

EUS-guided gastroenterostomy for the management of gastric outlet obstruction: A systematic review and meta-analysis

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ABSTRACT

Gastric outlet obstruction (GOO) is characterized by epigastric pain and postprandial vomiting secondary to mechanical obstruction. Management of GOO is usually focused on alleviating the symptoms of obstruction and can be achieved by surgical gastrojejunostomy or enteral stenting. Recent studies have shown success with EUS-guided gastroenterostomy (EUS-GE) in the management of GOO but data is limited. We, therefore, conducted a meta-analysis to evaluate the safety and efficacy of EUS-GE in the management of GOO. A comprehensive literature review was conducted by searching the Embase and PubMed databases from inception to January 2019 to identify all studies that evaluate the efficacy and safety of EUS-GE in GOO. Our primary outcome was to evaluate technical success and clinical success. Secondary outcomes were to evaluate the need for reintervention and adverse events of the procedure. Twelve studies including 285 patients were included in the meta-analysis. Technical success was achieved in 266 patients with a pooled technical success of 92% (95% confidence interval [CI]: 88%–95%). Clinical success was achieved in 90% of the patients (95% CI: 85%–94%). Recurrence of symptoms or unplanned reintervention was needed in 9% of the patients (95% CI: 6%–13%) and adverse events were reported in 12% of the patients (95% CI: 8%–16%). The heterogeneity tests among studies were nonsignificant with $I^2 = 0$. EUS-GE is a safe and efficacious treatment modality for the management of benign and malignant GOO. Larger prospective studies are needed to further evaluate its utility in GOO.

Key words: EUS, enteral stenting, gastric outlet obstruction, gastroenterostomy, gastrojejunostomy

INTRODUCTION

Gastric outlet obstruction (GOO) is a potential complication of pancreatic or distal gastric malignancy and may present in as many as 15%–20% of patients with pancreatic adenocarcinoma.^[1,2] Ampullary cancer,

lymphoma, and biliary malignancy may also cause GOO. There are also several benign etiologies of GOO including chronic pancreatitis, peptic ulcer

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disease, caustic ingestion, and others.^[3-6] Patients usually present with epigastric pain, postprandial vomiting and unable to tolerate an oral diet. Therefore, the primary goal in the management of GOO is to relieve the obstruction so that patients can tolerate an oral diet.^[2] This has been conventionally achieved by surgical gastrojejunostomy (SGJ) or enteral stenting (ES). Studies have reported comparable efficacy of both approaches though better short-term outcomes with ES compared to SGJ.^[7-10] SGJ can be associated with high morbidity and mortality.^[11]

EUS-guided gastroenterostomy (EUS-GE) has recently been successfully utilized in the management of GOO.^[12-24] In EUS-GE, an EUS-guided bypass is made by inserting a lumen apposing metal stent (LAMS) from the gastric lumen to the small bowel distal to the obstruction. Currently, limited evidence exists regarding the efficacy and safety of this procedure, and the literature is mostly limited to small case series and observational studies. We, therefore, conducted a systematic review and meta-analysis of the available literature to evaluate the safety and efficacy of this procedure in benign and malignant GOO.

MATERIALS AND METHODS

Search strategy

A systematic literature search was conducted in the PubMed and Embase databases to identify all studies from inception to January 2019 that assessed the efficacy of EUS-GE in GOO. The systematic literature review was independently conducted by two investigators using search terms as follows: (((“Gastric Outlet Obstruction” [Mesh] OR “Gastric Outlet Obstruction” [tiab])) AND (“Endosonography” [Mesh] OR “endosonography” [tiab])) AND (“Gastroenterostomy” [Mesh] OR “Gastroenterostomy” [tiab]) in PubMed. We also searched Embase using terms, “endoscopic ultrasonography”/exp OR “endoscopic ultrasonography” OR “endoscopic ultrasonography”:Ti, ab AND “gastroenterostomy”/exp OR “gastroenterostomy” OR “gastroenterostomy”:Ti, ab and “gastrojejunostomy”/exp OR “gastrojejunostomy” OR “gastrojejunostomy”:Ti, ab AND, “endoscopic ultrasonography”/exp OR “endoscopic ultrasonography” OR “endoscopic ultrasonography”:Ti, ab.

Selection criteria

Eligible studies were observational studies or case series that evaluated the efficacy of EUS-GE for the

management of GOO. Included studies should also report technical success and safety outcomes of the procedure. We did not include individual case reports. A sample size of the study did not restrict its inclusion in the meta-analysis. There was no language restriction for the study to be included in the meta-analysis. Abstracts that are not fully published were also eligible for inclusion if they reported our outcomes of interest. The Newcastle–Ottawa quality assessment scale was used to evaluate the quality of observational studies in three areas: the recruitment of cases and controls, the comparability of the two groups and the outcome of interest of the cohort study. We also evaluated the quality of the case series using NIH quality assessment tools. The results of the methodological quality assessment did not influence the eligibility of the studies. This study was conducted in agreement with the Preferred Reporting Items for Systematic Reviews and Meta-Analysis statement.^[25]

Data extraction

A structured data collection form was used to extract the following data from each study: demographic information, indications for EUS-GE, etiology of GOO, technical success, clinical success, adverse events, recurrence of symptoms or need for reintervention, procedure time if reported, and procedural technique utilized. Technical success was defined as successful EUS-guided deployment of the LAMS. Clinical success was defined as the ability to tolerate oral intake after the procedure. The data regarding stent diameter was inconsistently reported therefore was not abstracted. To ensure accuracy, data extraction was independently performed by two investigators and was reviewed by the third investigator. Any disagreement was resolved by mutual consensus.

Statistical analysis

Meta-analyses were conducted for each included outcome using the random-effects model. Incidence rates and 95% confidence intervals (CIs) were estimated for binary outcomes from included studies. Each included study’s pooled estimates and measures of variability were used to generate Forrest plots. Publication bias was evaluated by Egger’s test. Variability between included studies was assessed via heterogeneity tests using the I^2 statistics. The I^2 statistic was calculated to quantify the proportion of between-study heterogeneity attributable to variability in the association rather than sampling variation. A value of I^2 of 0%–25% represented no significant

heterogeneity, 26%–50% represented low heterogeneity, 51%–75% represented moderate heterogeneity, and $I^2 > 75\%$ represented high heterogeneity. All analyses were conducted in RStudio (Version 1.0.136, RStudio, Inc. Boston, MA, USA) using the “Meta” and “Metafor” package.^[26]

RESULTS

The initial search revealed 274 articles, 23 in PubMed and 251 in Embase. After the removal of duplicates, review articles, and editorials, 22 articles underwent title and abstract review and 17 articles were selected for full manuscript review. Articles were excluded if they evaluated the efficacy of EUS-GE for any indication other than GOO. If the article was presented in abstract form and fully published, we only included the fully published article to avoid duplication. After a full review, 12 articles including 285 patients were included in the final meta-analysis.^[12-15,17-24] We believe that Chen *et al.* 2017 study comparing EUS-GE with ES and Khashab *et al.* 2017 study comparing EUS-GE and SGJ has a similar patient population in EUS-GE group.^[16,17] Therefore, we excluded Chen *et al.* 2017 study from the meta-analysis to avoid duplication.^[16] Figure 1 elaborates on the systematic literature review process of our study.

Among 12 included studies 3 were case series, 1 prospective study, and 8 retrospective studies. 7 of

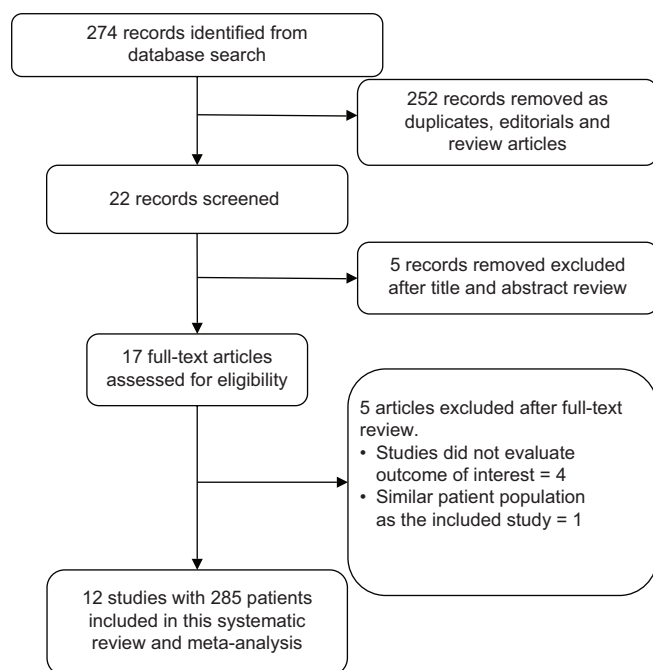


Figure 1. Literature review process

the included studies were good quality studies while 5 were of fair quality. EUS-GE was performed in 202 patients with GOO secondary to malignancy while 83 patients had benign etiologies of GOO. EUS-GE was performed with different procedural techniques with direct EUS-GE is the most common approach, followed by balloon-assisted technique and EUS-guided double-balloon occluded gastrojejunostomy bypass (EPASS). Baseline characteristics and quality assessment of the included studies were reported in Table 1.

Technical success was achieved in 266 of 285 patients who underwent EUS-GE with a pooled technical success of 92% (95% CI: 88%–95%) [Figure 2]. Clinical success was achieved in 249 patients with a pooled clinical success rate of 90% (95% CI: 85%–94%) [Figure 3]. The technical and clinical success of the individual study was reported in Table 1. Adverse events occurred in 28 patients with a pooled incidence of 12% (95% CI: 9%–17%) [Figure 4]. Adverse events are reported in detail in Table 1. Recurrence of GOO symptoms and the need for unplanned re-intervention occurred in 16 patients with a pooled incidence of 9% (95% CI: 6%–13%) [Figure 5]. There was no statistical heterogeneity existed among the included studies ($I^2 = 0\%$, $P > 0.05$). Egger’s test indicated no publication bias as the symmetry existed in the funnel plot ($P > 0.05$) [Figure 6].

DISCUSSION

This is the first meta-analysis done to evaluate the safety and efficacy of EUS-GE in the management of GOO. GOO carries a poor prognosis and is associated with high morbidity and mortality. GOO increases the risk of malnutrition and significantly impacts the quality of life. Therefore, the primary goal in these patients is to relieve the symptoms of obstruction that would support them tolerate the oral intake.^[2] SGJ has been conventionally done for the palliation of symptoms but it is invasive and associated with significant morbidity.^[11] Endoscopic stenting of the duodenum is an alternative to surgical bypass and has comparable efficacy and has the advantage of being less invasive and shorter time to tolerate oral intake.^[7-11,27,28] However, as compared to surgical bypass, endoscopic ES has a higher rate of stent occlusion which may require the need for reintervention.^[8,11]

EUS-GE provides a safe and efficient approach by utilizing LAMS to create a bypass to relieve symptoms

Table 1. Baseline characteristics of the included studies

Author's name, years, Country	Sample size	Study design	Quality of the study	Baseline characteristics	Efficacy of the procedure (%)	Adverse events	Recurrence/reintervention	Procedural technique
Barthet et al., 2015, France ⁽¹²⁾	3	Case series	Good	Benign GOO=1 Malignant GOO=2 Mean age=45 Male=3	TS=100 CS=100	1 minor adverse event due to excessive jejunal using needle knife None	None	NOTES endoscopic GI anastomosis
Khashab et al., 2015, USA ⁽¹³⁾	10	Retrospective cohort study	Fair	Benign GOO=7 Malignant GOO=3 Male=7 Mean age=55.8	TS=90 CS=100	None	None	Direct EUS-GE=1 Balloon-assisted EUS-GE=9
Tyberg et al., 2016, USA ⁽¹⁴⁾	26	Multicenter international retrospective study	Good	Benign GOO=9 Malignant GOO=17 Male=11 Mean age=66.2	TS=92 CS=85	Peritonitis=1 Bleeding=1 Abdominal pain requiring laparotomy=1	None	Assisted methods Contrast filled balloon=13 Nasobiliary drain=3 Ultra slim scope=5 Unassisted methods Direct EUS-GE=3 NOTES=2 EPASS=20
Itoi et al., 2016, Japan ⁽¹⁵⁾	20	Prospective cohort study	Fair	Benign GOO=None Malignant GOO=20	TS=90 CS=100	Stent misdeployment=2	None	EPASS=22
Chen et al., 2017, USA ⁽¹⁶⁾	30	Multicenter international retrospective study	Good	Benign GOO=0 Malignant GOO=30 Male=17 Mean age=70±13.3	TS=87 CS=83.3	Adverse events reported in 5 patients	1	Direct EUS-GE=2 Balloon-assisted EUS GE=6
Khashab et al., 2017, USA ⁽¹⁷⁾	30	Multicenter international retrospective study	Good	Benign GOO=0 Malignant GOO=30 Male=17 Mean age=70±13.3	TS=87 CS=87	Stent misdeployment=3 Abdominal pain requiring hospitalization=2	1	EPASS=22 Direct EUS-GE=2 Balloon-assisted EUS GE=7
Chen et al., 2018, USA ⁽¹⁸⁾	26	Multicenter retrospective study	Fair	Benign GOO=26 Malignant GOO=0 Male=14 Mean age=57.7±13.9	TS=96.2 CS=84	Stent misdeployment=2 Gastric leak needing surgical intervention=1	1	EPASS=4 Direct EUS-GE=15 Balloon-assisted EUS GE=7
Perez-Miranda et al., 2017, Spain ⁽¹⁹⁾	25	Multicenter retrospective cohort study	Fair	Benign GOO=8 Malignant GOO=17 Male=11 Mean age=63.9	TS=88 CS=84	Bleeding=2 Peritonitis=1	NR	Assisted methods Balloon catheter=9 Nasobiliary drain=3 Ultra slim scope=7 Unassisted methods Direct EUS-GE=6 Direct EUS-GE=27 Balloon-assisted EUS GE=10
Kerdisirichairat et al., 2018, USA ⁽²⁰⁾	37	Retrospective cohort study	Fair	Benign GOO=7 Malignant GOO=30 Male=18 Median age=63	TS=94.6 CS=85.7	1 patient had gastrocolonic fistula due to delayed LAMS migration	5	Direct EUS-GE=52 Balloon-assisted EUS GE=22
Chen et al., 2018, USA ⁽²¹⁾	74	Multicenter retrospective study	Good	Benign GOO=25 Malignant GOO=49 Male=33 Mean age=63±11.7	TS=94.2 CS=92.3	Stent misdeployment=5	7	None
Ge et al., 2018, USA ⁽²²⁾	22	Retrospective cohort study	Good	Benign GOO=0 Malignant GOO=22 Male (entire cohort)=56% Mean age (entire cohort)=65.9±11.9	TS=100 CS=91.7	5 patient had adverse events including 2 patients who had misdeployments resulting in perforation None	2	None
Urrehman et al., 2018, Singapore ⁽²³⁾	5	Case series	Good	Benign GOO=0 Malignant GOO=5 Median age=61.5	TS=100 CS=80	None	None	Balloon assisted
Brewer Gutierrez et al., 2017, USA ⁽²⁴⁾	7	Multicenter case series	Good	Benign GOO=0 Malignant GOO=7 Male=3 Mean age=64.6±12.5	TS=100 CS=100	None	None	Direct EUS-GE=5 Balloon-assisted EUS GE=2

¹⁹Study is excluded from the meta-analysis as EUS-GE patient population likely same as Khashab et al. 2017 as seen by similar baseline characteristics, techniques of EUS-GE used, similar study period, clinical success and authors of study. GOO: Gastric outlet obstruction, TS: Technical success, CS: Clinical success, GE: Gastroenterostomy, NR: Not reported, EPASS: EUS-guided double balloon occluded gastrojejunostomy bypass, NOTES: Natural orifice transluminal endoscopic surgery, LAMS: Lumen apposing metal stent, Gi: Gastrointestinal

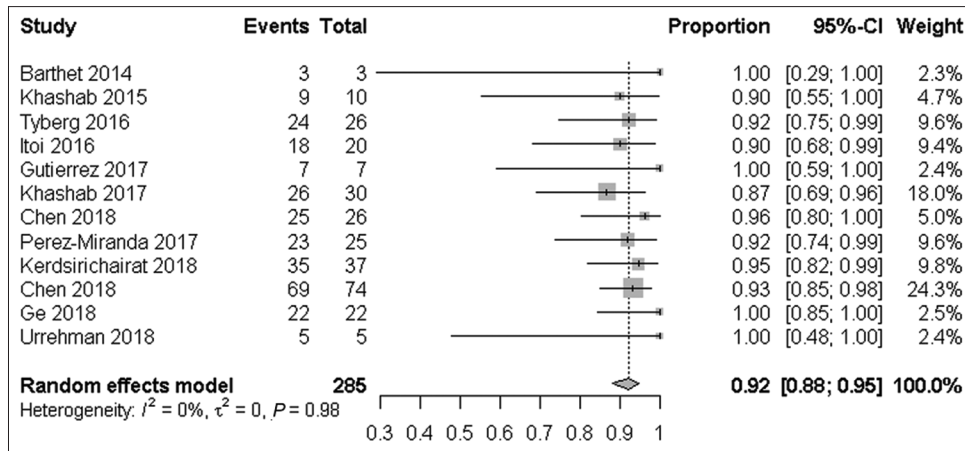


Figure 2. Forrest plot of all studies for technical success

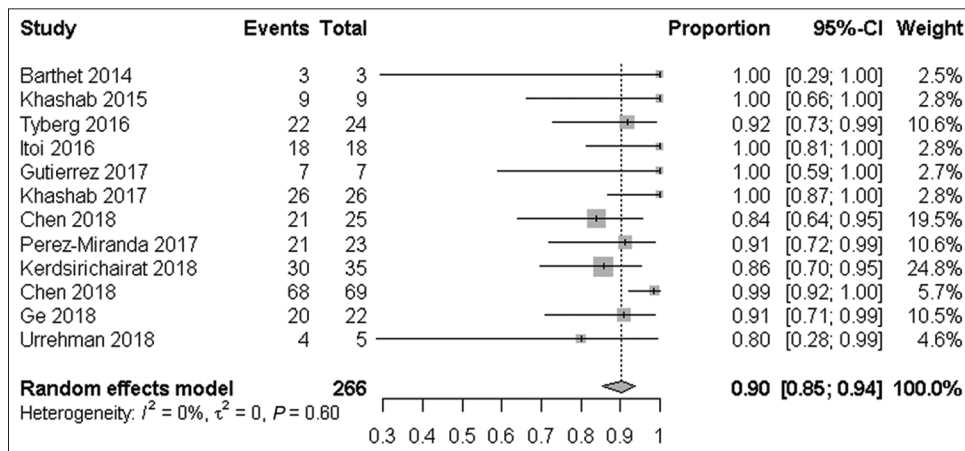


Figure 3. Forrest plot of all studies for clinical success

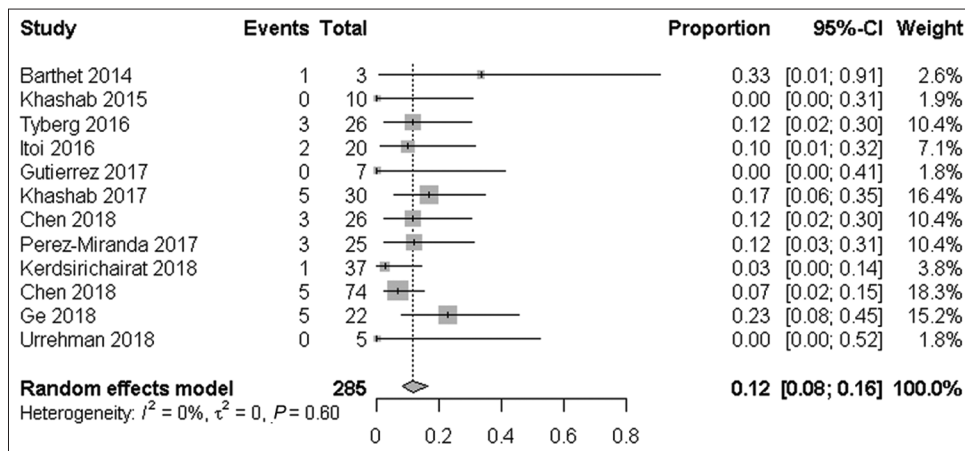


Figure 4. Forrest plot of all studies for adverse events

of obstruction. This meta-analysis revealed technical success and clinical success of EUS-GE (92% and 90% respectively) which is comparable to that of ES (technical success 96%–97% and clinical success 85%–90%) and SGJ (technical success of 99%–100% and clinical success of 80%–90%) as demonstrated

in previous studies.^[7-11] However, there are only a few studies to date that directly compares the efficacy and safety of EUS-GE with SGJ or ES. In a multicenter retrospective study that included 82 patients Chen *et al.* compared endoscopic duodenal stenting with EUS-GE in patients with malignant GOO.^[16] The study found

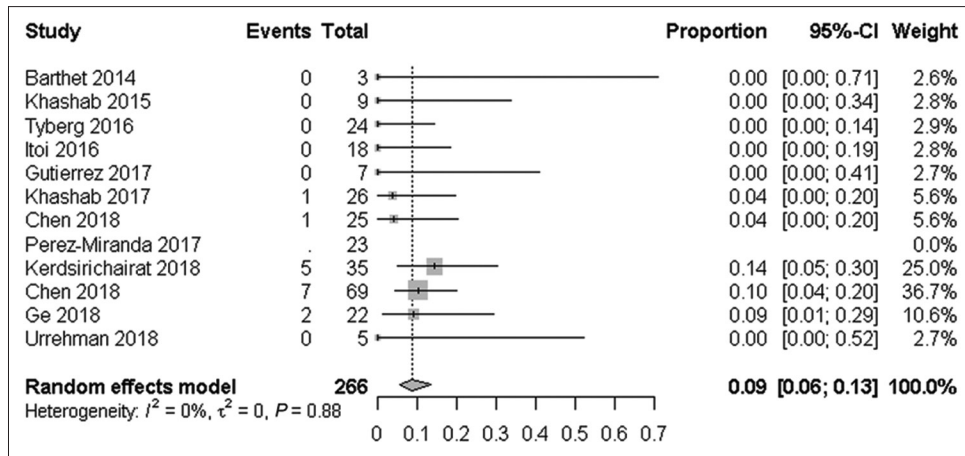


Figure 5. Forrest plot of all studies for recurrence of symptoms or need for re-intervention

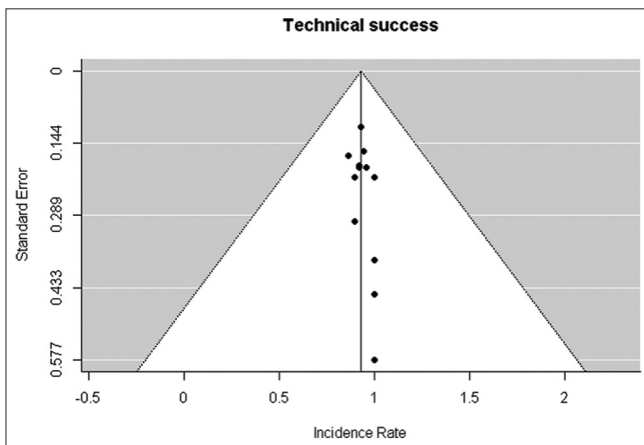


Figure 6. Funnel plot diagram to evaluate publication bias

no significant difference in technical success, clinical success, and rate of adverse events between the two groups. Recurrence of symptoms and the need for repeat intervention was higher in the ES group compare to EUS-GE (28.6% vs. 4%; $P = 0.015$).^[16] Similarly, in an international multicenter retrospective study by Perez-Miranda *et al.*, there was no difference in the technical and clinical success of EUS-GE and SGJ.^[19] However, the rate of adverse events was significantly lower in the EUS-GE group compare to SGJ. Khashab *et al.* compared EUS-GE with SGJ and showed higher technical success with SGJ. Despite this, there was no significant difference in clinical success, rate of adverse events, or need for reintervention.^[17] Kerdsirichairat *et al.* evaluated the long-term outcomes of EUS-GE using LAMS in 37 patients. This study showed promising long-term outcomes of the procedure with 82.3% and 77.8% of patients showed favorable outcomes at 6 and 12 months.^[20] There was only one adverse event reported in a patient who developed gastro-colonic fistula due to migration of LAMS.

Although malignant GOO is more prevalent, benign etiologies can also cause GOO. Endoscopic balloon dilation (EBD) has usually been considered as the initial treatment modality but its success largely depends upon the etiology of benign disease. EBD along with eradication of *Helicobacter pylori* is effective in around 80% of the patient with GOO secondary to PUD.^[3,29] EBD has poor efficacy in the management of strictures secondary to chronic pancreatitis and requires multiple sessions in management of injury to caustic substances.^[4-6,30-33] ES has also been considered in the management of benign GOO and has shown favorable results but is associated with stent migration.^[10,34] Chen *et al.* in a study done on 26 patients who underwent EUS-GE due to GOO secondary to benign etiologies demonstrated technical success in 96% and clinical success in 84%. Therefore, EUS-GE might be a promising procedure in patients who have failed EBD or who have a benign cause of GOO.

EUS-GE is also safe and successful in the management of GOO in patients with altered anatomy.^[14,19] It has also been utilized in the management of afferent loop syndrome (ALS) and in the reversal of altered anatomy in patients with previous gastric bypass.^[35-38] In a case series of 15 patients with altered anatomy EUS-GE was technically and clinically successful in all patients with complications reported in only two patients.^[38] In a multicenter retrospective series of 18 patients with ALS EUS-GE was technically successful in 100% of the patients.^[36] Resolution of symptoms occurred in 16 patients while the other two patients reported improvement in their ALS-related symptoms. Adverse events and re-intervention were required in 3 patients.^[36]

The optimal technique for EUS-GE is still unclear. Direct EUS-GE carries a risk of inadvertent colonic

access, but the use of methylene blue infusion into the small intestinal lumen followed by utilization of needle puncture and aspiration of infused bluish material may decrease that risk. Another technique is the injection of contrast via the access needle and evaluation under fluoroscopy to confirm small bowel lumen access *vs.* colonic puncture. Chen *et al.* compared the efficacy and safety of direct EUS-GE technique with balloon-assisted EUS-GE.^[21] No difference was found between the two groups in technical success, clinical success, rate of adverse events, need for repeat intervention, or survival. However, mean procedure time was significantly lower in direct GE group compared to the balloon-assisted group (35.7 min *vs.* 89.9 min).^[21] EPASS is also an alternative EUS-GE technique that is not currently available in the United States, and most of the included studies that utilized this technique were conducted in Japan. Future prospective studies are needed to further evaluate any difference in outcomes between different EUS-GE techniques.

The systematic literature search of our study is comprehensive, the sample size is fair, and all the included studies are fair to good quality; however, there are some limitations to our meta-analysis. First, the majority of the included studies are case series and retrospective studies which may introduce bias in the study results. There are only limited retrospective studies that directly compared the EUS-GE with ES or SGJ. Furthermore, most of the studies are done by the same group of authors; therefore, despite our best efforts to exclude duplication of patients, there is still a chance of this which also may introduce bias in our study results. The sample size of the studies is small to moderate and larger prospective studies are lacking. Finally, although the statistical heterogeneity is insignificant, methodological heterogeneity might still exist given differences in techniques of the procedure, patient population, and expertise of the clinician.

CONCLUSION

In summary, EUS-GE is an effective treatment modality for the management of benign and malignant GOO and might be associated with lesser adverse effects compared to other techniques. The rate of reintervention and recurrence of symptoms are also lower with EUS-GE. Further research is needed to directly compare the efficacy of EUS-GE with endoscopic duodenal stenting and SGJ in GOO and to evaluate optimal EUS-GE technique.

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Conflicts of interest

There are no conflicts of interest.

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