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Editorial Board Member of *World Journal of Gastrointestinal Oncology*, Rossana Berardi, MD, PhD, Director, Full Professor, Medical Oncology, Università Politecnica delle Marche, Ancona 60126, Italy. r.berardi@staff.univpm.it

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WJGO mainly publishes articles reporting research results and findings obtained in the field of gastrointestinal oncology and covering a wide range of topics including liver cell adenoma, gastric neoplasms, appendiceal neoplasms, biliary tract neoplasms, hepatocellular carcinoma, pancreatic carcinoma, cecal neoplasms, colonic neoplasms, colorectal neoplasms, duodenal neoplasms, esophageal neoplasms, gallbladder neoplasms, etc.

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

Anna Cominardi, Giacomo Tamanini, Nicole Brighi, Pietro Fusaroli, Andrea Lisotti

ORCID number: Anna Cominardi 0000-0002-7003-2855; Giacomo Tamanini 0000-0001-5795-9851; Nicole Brighi 0000-0002-1187-5481; Pietro Fusaroli 0000-0002-4397-9314; Andrea Lisotti 0000-0002-7724-7402.

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Anna Cominardi, Giacomo Tamanini, Andrea Lisotti, Department of Gastroenterology Unit, Hospital of Imola, University of Bologna, Imola 40026, BO, Italy

Nicole Brighi, Department of Medical Oncology, Istituto Scientifico Romagnolo Per Lo Studio Dei Tumori "Dino Amadori" (IRST) IRCCS, Meldola 47014, FC, Italy

Pietro Fusaroli, Department of Medical and Surgical Sciences, University of Bologna/Hospital of Imola, Bologna 40121, Italy

Corresponding author: Anna Cominardi, MD, Research Fellow, Senior Postdoctoral Fellow, Department of Gastroenterology Unit, Hospital of Imola, University of Bologna, Via Montericco 4, Imola 40026, BO, Italy. annacom26@gmail.com

Abstract

Gastric outlet obstruction (GOO) is a clinical syndrome characterized by post-prandial 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 an enteral self-expanding metal stent. Both treatments are effective; however, endoscopic stent placement is less invasive and it is associated with good short-term results, while surgery provides longer-lasting effects with a 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 of 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 EUS-view. EUS-GE has the advantage of being as minimally invasive as enteral stent placement, and of

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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

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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 rates to those of surgical gastro-jejunostomy and endoscopic enteral stent placement, but it also results in a lower rate of reintervention, adverse events, and costs.

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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 the 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; vagus nerve injuries occur more frequently in bariatric surgery, fundoplication, 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*) infection, 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 the 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* infection, 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 on 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 *limitis plastica*, gastric lymphomas and gastric metastases (*i.e.* breast cancer or melanoma), usually growing below the mucosal layer, may be difficult to diagnose 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 *nil per os*; high-dose proton pump inhibitor 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 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.

Table 1 Causes of malignant gastric outlet obstruction

Site	Pathology
Stomach	Distal gastric cancer
	Gastric lymphoma (<i>e.g.</i> , 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 (<i>e.g.</i> , 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.

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.

LAMSs were first 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 choledochoduodenostomy and EUS-guided gallbladder drainage. Other off-label indications have 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 being less invasive than surgery.

This endoscopic technique can be performed in cases with 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, as it is 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 the 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 airway intubation. Indeed, in patients with presumed gastric stasis and the presence of ingest in gastric lumen, it is mandatory to prevent aspiration. We recommend airway intubation as a basic safety issue in this field. Moreover, we strongly suggest nasogastric tube placement the day 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 the 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, Natick, Massachusetts, 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 of the choice of a target anastomotic site, as 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: The 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 Taewoong’s Hot-SPAXUS could provide promising innovations in this field.

The target site selection is mainly based on the proximity of the small bowel portion and its axis. Identification of the anastomotic site under EUS view is sometimes difficult: air insufflation and a 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 the duodenum or jejunum to improve acoustic coupling.

Recently, water-filling luminal techniques, consisting of filling the 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 stabilization of the target small bowel loop, but also 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, antegrade EUS-GE (the “rendezvous” method), antegrade direct method, retrograde EUS-GE, and EUS-guided double-balloon occluded gastrojejunostomy bypass (E-PASS)[21-27].

Direct EUS-GE-traditional/downstream method

The 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 can 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

The 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 can be punctured to confirm the correct target, avoiding the transverse colon. Free-hand insertion of the electrocautery-enhanced LAMS is carried out[21-27].

Retrograde EUS-GE-“enterogastrostomy”

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

EPASS

Using a double-balloon enteroscope, a guidewire is advanced through the proximal jejunum. The enteroscope is 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, at a distance of 20 cm. The inflation of these balloons is used to fix the jejunum, which is filled with contrast material and methylene blue. EUS is used to puncture or to directly deploy 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

On the day of the procedure no food intake is recommended, while clear fluids can be resumed 12 h later if no worrying symptoms are 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 correct placement of the LAMS, 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 develop any symptoms. 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 effective access to the punctured limb. However, in the case of a “proximally misdeployed” stent (with the distal flange in 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 a through-the-scope clip. In our experience, no complications have occurred. In the case of a “distally misdeployed” stent (with the distal flange in the jejunal limb and the proximal flange in 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) may be required to rescue the EUS-GE.

Long-term EUS-GE management

As 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 near future.

Outcomes of EUS-GE for malignant GOO

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

Since the first description of EUS-GE in a pig model in 2002[12], this technique has also been demonstrated to be feasible in humans with a significant success rate. Previous studies on 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 range from 80% to 100%, while clinical success ranges from 73% to 100%. However, the definition of “clinical success” is not univocal in the reported literature, as 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 misdeployment of the LAMS, bleeding, abdominal pain, peritonitis, pneumoperitoneum and fistula.

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

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

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

Although in this study different EUS-GE techniques were performed, in the same year Itoi *et al*[30] reported their experience on performing EPASS in 20 patients with malignant GOO, and showed 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] and Chen *et al*[34] reported their retrospective multicenter experience of EUS-GE for palliation of malignant GOO using several techniques. These studies showed a similar technical success rate of 88%, 87% and 86.7%, respectively, and a comparable clinical success rate (84%, 87% and 83.3%). AEs occurred in 12% to 16.7% of the procedures and in 4.3% of cases, GOO recurrence or need for reintervention were described[31-34].

In 2018, Chen *et al*[35] compared the safety and efficacy of the antegrade direct technique with the “traditional” balloon-assisted technique in a cohort of 77 patients

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

Ref.	Nation	Study design	Population (n)	Techniques	Technical success (%)	Clinical success (%)	Adverse events(%)	Follow-up (wk)	GOO recurrence (%)
Khashab <i>et al</i> [28], 2015	United States	Retrospective multicenter	10 (3 with malignant GOO)	Direct (n = 1). Balloon-assisted (n = 9)	90	100	0	21	0
Tyberg <i>et al</i> [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 <i>et al</i> [30], 2016	Japan	Prospective single center	20	EPASS	90	90	10	14	0
Brewer Gutierrez <i>et al</i> [31], 2017	United States	Retrospective multicenter	7	Direct (n = 5). Balloon-assisted (n = 2)	100	100	0	15	0
Perez-Miranda <i>et al</i> [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). Ultrastim-endoscope assisted (n = 7)	88	84	12	8	0
Khashab <i>et al</i> [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 <i>et al</i> [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 <i>et al</i> [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 <i>et al</i> [36], 2018	Singapore	Prospective single center	5	Balloon-assisted EUS-GE	100	80	0	-	-
Ge <i>et al</i> [37], 2019	United States	Prospective single center	22	Direct EUS-GE	100	95.8	20.8	24	4.5
Kerdsirichairat <i>et al</i> [38], 2019	United States	Retrospective multicenter	57 (34 with malignant GOO)	Direct EUS-GE	93	89.5	3.5	28	15.1
Xu <i>et al</i> [39], 2020	China	Retrospective single center	36	Double balloon-assisted EUS-GE	100	94.4	25	13	2.7
Hu <i>et al</i> [40], 2020	China	Prospective single center	9	RPAT-assisted EUS-GE	100	100	-	-	-
Kastelijm <i>et al</i> [41], 2020	Europe	Retrospective multicenter	45	Direct (n = 36). Balloon-assisted (n = 9)	86.7	73.3	26.7	10	5.1
Wannhoff <i>et al</i> [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.

(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 differences were found in the rate of AEs and the need for repeated intervention. Nevertheless, the procedure time for the direct technique was significantly lower than that for the balloon-assisted tech-

nique (35.7 min *vs* 89.9 min)[35].

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

With regard to 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% of patients[38].

Different to previous studies, Kastelijn *et al*[41] and Wannhoff *et al*[42] recently reported lower technical (86.7% and 80%, respectively) and clinical (73.3% and 74.3%, respectively) 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] showed that 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 relieve 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 of being less invasive than SGJ and resulted in fewer AEs, shorter time to oral intake restart, and shorter hospital stay; however, enteral SEMS placement was associated with a higher rate of reintervention due to stent obstruction. In recent years, the novel EUS technique of EUS-GE has been developed[43,44].

EUS-GE was first 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 rate (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 with 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 with 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 who underwent open SGJ. The cost-analysis of the two procedures showed that EUS-GE had lower overall costs when 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 with a shorter delay to resumption of oral intake and chemotherapy, a shorter length of stay and reduced hospital costs.

A comparative multicenter retrospective study of 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 rate of AEs (12% *vs* 41%, $P = 0.0386$). Moreover, the overall cost analysis showed that EUS-GE was less expensive than laparoscopic SGJ (\$4515 *vs* \$14778.80, respectively, $P < 0.00001$).

Comparison of EUS-GE with enteral stenting

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

Technical and clinical success rates 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 with a significantly lower reintervention rate and symptom recurrence (4.0 *vs* 28.6%, ($P = 0.015$)[34].

In 2019, the retrospective comparative study by Ge *et al*[37] confirmed that EUS-GE and enteral SEMS placement had a similar clinical success rate (100% in both groups), but EUS-GE not only showed a statistically significant better initial clinical success rate (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 was confirmed 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 minimally invasive as an endoscopic procedure; weak evidence suggests 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 has similar technical and clinical success rates compared to laparoscopic gastro-enterostomy. Interestingly, EUS-intervention seems to reduce the length of stay and incidence of AEs, suggesting possible advantages compared to surgery[46]. Finally, EUS-guided jejuno-jejunal anastomosis provides the opportunity to treat malignant GOO also in patients who have undergone 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 area from the mesenteric vessels could reduce this issue in patients with non-surgically modified anatomy. Moreover, a safe puncture is not feasible if the target loop is not distended enough; sometimes, despite a large amount of water injected into the small bowel, the target loop collapses due to peristaltic movements pushing water forward. The use of spasmolytic agents could represent a key factor in achieving this goal.

Currently, EUS-GE remains a technically difficult echoendoscopic procedure, whose outcome is strongly influenced by the endoscopist's 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 the patient's characteristics and comorbidities, in order to guarantee better prognostic outcomes and technical and clinical success.

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