

Endoscopic Ultrasound-guided Gastroenterostomy: A Promising Alternative to Surgery

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ABSTRACT

Recently, with the advancement of techniques, endoscopic ultrasound-guided therapies have shown distinct advantages, especially in relieving benign and malignant gastric outlet obstruction (GOO), as well as in postoperative pancreaticobiliary diseases. Herein, we present five currently used approaches in endoscopic ultrasound-guided gastroenterostomy (EUS-GE) using lumen-apposing biflanged metal stents (LAMS), along with several examples of LAMS-based EUS treatment of pancreaticobiliary diseases. Compared with traditional treatment methods, EUS-guided procedures have – to some degree – shown higher success rates, both technical and clinical. Moreover, EUS-guided therapies reduce the risk of multiple surgical adverse events, including delayed gastric emptying, prolonged hospital stay, increased costs, and delay in cancer treatment. Particularly in terms of postoperative pancreaticobiliary diseases, EUS-guided therapy has assumed an essential role as a treatment option in cases where traditional methods are difficult to perform. Nevertheless, EUS-guided gastrointestinal procedures are still relatively new, with some clinical failures, and additional prospective clinical trials are warranted.

Key words: endoscopic ultrasound, endoscopic ultrasound-guided gastroenterostomy, gastrojejunostomy, stents

INTRODUCTION

Surgical gastroenterostomy has been the standard palliative therapy for gastric outlet obstruction (GOO) due to malignant and benign diseases and postoperative pancreaticobiliary complications. Endoscopic intervention is an alternative treatment option for GOO, which is divided into two approaches – the placement of enteric self-expanding metal stents (SEMS) across the stricture and endoscopic ultrasound-guided gastroenterostomy (EUS-GE) using metal stents. Enteric SEMS placement may be complicated due to the recurrent obstruction caused by either stent migration or tumor infiltration.^[1,2] Therefore, EUS-GE may be ideal for GOO because of the short anastomotic length of the gastroenterostomy and the minimally invasive nature of the endoscopic intervention.^[3–9] This procedure was first introduced in 2002.^[10] Common

causes of GOO include gastric or duodenal cancer, pancreatitis, periampullary cancer, pancreatic cancer, bile duct cancer, gallbladder cancer, and postoperative therapy, among others.^[8,11–13] Symptomatic GOO is amenable to EUS-GE, regardless of the degree of stenosis or the type of disease (benign or malignant). Itoi *et al.*^[2] have recommended that the indications and contraindications for EUS-GE should be based on the stricture site. Obstructions in the antrum of the stomach and those in the first, second, and third portions of the duodenum are indications for EUS-GE, while EUS-GE may not be safe or technically feasible for obstructions in the body of the stomach, the fourth portion of the duodenum, and the proximal jejunum around the ligament of Treitz.^[2] According to recent trials, EUS-GE leads to the recovery of oral intake in 90% of patients, without the risk of tumor ingrowth and/or overgrowth, and meanwhile avoiding the potential morbidity of surgery.^[5,12,14–26]

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In this review, we aimed to summarize the current techniques in EUS-GE and to discuss future directions for EUS-GE.

TECHNIQUES IN ENDOSCOPIC ULTRASOUND-GUIDED GASTROENTEROSTOMY: AN OVERVIEW

The AXIOS™ lumen-apposing metal stent (LAMS) (15 mm in diameter and 10 mm in length; Boston Scientific, Natick, MA, USA) attaches to the gastric and enteric wall and has been shown to be an ideal device for EUS-GE in animal models.^[27–34]

The AXIOS-EC™ stent includes an electrocautery-enhanced delivery system that permits stent placement without needle puncture and guidewire placement, and may reduce the risk of missing the target during EUS-GE, which can lead to failed EUS-GE with adverse events.^[35–42] Bowen *et al.*^[16] successfully used a novel, double-flanged, fully covered, self-expandable metal stent with cautery to refine the EUS-GE procedure in a patient with paraduodenal pancreatitis and walled-off pancreatic necrosis due to biliary pancreatitis. The patient resumed a liquid diet on a postoperative day 2 without any adverse events.^[16]

Nonetheless, even if an ideal stent is available, EUS-GE is still a technically demanding procedure because access to the duodenum and jejunum is difficult and unpredictable.^[43] Moreover, given that air insufflation, which can seriously affect the accuracy of ultrasound images, precludes ultrasound imaging, safe puncture into the small bowel is not guaranteed. To overcome this problem, water-filling luminal techniques have been used. Wang *et al.*^[44] reported successful saline with methylene blue-assisted EUS-GE in a 65-year old man with malignant duodenal stenosis after a Roux-en-Y bypass and demonstrated that this method was simple and fast. However, rapid infusion of a large volume of water to sufficiently dilate the small bowel may cause serious adverse events, including hyponatremia, and fluid absorption may result in cardiovascular volume overload. Furthermore, the injection of a large amount of fluid distends not only the targeted portion of small intestine, but also the colon, leading to a risk of puncture into the colon and inadvertent creation of a gastrocolostomy. Several investigators have now developed unique and novel LAMS-based techniques for EUS-GE founded on the approaches above.^[2,43,45,46]

TRADITIONAL ENDOSCOPIC ULTRASOUND-GUIDED GASTROENTEROSTOMY

Briefly, the traditional approach to EUS-GE entails direct puncture of a small-bowel loop adjacent to the stomach.^[3,4,13,47,48] A linear echoendoscope is inserted into the stomach, and a duodenal or jejunal loop adjacent to the stomach is identified. After the transgastric puncture of the small bowel with a 19-gauge needle, a contrast is injected to ensure the entry. An enterogram is obtained, and the GE tract is dilated over a wire, followed by placement of a fully covered anastomotic stent. The diameter of the GE tract is gauged to allow the introduction of the anastomotic stent sheath (typically 10.8 F), and overly aggressive dilation is avoided to minimize luminal leakage. The flanged LAMS is deployed across the GE tract under combined EUS, fluoroscopic, and endoscopic guidance. The distal anchor flange is deployed first under EUS and fluoroscopic guidance. The proximal anchor flange is then deployed under endoscopic guidance. Usually, the procedure requires a transgastric puncture.^[49] Rodrigues-Pinto *et al.*^[49] have reported that retrograde EUS-GE performed from the duodenum to the stomach is also feasible, with a lesser risk of puncturing the duodenal lumen, which has a small caliber and is mobile.

ASSISTED ENDOSCOPIC ULTRASOUND-GUIDED GASTROENTEROSTOMY

Given that the traditional EUS-GE is not easily performed because of the blind transgastric puncture, an assisted EUS-GE using a retrieval/dilating balloon catheter, single balloon overtube, nasobiliary drain, and ultraslim endoscope is a good choice. A hydrophilic guidewire is advanced distally into the small bowel under fluoroscopic guidance, allowing the insertion of a retrieval or dilating balloon catheter (usually 15 to 18 mm); the balloon is passed over the wire and inflated with a contrast medium to serve as the target for transgastric puncture.^[50] A linear echoendoscope is then advanced into the stomach, the contrast-inflated balloon is identified under echosonographic and fluoroscopic visualization, and a 19-G needle is used to puncture the balloon. The balloon burst indicates the correct positioning of the needle tip within the small bowel lumen. The remaining steps are similar to the traditional EUS-GE technique.

Advancement of the dilating balloon over the guidewire can be challenging because of the looping of the wire

in the stomach and flaccidity of the balloon shaft, and additional assistive tools may be required. Another challenge is the potential loss of visualization and access to the small bowel due to the advancement of the wire through the needle pushing the small bowel away from the stomach. Both the need for extra steps and the loss of visualization can potentially result in technical failure and stent misdeployment.^[36,39,40]

RENDEZVOUS ENDOSCOPIC ULTRASOUND-GUIDED GASTROENTEROSTOMY

This technique consists of capturing the guidewire in the duodenum or proximal jejunum and pulling it back through the obstruction and out of the mouth, rather than passing the guidewire downstream into the jejunum, thus securing it at both ends.^[51] The specific steps include coiling the guidewire within the dilating balloon itself and trapping the wire with a snare or stone retrieval basket, or with an ultra-slim gastroscope and pediatric forceps. The LAMS can be deployed over this fixed guidewire from either end to create the gastroenterostomy. However, the multiple steps again create various challenges.

ENDOSCOPIC ULTRASOUND-GUIDED BALLOON-OCCLUDED GASTROJEJUNOSTOMY BYPASS

EUS-guided balloon-occluded gastrojejunostomy bypass (EPASS) was devised on the basis of animal studies.^[2,52–55] It is performed using a cautery tip-equipped fully covered LAMS and a special double-balloon enteric tube that traps water between the 2 balloons, thus dilating only the intestinal segment needed for the transgastric puncture.^[53] The procedure is similar to assisted EUS-GE using other instruments. EPASS is performed by either a one-step procedure (freestyle technique), using the direct electrocautery-enhanced tip delivery system, or a two-step procedure (standard technique), which is a more conventional method.^[56–59]

During a freestyle EPASS, the AXIOS-EC™ stent is directly advanced into the distended duodenum or jejunum while applying current. The stent is deployed across the GE tract under combined EUS, fluoroscopic, and endoscopic guidance. Finally, the deployed stent lumen is dilated to 10 mm with a dilating balloon.

A follow-up upper GI examination is required after EUS-GE, usually using water-soluble contrast to evaluate the

stent function by confirming that the contrast medium is flowing in the jejunum.^[50] Other examinations, such as CT, are also important. We usually evaluate the technical success of EUS-GE in terms of adequate positioning and deployment of the stent as determined endoscopically and radiologically, and clinical success is defined by the patient's ability to tolerate oral intake without vomiting.^[60]

ONE-STEP ENDOSCOPIC ULTRASOUND-GUIDED GASTROENTEROSTOMY: OTHER APPLICATIONS

Procedures similar to EUS-GE are also applied to other gastrointestinal diseases. Ikeuchi *et al.*^[56] reported a one-step, LAMS-based, EUS-guided gastrojejunostomy for treatment of afferent loop syndrome. The cautery-equipped AXIOS™ stent was transgastrically and directly advanced into the enlarged afferent loop under EUS guidance using the AutoCut electrosurgical mode without needle puncture, which proved to be safe and efficient. The device eliminated the need for guidewires, balloon catheters, and the advancement of devices over guidewires, and was performed with a single endoscope, making it the most efficient technique described so far. However, one of the challenges with this technique could be an inability to puncture the small bowel.

OUTCOMES OF ENDOSCOPIC ULTRASOUND-GUIDED GASTROENTEROSTOMY

Since EUS-GE was first reported using the pig model, several clinical trials have demonstrated the feasibility of the technique in humans, with a high success rate. Relatively large studies with novel devices or techniques have shown technical success rates of approximately 90%, regardless of the approach (Table 1). Complications were seen in several cases, but none were serious.

At present, the most common interventions for the treatment of GOO are endoscopic SEMS placement or surgical gastrojejunostomy (SGJ).^[8,61–63] EUS-GE is the latest breakthrough technique for the management of patients with GOO.^[18,20,58,64,65] Randomized trials have compared the outcomes of the 3 interventions with mixed results. The main shortcoming of the enteral SEMS placement is recurrent GOO due to tumor ingrowth/overgrowth.^[66] Chen *et al.*^[67] performed a comparative study between EUS-GE and endoscopic SEMS placement

and concluded that EUS-GE may be ideal for malignant GOO, with comparable efficacy and safety to endoscopic SEMS placement and fewer recurrences requiring reintervention.

The main limitation of SGJ is its invasive nature, especially in patients with advanced malignancies and poor nutritional status. In addition, SGJ is associated with frequent complications, including perioperative infection and gastroparesis.^[8,61–63,68] Khashab *et al.*^[69] conducted an international multicenter comparative trial of EUS-GE versus SGJ for the treatment of malignant GOO and recommended EUS-GE as a non-inferior but less invasive alternative to surgery.

FUTURE DIRECTIONS FOR ENDOSCOPIC ULTRASOUND-GUIDED GASTROENTEROSTOMY

Kedia *et al.*^[73] have performed EUS-guided biliary access and SEMS placement through the gastric pouch to treat obstructive jaundice after Roux-en-Y gastric bypass. Iwashita *et al.*^[74] have reported using an EUS-guided antegrade approach and temporary metal stent placement to treat biliary stones in the hepatic duct after a Whipple procedure. The use of a fully covered metal stent at the fistula enabled complete stone clearance through the stent with a basket catheter. Moreover, in place of endoscopic retrograde cholangiopancreatography (ERCP), which is challenging in patients with Roux-en-Y gastric bypass, EUS-directed transgastric ERCP (EDGE), using a linear echoendoscope has been used to access the excluded

stomach with deployment of a LAMS over a wire to create a gastrogastic or jejunogastric fistula, which allowed passage of the duodenoscope through the LAMS and performance of conventional ERCP.^[75] Jah *et al.*^[76] have reported EUS-guided drainage of an abdominal fluid collection following a Whipple procedure using an Olympus GF-UCT240 EUS endoscope (GF-UCT240, Olympus, UK), which was passed through the gastrojejunostomy. The serosanguinous collection was completely aspirated using a 19-gauge Echotip-Ultra needle (Wilson-Cook, Ireland) under EUS guidance. The amylase level in the fluid was normal, and all of the cultures were sterile.^[76] Especially for pancreatobiliary diseases, Ramesh *et al.*^[77] have recommended that traditional per-os EUS should be attempted first for the examination of the body and tail of the pancreas, while laparoscopy-assisted pancreatobiliary EUS should be considered as the preferred technique for the examination of the head of the pancreas and the common bile duct.

Perhaps the greatest potential drawback of EUS-GE is the risk of accidental puncture of the transverse colon, which can lie close to the stomach, or the small bowel, which is sensible and tents away easily. Zhang *et al.*^[22,51,78,79] have devised a retrievable puncture anchor (Vedkang Inc., Changzhou, China) for gallbladder puncture in EUS-guided gallbladder drainage. The retrievable anchor is attached to the gallbladder to provide traction, while the gallbladder is punctured and drained using a LAMS. The anchor can be easily removed after the procedure by changing the direction. We are inspired by the ways this new invention might be applied to EUS-GE to provide traction away from the LAMS, pulling the gastric wall closer to the intestinal

Table 1: Summary of reports in the literature of endoscopic ultrasonography-guided gastroenterostomy

Author	Year	Study design	Technique	Number of cases	Technical Success rate (%)	Clinical success rate (%)	Follow-up	Complications
Khashab <i>et al.</i> ^[61]	2015	Retrospective clinical study	Direct or balloon-assisted EUS-GE	10	90%	90%	21 weeks	-
Itoi <i>et al.</i> ^[70]	2016	Prospective clinical study	EPASS	20	90%	90%	14 weeks	1 case: pneumoperitoneum
Tyberg <i>et al.</i> ^[71]	2016	Retrospective clinical study	Water-filled intestine (various)	26	92%	85%	8 weeks	1 case: peritonitis 1 case: bleeding 1 case: pain
Perez-Miranda <i>et al.</i> ^[72]	2017	Retrospective comparative study	Balloon-assisted EUS-GE	EUS-GE: 25 Lap-GJ: 29	88% 100%	84% 90%	8 weeks 38.4 weeks	12% (3 cases) 41% (12 cases)
Khashab <i>et al.</i> ^[69]	2017	Retrospective comparative study	Direct puncture or EPASS	EUS-GE: 30 Surgery: 63	87% 100%	87% 90%	155 days 196 days	16% 25%
Chen Yi <i>et al.</i> ^[67]	2017	Retrospective comparative study	Direct puncture, balloon-assisted EUS-GE and EPASS	EUS-GE: 30 Enteral stent: 94.2% EUS-GE and EPASS 52	86.7% 94.2%	83.3% 67.3%	103 days 23.5 days	Re-intervention 4% 28.6%

EUS-GE: endoscopic-ultrasound-guided gastroenterostomy; EPASS: endoscopic ultrasound-guided balloon-occluded gastrojejunostomy bypass; Lap-GJ: laparoscopic gastrojejunostomy.

wall,^[80] and potentially increasing the probability of success while making the procedure safer and simpler.^[81]

We anticipate that in the near future, many patients suffering from malignant GOO will benefit from a safe GE that permits both secure anastomosis and passage of food. In addition, we believe that an endoscopic gastric bypass procedure using a simple anastomosis method with a LAMS has the potential to be a minimally invasive treatment strategy for obesity and type 2 diabetes. The global prevalence of these metabolic diseases has increased exponentially, and conventional bariatric surgery is currently the only treatment that reliably results in large, sustained weight loss and control of intractable type-2 diabetes.^[82,83] However, bariatric surgery carries considerable perioperative risk, and there is a great need for minimally invasive weight-loss procedures in the treatment sequence.^[55]

CONCLUSION

EUS-GE is a promising new technique for the treatment of benign and malignant GOO, although it is palliative only and is currently used mainly as an alternative for patients without other good treatment options. Limitations such as the risk of puncture of the small bowel, the necessity for stent removal after the procedure, and so on, need more investigation. Nevertheless, since EUS-GE was introduced in 2002, great improvements have been made, new techniques are regularly put forward, and treatment methods based on EUS-GE that are used for other gastrointestinal and biliary diseases especially support the suitability of EUS-GE in the clinical setting.^[84] Thus, additional prospective, multicenter trials are justified for the advancement of EUS-GE.

Conflict of Interest

None declared.

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