patients followed up for more than 6 months, permits us to reassure on the benefit of this technique.

Second of all, none of the included studies reported a head-to-head comparison with either surgical or endoscopic pylorus-directed therapies. The lack of interventional-designed studies keeps the overall level of evidence supporting G-POEM for GP still low. However, reassuring on the safety profile of G-POEM, our study may be informative for designing such comparative studies.

Conversely, one of the main strengths of our analysis is the only mild-to-moderate interstudy heterogeneity reported across the different outcomes, leading to robust estimates. Secondly, the precise overview on technical features (ie, site for tunnelling and myotomy, length of myotomy, closure strategy, procedural time, length of hospital stay) give to the reader the opportunity to become familiar even with the most practical aspects of this cutting edge technique.

In conclusion, G-POEM appears as a promising endoscopic technique with convincing data in terms of both subjective and objective efficacy outcomes in the short term, and a reassuring safety profile. While waiting to prove possible superiority to other pylorus-directed interventional approaches in large controlled trials, it may be suggested by expert endoscopists when dealing with refractory gastroparesis.

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Author	Publication	Year	Country	Design	Mono/multicenter	NOS	Patients (n)
J. Xu	Full text	2018	China	Retrospective	Mono	5	16
Z. Malik	Full text	2018	USA	Retrospective	Mono	5	13
E. Shlomovitz	Full text	2015	USA	Retrospective	Mono	5	7
J. Jacques	Full text	2019	France	Prospective	Mono	5	20
P. Mekaroonkamol	Full text	2019	USA	Retrospective	Mono	6	30
J.M. Gonzalez	Full text	2017	France	Retrospective	Mono	6	29
M. Kahaleh	Full text	2018	USA	Retrospective	Multicenter	6	33
M.A. Khashab	Full text	2017	USA	Retrospective	Multicenter	6	30
J.H. Rodriguez	Full text	2018	USA	Prospective	Mono	6	100
H.B. Xue	Full text	2017	USA	Retrospective	Mono	5	14

Table 1: studies characteristics. NOS: Newcastle-Ottawa Scale

Procedural outcomes	Results
Technical success (%)	292/292 (100)
Endoscopic approach (%)	
<ul style="list-style-type: none"> • Great curvature • Lesser curvature • Anterior wall • Posterior wall 	<ul style="list-style-type: none"> • 162/292 (55,5) • 97/292 (33,2) • 16/292 (5,5) • 17/292 (5,8)
Mean myotomy length (cm)	2,7 ± 0,7
Closure strategy (%)	285/292 (97,6)
<ul style="list-style-type: none"> • Clipping • Suturing 	<ul style="list-style-type: none"> • 266/285 (93,3) • 21/285 (7,7)
Mean procedure duration (min)	62,4 ± 27,0

Table 2: procedural outcomes. Two patients underwent both endo-suturing and clip placement.

Variable	Coefficient	lower limit of 2.5%	upper limit of 97.5%	P value
Mean Age	0,00	-0,08	0,08	0,947
Male (%)	-0,17	-2,49	2,14	0,884

Etiology: postsurgical GP (%)	-0,41	-2,12	1,30	0,637
Etiology: diabetic GP(%)	1,18	-2,02	4,38	0,470
Etiology: idiopathic GP(%)	-0,57	-3,01	1,87	0,646
Mean GCSI score	0,48	-0,68	1,65	0,415
GES (half emptying time)	0,00	-0,01	0,01	0,446
GES (retention at 2 hours)	0,04	-0,08	0,15	0,551
GES (retention at 4 hours)	-0,01	-0,04	0,03	0,784
Previous treatment: dilation (%)	-6,79	-22,11	8,52	0,384
Previous treatment: Botox (%)	-0,32	-1,72	1,09	0,660
Previous treatment: pyloric surgery (%)	-5,74	-17,45	5,97	0,336
Previous treatment: transpyloric stenting (%)	2,90	-5,64	11,44	0,505
Previous treatment: gastric stimulator (%)	-3,25	-8,16	1,667	0,195

Table 3: Metaregression analysis * All continuous variables were mean-centered variables. GP: Gastroparesis; GCSI: Gastroparesis Cardinal Symptom Index; GES: Gastric Emptying Scintigraphy.

FIGURE Legends

Figure 1: Flow chart of the study selection process.

Figure 2: Forest plot reporting the rates of clinical success. CI: confidence interval. RE: random effect.

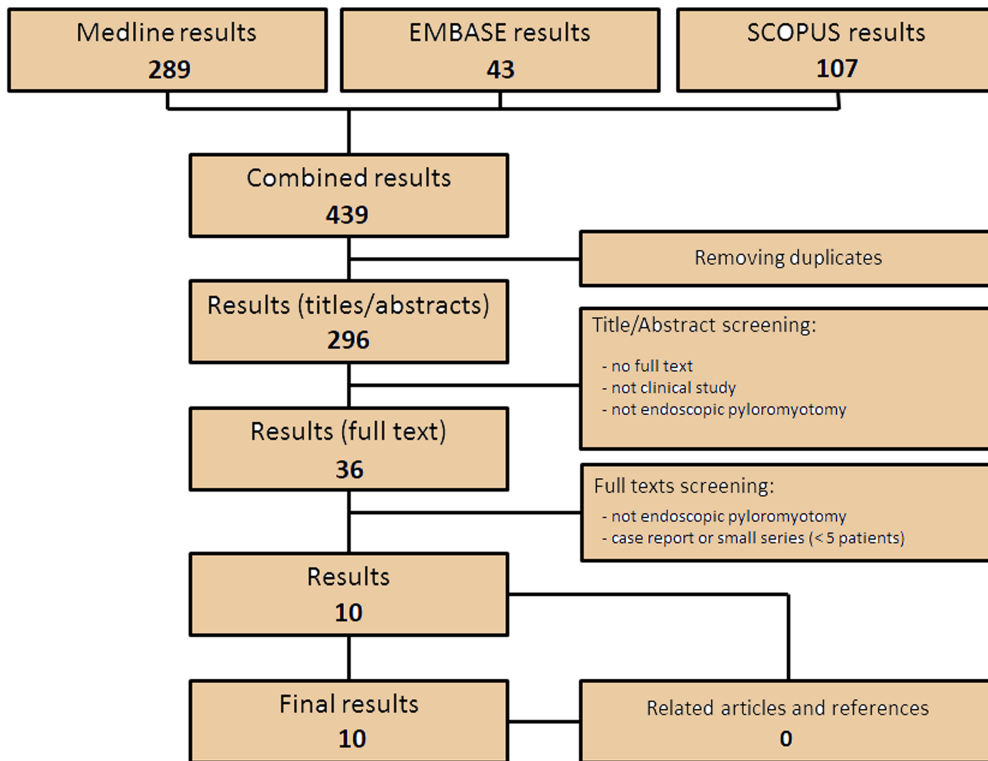
Figure 3: Forest plot reporting the rates of adverse events. CI: confidence interval. RE: random effect.

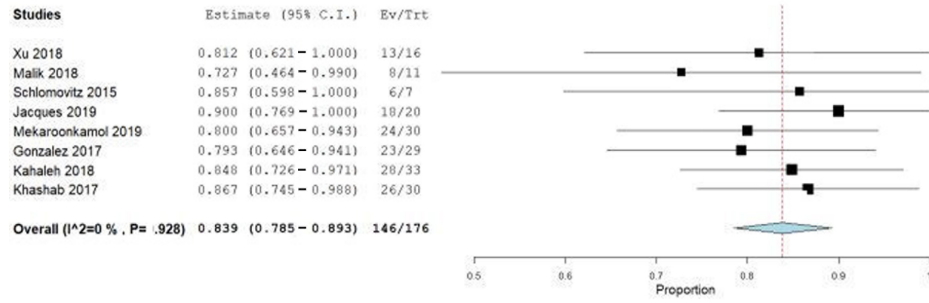
Supplementary figure 1: Forest plot reporting the rates of intraprocedural bleeding. CI: confidence interval. RE: random effect.

Supplementary figure 2: Forest plot reporting the rates of postprocedural bleeding. CI: confidence interval. RE: random effect.

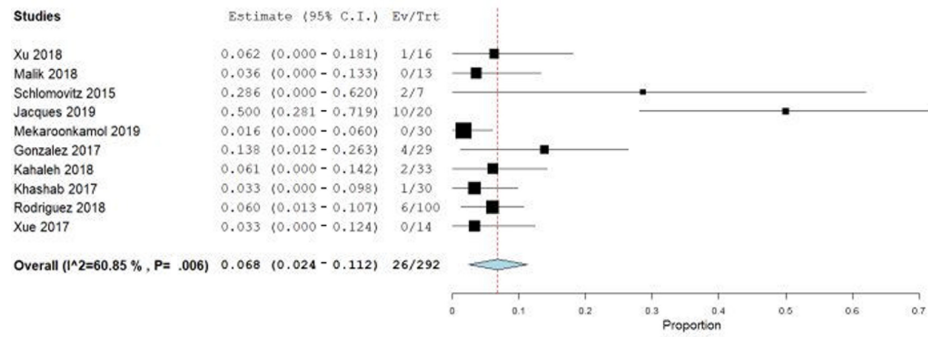
Supplementary figure 3: Forest plot reporting the rates of ulcer formation. CI: confidence interval. RE: random effect.

Supplementary figure 4: Forest plot reporting the rates of stricture. CI: confidence interval. RE: random effect.





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Appendix 1

Data sources and search strategy

A comprehensive electronic literature search was conducted in PubMed/MEDLINE, EMBASE and Scopus (up to January 20th 2019) to identify eligible studies that performed Gastric Peroral Endoscopic Pyloromyotomy (G-POEM) for Refractory Gastroparesis. PROSPERO was searched for ongoing or recently completed systematic reviews. Electronic searches were supplemented by manual searches of references of included studies and review articles. Literature search was performed and verified by two authors (MS; MC).

The search for studies of relevance was performed using the following text words and corresponding Medical Subject Heading/Entree terms when possible: “pyloromyotomy”, “G-POEM”. The Medline search strategy was: ("pyloromyotomy"[MeSH Terms] OR "pyloromyotomy"[All Fields] OR "g poem"[All Fields]) OR ("pyloromyotomy"[MeSH Terms] OR "pyloromyotomy"[All Fields]).

Selection process

Two review authors (MS; MC) independently screened the titles and abstracts yielded by the search against the inclusion criteria. Full reports were obtained for all titles that appeared to meet the inclusion criteria or where there was any uncertainty. Review author pairs then screened the full text and abstract reports and decided whether these met the inclusion criteria. Disagreements were resolved through discussion of all the authors. The reasons for excluding trials were recorded. Neither of the review authors was blinded to the journal titles or to the study authors or institutions. When there were multiple articles for a single study, we used the latest publication and supplemented it, if necessary, with data from the more complete version.

Data extraction

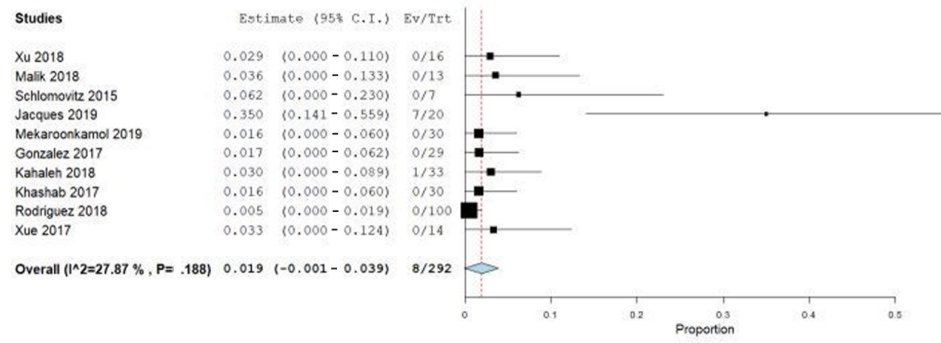
Using standardized forms, two reviewers (MS, MC) extracted data independently and in duplicate from each eligible study. Reviewers resolved disagreements by discussion, and the arbitrators (RM and AR) unresolved disagreements. The following data were extracted for each study: first author, year of publication, study design, number of centers, number of patients, age, gender, gastroparesis aetiology, previous interventional treatments, endoscopic approach (greater or lesser curvature) myotomy length, mean procedural time, technical success, clinical success, pre- and post-procedural assessment of gastroparesis cardinal symptom index (GCSI), pre- and post-procedural assessment of gastric emptying scintigraphy, mean hospital stay, adverse events such as intra-procedural bleed, post-procedural bleed, stricture and perforation. In order to retrieve all data with homogeneity among studies, we had requested the corresponding authors from studies for necessary information if not reported in the manuscript.

Quality assessment

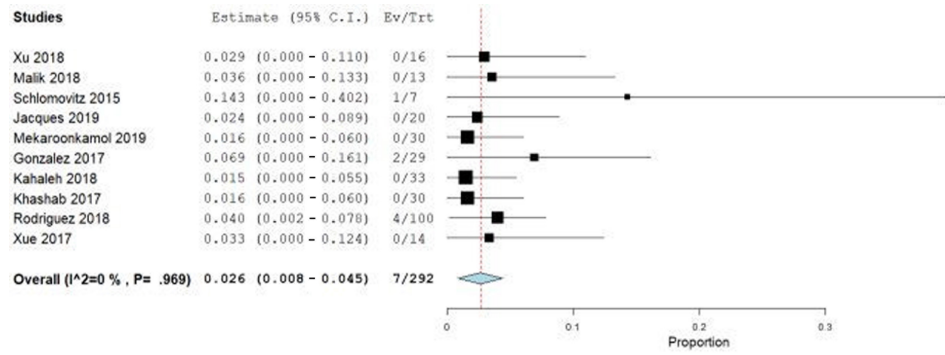
Quality was assessed by the modified Newcastle-Ottawa Scale for non-randomized studies, ranging from 0 (low-quality) to 5 (high-quality). Two reviewers (MS, MC) assessed quality measures for included studies and discrepancies were adjudicated by collegial discussion.

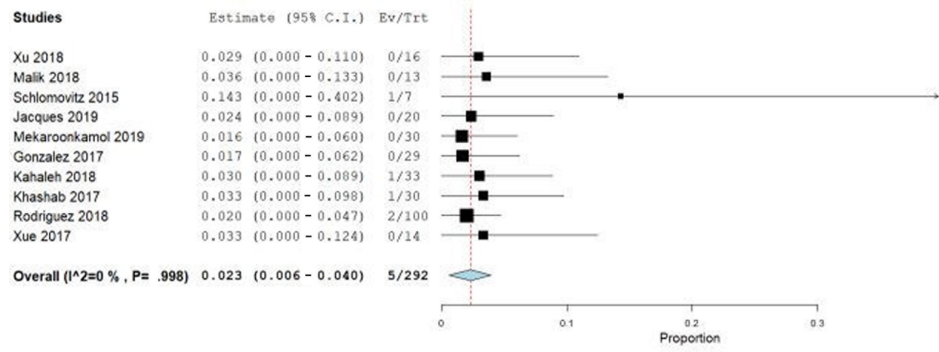
G-POEM uses the principles of submucosal endoscopy to identify and dissect the pyloric ring. Technical variations of G-POEM include different myotomy orientations, myotomy length, and mucosotomy closure tools. Most experts utilize a greater curvature approach as it permits easy entry into the tunnel and subsequent myotomy. Recently, a lesser curvature approach was described.¹ One advantage of this latter approach is that it avoids the dependent area of the stomach and, thus, stomach contents do not interfere with visualization during the procedure. There are currently no comparative studies between both approaches. In terms of tunnel and myotomy length, most experts perform a short (3–4-cm) tunnel to (1) ensure straight and direct access to the pylorus and avoid tunneling away from the ring and (2) avoid a long antral myotomy which theoretically may worsen gastroparesis. The final step of mucosal closure can be harder in the stomach as compared with the esophagus because of the thick mucosa, frequent presence of mucosal edema, and decreased tissue elasticity in the stomach. Nevertheless, mucosal closure using endoclips is successful in the vast majority of cases. Closure using endoscopic suturing can be utilized if clip closure is not possible.

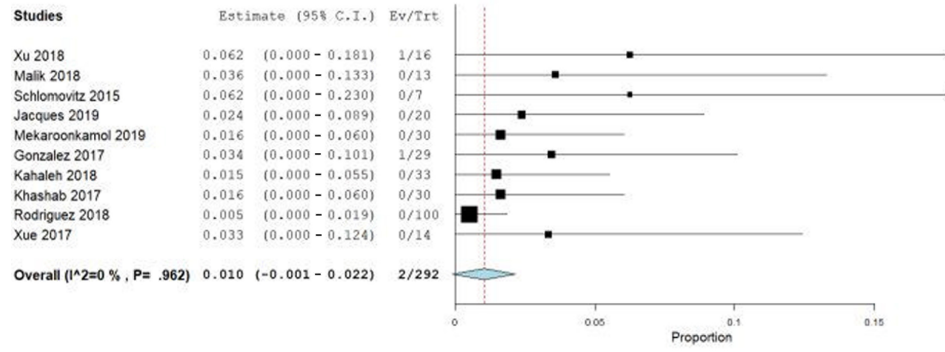
1. Rodriguez J, Strong AT, Haskins IN, et al. Per-oral Pyloromyotomy (POP) for Medically Refractory Gastroparesis: Short Term Results From the First 100 Patients at a High Volume Center. *Ann Surg* 2018;268:421-430.



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Reference	Patients (n)	Mean Age (years)	M (n)	Aetiology			
				PS (n)	Diabetic (n)	Idiopathic (n)	Other (n)
J. Xu, 2018	16	63.5	11	13	3	0	0
Z. Malik, 2018	13	45.7	6	8	1	4	0
E. Shlomovitz, 2015	7	51.0	0	2	0	5	0
J. Jacques, 2019	20	NA	NA	1	10	4	5
P. Mekaroonkamol, 2019	30	47.0	4	5	12	12	1
J.M. Gonzalez, 2017	29	52.8	10	5	7	15	2
M. Kahaleh, 2018	33	52.0	11	12	7	12	2
M.A. Khashab, 2017	30	47.0	13	12	11	7	0
J.H. Rodriguez, 2018	100	45.0	15	19	21	56	4
H.B. Xue, 2017	14	NA	6	1	6	6	1

Supplementary Table 1: Preprocedural patients characteristics. M: males; PS: postsurgical; NA: not available

Reference	Patients (n)	Previous treatment						
		Dilation (n)	EFT (n)	BT (n)	PS (n)	PEJ (n)	T-S (n)	G-S (n)
J. Xu, 2018	16	0	5	0	0	0	0	0
Z. Malik, 2018	13	1	0	11	1	0	0	3
E. Shlomovitz, 2015	7	NA	NA	NA	NA	NA	NA	NA
J. Jacques, 2019	20	0	0	2	0	0	0	0
P. Mekaroonkamol, 2019	30	0	4	1	2	2	0	4
J.M. Gonzalez, 2017	29	0	0	1	0	0	0	4
M. Kahaleh, 2018	33	0	0	4	0	0	0	2
M.A. Khashab, 2017	30	0	0	12	0	1	4	0
J.H. Rodriguez, 2018	100	0	26	46	1	12	0	21
H.B. Xue, 2017	14	0	0	3	0	0	0	2

Supplementary Table 2: Pre-procedural patients characteristics. EFT: enteral feeding tube; BT: botulinum toxin; PS: pyloric surgery; PEJ: percutaneous endoscopic jejunostomy; T-S: transpyloric stent placement; G-S: gastric stimulator; NA: not available.

Reference	Patients (n)	Endoscopic approach				Myotomy length (cm)	Closure incision		Technical success (n)	Mean time (min)
		GC (n)	LC (n)	AW (n)	PW (n)		M-C (n)	S-D (n)		
J. Xu, 2018	16	16	0	0	0	NA	13	3	16	45
Z. Malik, 2018	13	13	0	0	0	3.5	0	13	13	119
E. Shlomovitz, 2015	7	0	0	7	0	2.0	NA	NA	7	N.A.
J. Jacques, 2019	20	20	0	0	0	NA	20	0	20	56
P. Mekaroonkamol, 2019	30	30	0	0	0	NA	30	0	30	48
J.M. Gonzalez, 2017	29	29	0	0	0	2.0	29	0	29	47
M. Kahaleh, 2018	33	31	2	0	0	3.3	32	3	33	77
M.A. Khashab, 2017	30	19	0	9	2	2.6	28	2	30	72
J.H. Rodriguez, 2018	100	4	95	0	1	NA	100	0	100	33
H.B. Xue, 2017	14	0	0	0	14	3.0	14	0	14	N.A.

Supplementary Table 3: Procedural characteristics. Myotomy length is reported asy mean (cm). GC: great curvature; LC: lesser curvature; AW: anterior wall; PW: posterior wall; M-C: metal clips; S-D: suturing device; NA: not available.

Reference	Patients (n)	Mean GCSI		Mean GES pretreatment			Mean GES post-treatment		
		pre-GPOEM	post-GPOEM	H-E time (min)	Ret at 2h (%)	Ret at 4h (%)	H-E time (min)	Ret at 2h (%)	Ret at 4h (%)
J. Xu, 2018	16	N.A.	N.A.	183	69	N.A.	84	33	N.A.
Z. Malik, 2018	13	2,2	1,9	NA	78	49	NA	60	33
E. Shlomovitz, 2015	7	NA	NA	124	NA	21	58	NA	4
J. Jacques, 2019	20	3,5	1,8	345	82	58	100	56	15
P. Mekaroonkamol, 2019	30	3,5	1,8	N.A.	N.A.	63	N.A.	N.A.	22
J.M. Gonzalez, 2017	29	3,3	0,95	202	70	40	130	55	28
M. Kahaleh, 2018	33	3,3	0,8	222	76	45	143	58	30
M.A. Khashab, 2017	30	N.A.	N.A.	N.A.	N.A.	37	N.A.	N.A.	17
J.H. Rodriguez, 2018	100	3,8	2,4	N.A.	N.A.	40	N.A.	N.A.	16
H.B. Xue, 2017	14	N.A.	N.A.	N.A.	N.A.	N.A.	N.A.	N.A.	N.A.

Supplementary Table 4: Pre- and postprocedural GCSI and scintigraphic evolution. GCSI: Gastroparesis Cardinal Symptom Index; GPOEM: gastric peroral endoscopic pyloromyotomy; H-E: half-emptying; Ret at 2h/4h: retention at 2 hours/4hours; N.A.: not available.

Reference	Patients (n)	Hospital stay (days)	Adverse events						
			Immediate bleeding (n)	Late bleeding (n)	Ulcer (n)	Peritoneal abscess (n)	Str (n)	Prf (n)	Overall (n)
J. Xu, 2018	16	6,0	0	0	0	0	1	0	1
Z. Malik, 2018	13	2,5	0	0	0	0	0	0	0
E. Shlomovitz, 2015	7	2,3	0	1	1	0	0	0	2
J. Jacques, 2019	20	3,7	7	0	0	0	0	3	10
P. Mekaroonkamol, 2019	30	2,4	0	0	0	0	0	0	0
J.M. Gonzalez, 2017	29	NA	0	2	0	1	1	0	4
M. Kahaleh, 2018	33	5,4	1	0	1	0	0	0	2
M.A. Khashab, 2017	30	3,3	0	0	1	0	0	0	1
J.H. Rodriguez, 2018	100	1,3	0	4	2	0	0	0	6
H.B. Xue, 2017	14	NA	0	0	0	0	0	0	0

Supplementary Table 5: Safety outcomes. Hospital stay: mean duration of hospital stay; Str: stricture; Prf: perforation; NA: not available.

ACRONYMS

GP: Gastroparesis

G-POEM: Gastric Peroral Endoscopic Pyloromyotomy

POEM: Peroral Endoscopic Myotomy

PRISMA: Preferred Reporting Items for Systematic Reviews and Meta-Analyses

GCSI: Gastroparesis Cardinal Symptom Index

GES: Gastric Emptying Scintigraphy

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