**Name of Journal:** *World Journal of Gastrointestinal Oncology*

**Manuscript NO:** 64447

**Manuscript Type:** MINIREVIEWS

**Conservative management of malignant gastric outlet obstruction syndrome-evidence based evaluation of endoscopic ultrasound-guided gastroentero-anastomosis**

Cominardi A *et al*. EUS-GA for malignant gastric obstruction

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**Received:** February 21, 2021

**Revised:** April 16, 2021

**Accepted:** July 21, 2021

**Published online:**

**Abstract**

Gastric outlet obstruction (GOO) is a clinical syndrome characterized by postprandial vomiting, abdominal pain, bloating and, in advanced cases, by weight loss secondary to inadequate oral intake. This clinical entity may be caused by mechanical obstruction, either benign or malignant, or by motility disorders. In this review we will focus on malignant GOO and on its endoscopic ultrasound (EUS)-guided palliative treatment. The most frequent malignant causes of this syndrome are gastric and locally advanced pancreatic carcinomas; other causes include duodenal or ampullary neoplasms, gastric lymphomas, retroperitoneal lymphadenopathies and, more infrequently, gallbladder and bile duct cancers. Surgery represents the treatment of choice when radical and curative resection is potentially feasible; if the malignant cause is not likely to be completely resected, palliative treatments should be proposed. Palliative treatments for malignant GOO are primarily based on surgical gastro-jejunostomy and endoscopic placement of enteral self-expanding metal stent. Both treatments are effective; however, endoscopic stent placement is less invasive and it is associated to good short-term results, while surgery provides longer-lasting effects with lower frequency of reintervention. In the last few years, EUS-guided gastroenterostomy (GE) has been proposed as palliative treatment for malignant GOO. This novel technique consists in the creation of an anastomosis between the gastric lumen and a small bowel loop distal to the malignant obstruction, through the deployment of a lumen-apposing metal stent under endoscopic ultrasound-view. EUS-GE has the advantage of being as minimally invasive as enteral stent placements, and of guaranteeing long-term results similar to those of surgery.

**Key Words:** Gastric outlet obstruction; Endoscopic ultrasound-guided gastroenterostomy; Endoscopic ultrasound; Enteric anastomosis; Lumen-apposing metal stents

Cominardi A, Tamanini G, Brighi N, Fusaroli P, Lisotti A. Conservative management of malignant gastric outlet obstruction syndrome-evidence based evaluation of endoscopic ultrasound-guided gastroentero-anastomosis. *World J Gastrointest Oncol* 2021; In press

**Core Tip:** Malignant gastric outlet obstruction is a clinical syndrome affecting patients with advanced pancreatic adenocarcinoma, gastric and duodenal cancer, or retroperitoneal neoplasms. Recently, endoscopic ultrasound-guided gastroenterostomy using a lumen-apposing metal stent has been proposed as a minimally invasive and long-lasting endoscopic palliative treatment for this condition. This technique has not only shown similar technical and clinical success rate to those of surgical gastro-jejunostomy and endoscopic enteral stent placement, but it also presents with lower rate of reintervention, adverse events, and costs.

**INTRODUCTION**

Gastric outlet obstruction (GOO) is a clinical syndrome caused by the presence of any obstacle to gastric emptying. However, the definition “gastric outlet obstruction” is misleading, since this condition is caused not only by intrinsic gastric, but also by duodenal, jejunal or extra-luminal conditions.

**ETIOLOGY**

The two main etiologies of GOO are motility disorders and mechanical obstructions.

***Motility disorders***

The most common motility disorder causing GOO is gastroparesis, usually secondary to long-standing diabetes. Gastroparesis may also be idiopathic or be a result of viral infections, chronic use of medications (*e.g.,* opioids, anticholinergics and antidepressants), connective tissue diseases (*e.g.,* scleroderma, Ehlers-Danlos syndrome), or neurological conditions, such as Parkinson’s disease and multiple system atrophy[1].

Some solid and hematologic malignancies may induce gastric and intestinal dysmotility through a paraneoplastic syndrome or a secondary infiltrative process (*e.g.,* amyloidosis or carcinomatosis).

Moreover, thoracic and abdominal surgery may cause vagus nerve injuries, resulting in an alteration of gastric motility; vague nerve injuries occur more frequently in bariatric surgery, fundoplicatio, surgery for peptic ulcer disease (PUD) and esophagectomy[1].

***Mechanical obstruction***

Mechanical obstruction may be caused by either benign or malignant causes.

Benign causes are PUD, nonsteroidal anti-inflammatory drug use, *Helicobacter Pylori* (*H. Pylori*), ingestion of corrosive or caustic agents, abdominal tuberculosis, gastric or duodenal polyps, anastomotic strictures, Crohn’s disease, sarcoidosis, gastric bezoars, gastric antral webs, gastric volvulus, Bouveret syndrome, acute and chronic pancreatitis, pancreatic pseudocyst and annular pancreas.

Malignant mechanical GOO is usually secondary to gastric, duodenal or pancreatic neoplasms. In particular, up to 35% of cases of GOO is caused by distal gastric cancer. Pancreatic adenocarcinoma is also a common cause of GOO, especially in presence of gastric and duodenal infiltration. Almost 15%-25% of patients with a diagnosis of pancreatic adenocarcinoma present with GOO[2].

Other causes of malignant GOO are gastric lymphomas (*e.g.*, MALT lymphoma), large neoplasms of the proximal duodenum and ampulla, cystic neoplasms of the pancreas, local extension of advanced gallbladder and bile duct cancer, neuroendocrine neoplasms, retroperitoneal lymphadenopathies (*e.g.*, metastatic tumor, lymphoma), retroperitoneal sarcomas, leiomyosarcomas, gastrointestinal (GI) stromal tumors and metastases(Table 1)[2-7].

**EPIDEMIOLOGY**

A precise estimate of GOO incidence is difficult to extrapolate. Until the late 1970s PUD was the cause of up to 90% of cases of GOO. However, after the advent of histamine H2-receptor antagonists and proton pump inhibitors and more effective treatment regimens for *H. Pylori* infections, less than 5% of cases of GOO are due to PUD. To date, malignancies represent the most common cause of GOO, accounting for almost 50%-80% of cases of GOO[2,3].

**CLINICAL MANIFESTATIONS AND DIAGNOSIS**

The onset of symptoms of GOO depends on the etiology of the obstruction. Patients with a malignant mechanical obstruction usually show a shorter duration of symptoms than those with benign disease[3-7]. Patients may also present hypokalemia and hypochloremic metabolic alkalosis at laboratory tests, as a consequence of protracted vomiting.

When GOO is suspected, abdominal imaging (abdominal radiography, contrast upper GI studies, or contrast-enhanced computed tomography) and upper endoscopy may confirm luminal obstruction. Additional tests, such as endoscopic ultrasound (EUS) with fine-needle aspiration or full-thickness surgical biopsies, may be useful in patients with suspected malignant GOO with negative endoscopic biopsies obtained during a gastroscopy. Indeed, diffuse-type gastric adenocarcinomas causing *linitis plastica,* gastric lymphomas and gastric metastases (*i.e.* breast cancer or melanoma), usually growing below the mucosal layer, may be difficult to be diagnosed with endoscopic biopsies[2-7].

**MANAGEMENT OF MALIGNANT GOO**

***Supportive management***

Patients with symptomatic GOO, regardless of its cause, should receive intravenous fluids support and correction of electrolyte alterations. Patients should be fasted and receive *nihil per os*; high-dose proton pump inhibitors therapy is suggested to decrease the volume of gastric secretions and associated inflammation. Nasogastric tube placement should be considered[1,8,9].

***Malignant GOO management***

Surgical approach represents the treatment of choice in patients with malignant GOO. However, radical resection (gastrectomy) is often not indicated or feasible, since most of underlying malignant conditions present as unresectable (almost 40% of gastric cancers and 80%-90% of periampullary cancers) or even metastatic.

Therefore, most patients require palliative interventions for GOO. Several palliative treatment strategies are available, such as surgery (bypass), endoscopy [endoscopic stenting, decompressive gastrostomy with or without feeding tube placement or EUS-guided gastroenterostomy (EUS-GE)] or radiotherapy (Table 2). Finally, primary curative chemotherapy is usually indicated in patients with gastric lymphomas. However, in this subset of patients, gastrectomy may be indicated in advanced T stages due to the high risk of chemotherapy-induced gastric perforation[10].

The aim of this review is to focus on procedural aspects and clinical outcomes of EUS-GE.

**EUS-GE**

EUS-GE was initially hypothesized and tested in animal models by Fritscher-Ravens *et al*[11] in 2002. This technique has progressively evolved; it involves the creation of a bypass between the stomach and a small bowel limb placed distal to the obstruction, through the insertion of a lumen-apposing metal stent (LAMS) under EUS and fluoroscopic guidance.

LAMS were firstly designed for the drainage of pancreatic fluid collections and, in the last decade, they have been used for other indications such as EUS-guided biliary drainage, including EUS-guided choledocoduodenostomy and EUS-guided gallbladder drainage. Other off-label indications had been described, such as drainage of post-surgical fluid collections, drainage of pelvic fluid collection, EUS-directed transgastric-endoscopic retrograde cholangiopancreatography (ERCP) and EUS-guided drainage of benign strictures[12-14].

EUS-GE represents a good alternative to surgical bypass in patients with symptomatic advanced malignant GOO regardless of the stenosis size, and it has the advantage to be less invasive than surgery.

This endoscopic technique can be performed in case of mechanical obstructions occurring in the antro-pyloric region, in the duodenal bulb and in the second or third portion of the duodenum. On the other hand, it is contraindicated for obstructions in the gastric body, in the fourth portion of the duodenum and in the proximal jejunum, around the ligament of Treitz, since considered unsafe or unfeasible. Other absolute contraindications for EUS-GE are the presence of a large amount of ascites interposed between the gastric wall and the target small intestine loop, and the presence of severe portal hypertension with peri-gastric varices[15-18].

***Pre-operative management***

A careful and complete explanation of the indications, contraindications, techniques and possible adverse events (AEs) of EUS-GE should be offered to all patients, due to the “off-label” nature of this procedure. An informed consent should be signed by all patients undergoing EUS-GE procedures. Patients should be clearly informed regarding the possibility of requiring urgent or emergent surgery in case of procedural complications.

Complete cross-sectional imaging and dynamic contrast radiology scans before the procedure are recommended, in order to evaluate and confirm the close apposition between the gastric wall and duodenum or the target small intestine loop.

No food intake for at least 8 h before the procedure should be recommended; endoscopic removal of gastric residue should be performed before the procedure in case of presence of large amounts of ingest. Antibiotic prophylaxis (gram-negative and anaerobe coverage) is suggested, in order to reduce the risk of peritonitis, although no clear evidence is available to date. EUS-GE must be performed under general anesthesia, with airways intubation. Indeed, in patients with presumed gastric stasis and presence of ingest in gastric lumen, it is mandatory to prevent aspiration. We recommend airways intubation a basic safety issue in this field. Moreover, we strongly suggest nasogastric tube placement the days before EUS-GE, in case of gastric distension. Carbon dioxide insufflation is recommended. A standard echoendoscope and a standard gastroscope are required for this procedure; however, sometimes, an enteroscope or a forward-view echoendoscope, especially in post-surgical anatomy of upper GI tract patients, may be useful[19].

***Endoscopic equipment***

A linear echoendoscope and a standard gastroscope are used to perform EUS-GE. The LAMS firstly used for EUS-GE in an animal model by Binmoeller and Shah[20] was the AXIOS stent (Boston Scientific, Natik, Massachussets, United States). The AXIOS stent is a bi-flanged fully-covered nitinol LAMS[20]. Originally, an AXIOS stent was placed into the newly-generated anastomotic tract after puncture, guidewire placement and tract dilation (Seldinger technique). More recently, two electrocautery-enhanced LAMS delivery systems have been developed and commercialized, namely Hot-AXIOS Stent (Boston Scientific, United States) and Hot-SPAXUS Stent (Taewoong Medical, South Korea), thus allowing the creation of the anastomotic conduit through an electrocautery-enabled access catheter and the subsequent release of a LAMS without guidewire passage and pre-dilatation of the passage.

***Techniques***

EUS-GE is an EUS technique based on the creation, under linear echoendoscope view, of a communication between the stomach and an adjacent duodenal or jejunal loop.

The first step consists in the choice of a target anastomotic site, since EUS-guided gastroduodenostomy into the third part of the duodenum or EUS-guided gastrojejunostomy represent the two anatomical options [21]. Moreover, the short length (about 10 mm) of the AXIOS stent has to be considered: duodenum or jejunum must be in close proximity to the gastric wall in order to prevent LAMS displacement after deployment and to facilitate the formation of a mature anastomosis over time. The different conformation of the Taewoong’s Hot-SPAXUS could provide promising innovations in this field.

The target site selection is mainly based on the proximity of that small bowel portion and its axis. The identification of the anastomotic site under EUS view is sometimes difficult: air insufflation and large amount of ascites can seriously undermine the accuracy of EUS images; moreover, EUS-morphology of the transverse colon may be mistaken for small bowel. In order to overcome these challenges, a controlled-radial expansion balloon or ERCP extraction balloon can be advanced up to duodenum or jejunum to improve acoustic coupling.

Recently, water-filling luminal techniques, consisting in filling duodenum or jejunum with water or isotonic saline with or without contrast or tinged with a dye, have been proposed; however, the rapid infusion of a volume of water sufficient to dilate the target small bowel loop may cause serious AEs such as hyponatremia and cardiovascular volume overload due to fluid absorption[22].

Lately, a novel double-balloon catheter has been developed, in order to enable not only the stabilization of the target small bowel loop, but also the distension of the lumen between the two balloons with fluid, to provide an easier target[23].

Due to increasing innovations, several techniques for EUS-GE are currently available: direct EUS-GE, anterograde EUS-GE (the “rendez-vous” method), anterograde direct method, retrograde EUS-GE, and EUS-guided double-balloon occluded gastrojejunostomy bypass (E-PASS)[21-27].

***Direct EUS-GE-traditional/downstream method***

Stricture is passed using a long stiff guidewire, placed into the proximal jejunum. A dilation balloon catheter (usually 18-20 mm) or a nasal biliary drainage catheter (NBDC) is passed over this wire into the jejunum and inflated with contrast to locate the jejunal loop.

A linear echoendoscope is used to identify the inflated balloon or the dilated target limb. In patients with no previous abdominal surgery, after the identification of the mesenteric vessels, the echoendoscope should be turned (either clockwise or anticlockwise) to find the Treitz area and first proximal jejunal limb. EUS-GE could be performed using a 15 mm × 10 mm or 20 mm × 10 mm Hot-AXIOS delivery system or the recently commercialized Hot-SPAXUS stent (Taewoong Medical, South Korea), with a free-hand technique; in this case, the use of a pure cut setting of the electrosurgical unit with high power is necessary. The procedure could be performed with a previous puncture with a 19-gauge needle and passing a 0.035” guidewire[21-27].

***Antegrade EUS-GE-the “rendezvous” method***

Stricture is passed using a long stiff guidewire, placed into the proximal jejunum. A dilation balloon catheter (usually 18-20 mm) or a NBDC is passed over this wire into the jejunum and inflated with contrast to locate the jejunal loop.

Instead of passing a guidewire downstream into the jejunum, in this technique the guidewire is captured in the duodenum or proximal jejunum and it is pulled back through the obstruction and the mouth in order to secure it. The LAMS is deployed over the fixed guidewire to create the gastroenterostomy[21-27].

***Antegrade direct method***

The small bowel distal to the stenosis is distended with saline solution and contrast, as well as a staining agent (*e.g.,* methylene blue) using a NBDC through the stricture or just flushing the lumen through the scope operative channel. The jejunal limb could be punctured to confirm the correct target, avoiding transvers colon. Free-hand insertion of the electrocautery-enhanced LAMS[21-27].

***Retrograde EUS-GE-“enterogastrostomy”***

This technique is a modification of the “rendez-vous” method. A long, stiff guidewire, was passed through the stricture and the anastomotic tract, punctured with an EUS-fine-needle aspiration needle. A therapeutic gastroscope was advanced, over the wire, through the stricture until the duodenum-jejunal junction. A LAMS is deployed from the small bowel to the stomach (the gastric flange was opened first). However, this technique is not feasible in most cases and the risk of iatrogenic perforation due to endoscope pass through the stenosis should limit its use[21-27].

***EPASS***

Using a double-balloon enteroscope, a guidewire is advanced through the proximal jejunum. Enteroscope was removed, leaving the overtube in place. A dedicated double-balloon enteric tube (Tokyo Medical University type; Create Medic Co., Ltd, Yokohama, Japan) is advanced through the stricture using the overtube to avoid loop formation in the stomach. The device is made with 2 balloons, distant 20 cm. The inflation of these balloons was used to fix the jejunum, which is filled with contrast material and methylene blue. EUS was used to puncture or to deploy directly the LAMS. Unfortunately, to date, this device has not been registered in Europe and the United States for human use[21-27].

***Post-operative management***

The day of the procedure no food intake is recommended, while clear fluids could be resumed 12 h later if no worrisome symptoms were observed. The day after the procedure a liquid diet should be started and it should be converted, if tolerated, into a low residue diet within the next 1-2 d.

The day after the procedure, abdominal radiography or CT may be performed to confirm LAMS correct placement, especially if dislodgment or migration or perforation are suspected. Nevertheless, performing imaging the day after EUS-GE is not necessary if the procedure was uneventful and the patient did not refer any symptom. Systemic antibiotics may be continued for 3 d after the procedure, although no solid evidence is available to date.

***Misdeployment***

In case of LAMS misdeployment, the use of a preloaded guidewire could provide an effective access to the punctured limb. However, in case of a “proximally misdeployed” stent (with the distal flange into the peritoneum and the proximal flange in the stomach), we suggest removing the stent and restarting the procedure. The site of puncture could be closed with through-the-scope clip. In our experience, no complication has occurred. In case of a “distally misdeployed” stent (with the distal flange into the jejunal limb and the proximal flange into the peritoneum), the presence of a preloaded guidewire could be useful for a salvage procedure; on the other hand, peritoneal exploration (either with laparoscopy or with a NOTES procedure) seems required to rescue the EUS-GE.

***Long-term EUS-GE management***

Since no large study reporting EUS-GE long-term outcomes is available, there is no robust evidence in the field. Long term complications due to LAMS traumatism on the contralateral wall could be hypothesized, based on pancreatic fluid collection drainage experience. The long-term management represents an unsolved issue in EUS-GE. Data on long-term AEs and LAMS management are required in the next future.

***Outcomes of EUS-GE for malignant GOO***

Patients suffering from malignant GOO could be treated either with surgical gastro-jejunostomy (SGJ), endoscopic enteral self-expanding metal stents (SEMS) placement or EUS-GE[10].

Since the first description of EUS-GE in a pig model in 2002[12], this technique has been demonstrated to be feasible also in human beings with a significant success rate. Previous studieson EUS-GE for malignant GOO are summarized in Table 3[28-42].

The technical success rate of EUS-GE for the treatment of malignant GOO, regardless of the technique performed, has been reported to be ranging from 80% to 100%, while clinical success ranges from 73% to 100%. However, the definition of “clinical success” is not univocal in the literature reported, since some authors defined “clinical success” as resumption of solid oral intake, while others as the ability to tolerate at least a full liquid diet.

The rate of AEs varies from 0% to about 27%; the most frequent AEs reported are misemployment of the LAMS, bleeding, abdominal pain, peritonitis, pneumoperitoneum and fistula.

The rate of GOO recurrence or the need of a reintervention of GOO is reported to be 0%-15%.

In 2015, Khashab *et al*[28] reported technical and clinical success of EUS-GE in their retrospective cohort of 10 patients (among them, 3 presented with malignant GOO), respectively of 90% and 100%. During follow-up no AEs or recurrence occurred[28].

Tyberg *et al*[29] showed similar results in 2016 by retrospectively evaluating 26 patients, among which 17 presented with malignant GOO. EUS-GE presented a technical success of 92% in the entire population and a clinical success of 88% between patients affected by malignant GOO. However, this study reported an AEs rate of 11.5%[29].

While in this study different EUS-GE techniques were performed, in the same year Itoi *et al*[30] reported their experience about performing EPASS in 20 patients with malignant GOO, showing a technical and clinical success of 90% with AEs in 10% of cases. In addition, no stent occlusion or migration occurred during a median follow-up of 100 d[30].

Studies enrolling a greater number of patients date back to 2017; in this year Perez-Miranda *et al*[32], Khashab *et al*[33] andChen *et al*[34] reportedtheir retrospective multicenter experience of EUS-GE for palliation of malignant GOO performing several techniques. These studies showed a similar technical success rate, respectively of 88%, 87% and 86.7%, but also a comparable clinical success (84%, 87% and 83.3%). AEs occurred from 12% to 16.7% of procedures and at the least in the 4.3% of cases GOO recurrence or need of reintervention were described[31-34].

In 2018 Chen *et al*[35] compared safety and efficacy of the antegrade direct technique with the “traditional” balloon-assisted technique in a cohort of 77 patients (52 affected by malignant GOO). This retrospective multicenter study showed no significant difference between these two methods, in terms of technical success rate (94% for the direct and 91% for balloon-assisted). Moreover, clinical success (defined as the ability to tolerate at least a full liquid diet) of these two methods was similar, (92% and 91%, respectively). Finally, no significant difference was showed for AEs rate and need of repeated intervention. Nevertheless, direct technique procedure time was significantly lower than that of balloon-assisted technique (35.7 min *vs* 89.9 min)[35].

The single center experience of Urrehman *et al*[36], reported a 100% technical success and 80% clinical success. Remarkable technical and clinical success was reported for the double balloon-assisted EUS-GE (respectively of 100% and 94.4%) with an AEs rate of 25% and need of reintervention in almost 3% of cases[36].

In terms of long-term outcomes of EUS-GE, Kerdsirichairat *et al*[38] reported their retrospective experience of 34 patients with malignant GOO undergoing the direct technique, with a median follow-up of 196 d. In this cohort, technical and clinical success was achieved in 93% and 89.5% of cases, respectively with AEs occurring in 3.5%[38].

Differently from previous studies, Kastelijn *et al*[41] and Wannhoff *et al*[42] recently reported lower technical (respectively of 86.7% and 80%) and clinical (73.3% and 74.3%) success rates for EUS-GE performed with various techniques for palliation of malignant GOO. While Kastelijn *et al*[41] showed the occurrence of AEs in 26.7% of cases, Wannhoff *et al*[42] reported reintervention in 10% of cases. Moreover, Wannhoff *et al*[42] showedthat the distance between the two lumina connected with the LAMS was a predictor of success of the procedure[41,42].

***Comparison of EUS-GE with surgical bypass***

Malignant GOO palliative treatment is fundamental to relief symptoms, to guarantee an adequate nutritional status and to improve patients’ quality of life.

Traditionally, the palliative therapy proposed for malignant GOO was surgery, either open or laparoscopic SGJ. Over the years, a new mini-invasive endoscopic technique has been developed for the palliation of malignant GOO: Enteral SEMS placement. This endoscopic technique had the advantage to be less invasive than SGJ and it showed lower occurrence of AEs, shorter time to oral intake restart, and shorter hospital stay; however, enteral SEMS placement was associated to a higher rate of reintervention due to stent obstruction. Finally, in recent years the novel EUS technique of EUS-GE has been developed[43,44].

EUS-GE was firstly compared to open SGJ in 2017 by Khashab *et al*[33]; 93 patients with malignant GOO were enrolled: 30 underwent EUS-GE and 63 open SGJ. Open surgery showed a significantly higher technical success (100 % *vs* 87 %, *P*  =  0.009); however, it has to be considered that the EUS-GE group included more patients with carcinomatosis than the SGJ group[43].

A comparable clinical success (90 % for SGJ and 87 % for EUS-GE) and a similar mean time to reintervention (88 d and 121 d, respectively) characterized both procedures, although EUS-GE was associated to a lower occurrence of AEs (16% *vs* 25%).

Recently, a comparison study between EUS-GE and SGJ was performed by Kouanda *et al*[45]; EUS-GE was associated to a statistically significant faster resumption of oral intake (1.3 d *vs* 4.7 d, *P* < 0.001) and a significant shorter length of stay (5 d *vs* 14.5 d, *P* < 0.001). EUS-GE and open SGJ showed similar technical success (92.5% and 100% respectively) and no significant differences were found for symptoms recurrence, reintervention rate, death within 30 d or 30 d readmission. Moreover, patients treated with EUS-GE could start chemotherapy earlier than those undergoing open SGJ. The cost-analysis of the two procedures showed that EUS-GE had lower overall costs if compared to open SGJ ($49387 *vs* $124192, *P* < 0.001)[45].

In conclusion, EUS-GE has been demonstrated to be non-inferior to open SGJ, but the EUS-guided procedure is not only less invasive, but it is also associated to a shorter delay to resumption of oral intake and chemotherapy, a shorter length of stay and reduced hospital costs.

A comparative multicenter retrospective study between EUS-GE and laparoscopic SGJ was performed in 2017 by Perez-Miranda *et al*[32]; although there was no difference in technical success between the two procedures (100% for laparoscopic SGJ and 88% for EUS-GE), EUS-GE showed a significantly lower AEs rate (12% *vs* 41%, *P* = 0.0386). Moreover, the overall cost analysis reported that EUS-GE was less expensive than laparoscopic SGJ ($4515 *vs* $14778.80 respectively, *P* < 0.00001).

***Comparison of EUS-GE with enteral stenting***

The comparison between EUS-GE and enteral SEMS placement was reported by Chen *et al*[34] and Ge *et al*[37].

Technical and clinical success were not significantly different between EUS-GE and enteral SEMS placement according to the comparative multicenter retrospective study by Chen *et al*[34]: Technical success was 86.7% for EUS-GE and 94.2% for SEMS placement, while clinical success was 83.3% and 67.3%, respectively. The two procedures showed a similar rate and severity of AEs (16.7% for EUS-GE *vs* 11.5% for SEMS placement) and a similar post-procedure mean length of hospitalization. However, EUS-GE was associated to a significantly lower reintervention rate and symptom recurrence (4.0 *vs* 28.6%, (*P* = 0.015)[34].

In 2019, the retrospective comparative study of Ge *et al*[37] confirmed thatEUS-GE and enteral SEMS placement had a similar clinical success (100% in both groups), but EUS-GE not only showed a statistically significant better initial clinical success (95.8% *vs* 76.3%, *P* = 0.042) and a lower rate of procedure failure requiring reintervention (32% *vs* 8.3%, *P* = 0.021), but also a lower incidence of AEs compared to enteral SEMS placement (20.8% *vs* 40.2%)[37].

Thus, EUS-GE confirmed itself as a valid alternative option to enteral SEMS placement, achieving similar technical and clinical success rates, but with lower costs and a lower rate of AEs and reinterventions.

**CONCLUSION**

Although EUS-GE is a relatively recent technique and available literature is limited, it has been demonstrated to be a safe and effective technique for the palliative treatment of patients with malignant GOO. Moreover, considering the advances in chemotherapy regimens and the consequent increased survival of these patients, it is essential to dispose of long-term palliative techniques.

EUS-GE has the advantage of being minimal invasive as an endoscopic procedure; weak evidence suggest that EUS-GE could provide long-lasting effects with lower recurrence rates[10,34]. Large high-quality evidence is still required in this field.

Moreover, a recent study suggests that EUS-GE present similar technical and clinical success rate compared to laparoscopic gastro-enterostomy. Interestingly, EUS-intervention seems to reduce length of stay and incidence of AEs, suggesting possible advantages compared to surgery[46]. Finally, EUS-guided jejuno-jejunal anastomosis gives the opportunity to treat malignant GOO also in patients who underwent gastrectomy.

The main limitation of EUS-GE is the position of the target small bowel loop; if the latter is too distant from the gastric wall, it may not be punctured under EUS-view. However, the above-described correct identification of the Treitz’s area from the mesenteric vessels could reduce this issue in patients with not surgically modified anatomy. Moreover, a safe puncture could not be feasible if the target loop is not enough distended; sometimes, despite a large amount of water injected into the small bowel, the target loop collapses because of peristaltic movements pushing water forward. The use of spasmolytic agents could represent a key factor to achieve the goal.

Currently, EUS-GE remains a technically difficult echoendoscopic procedure, whose outcome is strongly influenced by endoscopist skills and LAMS design. For this reason, larger anastomotic tracts with minimal risk of obstruction or stent migration are desirable.

In conclusion, EUS-GE, enteral SEMS placement and SGJ all represent valid options for the palliative treatment of malignant GOO; the appropriate treatment should always be chosen according to patients’ characteristics and comorbidities, in order to guarantee better prognostic outcomes and technical and clinical success.

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**Footnotes**

**Conflict-of-interest statement:** Authors declare no conflict of interests for this article.

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**Manuscript source:** Invited manuscript

**Peer-review started:** February 21, 2021

**First decision:** April 6, 2021

**Article in press:**

**Specialty type:** Oncology

**Country/Territory of origin:** Italy

**Peer-review report’s scientific quality classification**

Grade A (Excellent): A, A

Grade B (Very good): B

Grade C (Good): C

Grade D (Fair): D

Grade E (Poor): 0

**P-Reviewer:** Gornals JB, Matsubara S, Miura S **S-Editor:** Fan JR **L-Editor: P-Editor:**

**Table 1** **Causes of malignant gastric outlet obstruction**

|  |  |
| --- | --- |
| **Site** | **Pathology** |
| Stomach | Distal gastric cancer |
| Gastric lymphoma (*e.g.*, MALT lymphoma) |
| Leiomyosarcoma |
| Gastrointestinal stromal tumor |
| Gastric neuroendocrine neoplasms |
| Pancreas | Pancreatic adenocarcinoma |
|  | Cystic neoplasm of the pancreas |
| Duodenum | Duodenal cancer |
| Leiomyosarcoma |
| Neoplasm of the ampulla |
| Gastrointestinal stromal tumor |
| Metastasis |
| Gallbladder and bile duct | Gallbladder and bile duct cancer |
| Other | Retroperitoneal lymphadenopathy (*e.g.*, metastatic tumor, lymphoma) |
| Retroperitoneal sarcoma |

MALT: Mucosa-associated lymphoid tissue.

**Table 2 Treatment of mechanical malignant gastric outlet obstruction**

|  |  |  |
| --- | --- | --- |
|  | **Curative** | **Palliation** |
| Surgery | Surgery (gastrojejunostomy) | Surgical bypass |
| Endoscopy |  | Endoscopic stenting |
| EUS-GE |
| Decompressive gastrostomy with or without feeding tube placement |
| Chemotherapy and radiotherapy | Chemotherapy (especially for GI lymphoma) | Radiotherapy |

GI: Gastrointestinal; EUS-GE: Endoscopic ultrasound-guided gastroenterostomy.

**Table 3 Summary of reports in literature about endoscopic ultrasound-guided gastroenterostomy for malignant gastric outlet obstruction**

|  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Ref.** | **Nation** | **Study design** | **Population (N)** | **Techniques** | **Technical success (%)** | **Clinical success (%)** | **Adverse events**  **(%)** | **Follow-up (weeks)** | **GOO recurrence (%)** |
| Khashab *et al*[28], 2015 | United States | Retrospective multicenter | 10 (3 with malignant GOO) | Direct (*n* = 1). Balloon-assisted (*n* = 9) | 90 | 100 | 0 | 21 | 0 |
| Tyberg *et al*[29], 2016 | United States | Retrospective multicenter | 26 (17 with malignant GOO) | Direct (*n* = 3). Balloon-assisted (*n* = 13). NB catheter assisted (*n* = 3). Hybrid rendezvous (*n* = 5) | 92 | 88 | 11.5 | 8 | 0 |
| Itoi *et al*[30], 2016 | Japan | Prospective single center | 20 | EPASS | 90 | 90 | 10 | 14 | 0 |
| Brewer Gutierrez *et al*[31], 2017 | United States | Retrospective multicenter | 7 | Direct (*n* = 5). Balloon-assisted (*n* = 2) | 100 | 100 | 0 | 15 | 0 |
| Perez-Miranda *et al*[32], 2017 | United States and Europe | Retrospective multicenter | 25 (17 with malignant GOO) | Direct (*n* = 6). Balloon-assisted (*n* = 9). NB catheter assisted (*n* = 3). Ultraslim-endoscope assisted (*n* = 7) | 88 | 84 | 12 | 8 | 0 |
| Khashab *et al*[33], 2017 | United States and Japan | Retrospective multicenter | 30 | Direct (*n* = 2). Balloon-assisted (*n* = 6). EPASS (*n* = 22) | 87 | 87 | 16 | 22 | 3 |
| Chen *et al*[34], 2017 | United States and Japan | Retrospective multicenter | 30 | Direct (*n* = 2). Balloon-assisted (*n* = 6). EPASS (*n* = 22) | 86.7 | 83.3 | 16.7 | 14 | 4.3 |
| Chen *et al*[35], 2018 | United States and Europe | Retrospective multicenter | 77 (52 with malignant GOO) | Direct (*n* = 52). Balloon-assisted (*n* = 22) | 94.2  90.9 | 92.3  90.9 | 6.8 | 17 | 7  9 |
| Urrehman *et al*[36], 2018 | Singapore | Prospective single center | 5 | Balloon-assisted EUS-GE | 100 | 80 | 0 | - | - |
| Ge *et al*[37], 2019 | United States | Prospective single center | 22 | Direct EUS-GE | 100 | 95.8 | 20.8 | 24 | 4.5 |
| Kerdsirichairat *et al*[38], 2019 | United States | Retrospective multicenter | 57 (34 with malignant GOO) | Direct EUS-GE | 93 | 89.5 | 3.5 | 28 | 15.1 |
| Xu *et al*[39], 2020 | China | Retrospective single center | 36 | Double balloon-assisted EUS-GE | 100 | 94.4 | 25 | 13 | 2.7 |
| Hu *et al*[40], 2020 | China | Prospective single center | 9 | RPAT-assisted EUS-GE | 100 | 100 | - | - | - |
| Kastelijn *et al*[41], 2020 | Europe | Retrospective multicenter | 45 | Direct (*n* = 36). Balloon-assisted (*n* = 9) | 86.7 | 73.3 | 26.7 | 10 | 5.1 |
| Wannhoff *et al*[42], 2020 | Germany | Retrospective single center | 35 (33 with malignant GOO) | Direct (*n* = 22). Others (*n* = 12) | 80 | 74.3 | 14.3 | 8 | 10 |

GOO: Gastric outlet obstruction; NB: Nasobiliary; EUS-GE: Endoscopic ultrasound-guided gastroenterostomy; EPASS: EUS-guided double balloon-occluded gastrojejunostomy bypass; RPAT: Retrievable puncture anchor traction.