Review

Technical review of endoscopic ultrasonography-guided gastroenterostomy in 2017

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Gastric outlet obstruction (GOO) can be caused by benign and malignant diseases and often leads to a reduction in patient quality of life. Lately, endoscopic ultrasonography (EUS)-guided gastroenterostomy (EUS-GE) has emerged. At the present time, there are three types of EUS-GE using lumen-apposing biflanged metal stents (LAMS): (i) direct EUS-GE; (ii) assisted EUS-GE using retrieval/dilating balloon, single balloon overtube, nasobiliary drain and ultraslim endoscope; and (iii) EUS-guided double-balloon-occluded gastrojejunostomy bypass (EPASS). Overall technical success rate is approximately 90% regardless of technique used, although this is based on two retrospective studies only. In the EPASS procedure, the success rate of the one-step procedure was higher than that of the two-step procedure (100% *vs* 82%). Clinical success was almost uniform when stent placement was technically successful. Although there have been no-stent induced procedural deaths, adverse events were seen in several cases. One technically failed case carried out using balloon-assisted EUS-GE was converted to laparoscopic gastrojejunostomy. Two failed cases in EPASS procedure improved with conservative treatment. In the present review, we show the feasibility and outcomes using novel EUS-GE using LAMS. Clinical prospective trials with comparison to luminal enteral stents and surgical GE are warranted.

Key words: anastomosis, endoscopic ultrasonography, endoscopic ultrasonography-guided gastroenterostomy, gastrojejunostomy, lumen-apposing metal stent

INTRODUCTION

GASTRIC OUTLET OBSTRUCTION (GOO) can be caused by benign and malignant diseases (Table 1) and often leads to a reduction in patient quality of life because of nausea, vomiting, and poor oral food intake. Furthermore, in patients with malignancy who develop GOO, chemotherapy must be temporarily or permanently discontinued as a result of poor general condition and/or need for surgical intervention. Traditionally, surgery, either open or laparoscopic, has been the primary treatment for both benign and malignant GOO. Endoscopic intervention using lumenal self-expanding metal stents (SEMS) placed across the obstruction has been carried out for the treatment of malignant GOO. One randomized trial[1] of endoscopic enteral stent placement using a luminal SEMS and surgical gastrojejunostomy (GJ) showed that surgery had better long-term results as a result of reduced need for re-intervention and is therefore the treatment of choice in patients with a life expectancy of 2 months or longer. As endoscopic enteral stent placement was associated with better short-term outcomes, this treatment is preferable for patients expected to live <2 months. However, surgical intervention is more invasive, especially for operative patients in poor condition with benign disease and in patients with malignant disease. However, stent patency of uncovered duodenal SEMS is always of concern because of tumor ingrowth and overgrowth. Furthermore, recent developments in chemotherapy regimens have resulted in prolongation of life expectancy. Therefore, advances in minimally invasive strategies and techniques to relieve gastric outlet obstruction are needed.

Lately, endoscopic ultrasonography (EUS)-guided gastroenterostomy (EUS-GE) has emerged.[2–6] The concept of EUS-GE was first introduced by Fritscher-Ravens *et al.*[7,8] However, as the technique is complicated because of the use of special devices and need for endoscope exchange, the technique was not adopted. Nowadays, there are several

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Table 1 Etiology of gastric outlet obstruction

Patient condition	
Benign	Malignant
Gastric ulcer	Gastric cancer
Duodenal ulcer	Duodenal cancer
Acute pancreatitis	Periampullary cancer
Chronic pancreatitis	Pancreatic cancer
Post-endoscopic therapy	Bile duct cancer
Post-surgical therapy	Gallbladder cancer
Miscellaneous	Miscellaneous

proposed techniques from various institutions with expertise in EUS. Herein, we describe the current status and perspective of EUS-guided gastroenterostomy.

TERMINOLOGY AND INDICATION FOR EUS-GE

EUS-GE INCLUDES TWO procedures, namely EUS-guided gastroduodenostomy and gastrojejunostomy. These two procedures are the result of anatomical puncture sites from the stomach during EUS-GE into the third portion of the duodenum (gastroduodenostomy) and jejunum (gastrojejunostomy), respectively (Fig. 1).

Symptomatic GOO is amenable for EUS-GE regardless of size of stenosis and type of disease, benign or malignant. Indication and contraindication of EUS-GE are shown in Table 2. The targeted site within the duodenum or jejunum should be adjacent to the stomach. Pre-procedural computed

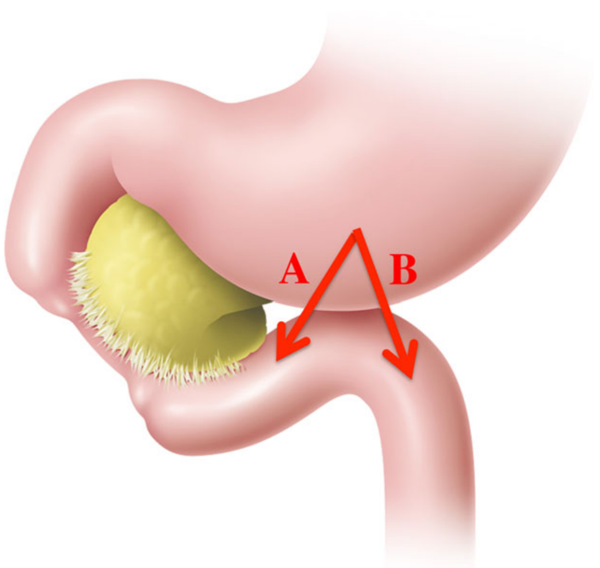

Figure 1 Endoscopic ultrasonography (EUS)-guided gastroenterostomy. (A) EUS-guided gastroduodenostomy. (B) EUS-guided gastrojejunostomy.

Table 2 Indication for EUS-guided gastroenterostomy according to stricture site

Indication of obstruction site	Contraindication
Antrum in the stomach	Body in the stomach
Ist, IInd and IIIrd portion in the duodenum	IVth portion in the duodenum
	Proximal jejunum

tomography (CT) scan is valuable in selecting the site of puncture as a preoperative road map, with the coronal view often being the most helpful. In general, as the anastomotic site is usually from the body of stomach, care should be taken in case of cancer invasion into the gastric wall in patients with gastric or pancreatic cancer. Similarly, in cases of cancer extending into the body of the stomach, IVth portion of duodenum and proximal jejunum around the ligament of Treitz, EUS-GE may not be safe and technically feasible. In the presence of small amounts of ascites, EUS-GE may be possible, but should be avoided if a large volume of ascites is present, because of poor fixation of the jejunum as a result of a small bowel floating phenomenon. Patients with GOO often have a large amount of gastric residue which may preclude successful EUS-GE and potential serious adverse events. Thus, no food intake or low-residue diet may be ideal until scheduled EUS-GE. However, in cases of a large amount of gastric residue, residue should be removed as much as possible using several devices (e.g. snare catheter, basket catheter, net catheter) before carrying out EUS-GE.

THEORY OF LUMEN-APPOSING METAL STENT OF EUS-GE

IN 2012, BINMOELLER and Shah[9] introduced a lumen-apposing metal stent (LAMS) (15 mm in diameter and 10 mm in length, AXIOS™ stent; Boston Scientific, Marlborough, MA, USA) which can attach the gastric and enteric wall and was shown to be an ideal device for EUS-GE in a pig model. Theoretically, LAMS allows adhesion between two organs as is done with a surgical anastomosis. In other words, a true anastomosis is not always completed unless a LAMS is used for this procedure because the stomach is not adherent to the duodenum or jejunum. Furthermore, the AXIOS-EC™ stent (often referred to as 'Hot Axios') (Fig. 2) includes an electrocautery enhanced delivery system which makes it possible to place the stent without needle puncture and guidewire placement, and may avoid missing the target during EUS-GE, which can lead to failed EUS-GE with adverse events. AXIOS-EC™ stent consists of a fully covered metal stent with bilateral anchor

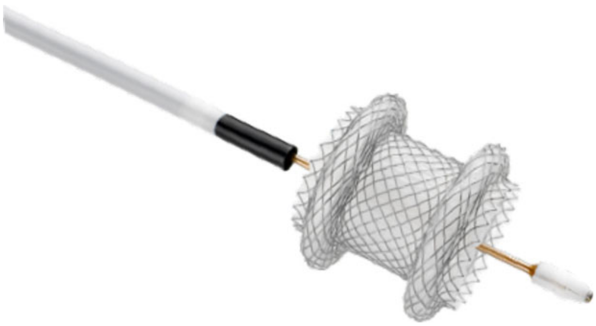

Figure 2 Electrocautery enhanced delivery system (AXIOS-EC^{TM} stent; Boston Scientific, Marlborough, MA, USA).

flanges. Fully expanded, the anchor flange diameter is twice that of the 'saddle' section (24 mm and 15 mm, respectively). The stent anchors are designed to distribute pressure evenly on the luminal wall and securely anchor the stent, preventing migration. The proximal and distal anchor flanges also securely hold the jejunal or duodenal wall to the gastric wall, preventing detachment.

Nonetheless, even if an ideal stent is available, EUS-GE is still a technically challenging procedure because access to the duodenum and jejunum is difficult and unpredictable. Ordinarily, endoscopy of the duodenum and jejunum often involves air insufflation as a result of endoscope insertion. However, air insufflation precludes ultrasound imaging, the duodenal and jejunal lumens are collapsed, and safe puncture into the small bowel is not guaranteed. To overcome this problem, water-filling luminal techniques with or without inflated balloons have been used.[7–9] However, rapid infusion of a large volume of water to sufficiently dilate the small bowel may cause serious adverse events, including hyponatremia and absorption of fluid, which could cause volume overload of the cardiovascular system. In addition, the injection of a large amount of fluid distends not only the targeted small intestine, but also the colon, leading to miss-puncture into colon and inadvertent creation of gastrocolostomy. At the present time, several investigators developed unique and novel techniques in combination with LAMS for EUS-GE based on the previous techniques. All patients are given i.v. antibiotics immediately before the procedure.

TECHNIQUES OF EUS-GE[4–6]

Direct EUS-GE technique

THE DIRECT EUS -GE method entails direct puncture of a small-bowel loop adjacent to the stomach using a 22-guage needle to distend the duodenum and jejunum by saline. After transgastric puncture using a 19-gauge fine-needle aspiration (FNA) needle, an enterogram is obtained, and a wire passed through the needle into the small bowel. The GE tract is dilated over the wire, followed by placement of a LAMS. GE tract dilation diameter is gauged to allow the introduction of the anastomotic LAMS delivery system (typically 10.8 Fr in diameter), and overly aggressive dilation is avoided to minimize luminal leakage during the exchange and prior to stent deployment.

Assisted EUS-GE technique

Assisted EUS-GE technique includes use of retrieval/dilating balloon, nasobiliary drain, or ultraslim endoscope insertion around the duodenal-jejunal flexure, although it is often difficult or impossible. Of these assisted techniques, retrieval/dilating balloon-assisted EUS-GE is the preferred technique.[4,5] Balloon-assisted EUS-GE involves transoral passage of a retrieval or dilating balloon catheter over a wire placed into the small bowel, which is then inflated with fluid (contrast and/or water) while positioned in the duodenum or jejunum. The fluid-filled balloon is localized transgastrically by EUS after the echoendoscope is passed alongside the balloon. The balloon is punctured with a 19-gauge fine-needle aspiration (FNA) needle. Bursting of the balloon indicates correct positioning of the needle tip within the small-bowel lumen. A guidewire is advanced through the FNA needle, and a LAMS stent is subsequently placed. Intravenous glucagon injection is given as needed to decrease small-bowel peristalsis. When nasobiliary drains are placed, contrast material is injected into the duodenum and jejunum through to distend and identify the duodenal or jejunal loop both endosonographically and fluoroscopically. In case of ultraslim endoscope-assisted EUS-GE, the small caliber endoscope is passed perorally or through an existing gastrostomy site into the stomach and then beyond the stricture. Saline is injected through the ultraslim scope to distend the bowel lumen. The echoendoscope is then advanced into the stomach (alongside the ultraslim scope in cases in which the ultraslim scope is introduced perorally). A guidewire is advanced through the needle and coiled within the bowel lumen. If possible, a forceps through the ultraslim scope is used to grasp the guidewire for traction as an internal rendezvous technique. The fistulous tract is created and the LAMS deployed.

EUS-guided balloon-occluded gastrojejunostomy bypass

EUS-guided balloon-occluded gastrojejunostomy bypass (EPASS) is conducted based on the results of an animal study[10] (Figs 3,4). A special double-balloon enteric tube (Tokyo Medical University type; Create Medic Co., Ltd, Yokohama, Japan) is used for this procedure. In this type of balloon, saline can basically be delivered into the drainage lumen of the enteric tube between the two inflated balloons.

A standard upper gastrointestinal (GI) endoscope is advanced into the third portion of the duodenum. A guidewire is advanced as far as possible beyond the duodenum and jejunum loop. Then, the endoscope is removed, leaving the guidewire in place. Recently, an overtube is used to facilitate passage of the pre-inflated balloon catheter to avoid looping in the fornix of the stomach as it passes through the pyloric-duodenal stenosis. A double-balloon tube is perorally inserted over the guidewire in combination with a 0.89-inch dedicated guidewire for better torquability, and two balloons are placed in the duodenum and jejunum in an area adjacent to the stomach. Both balloons are filled with saline and

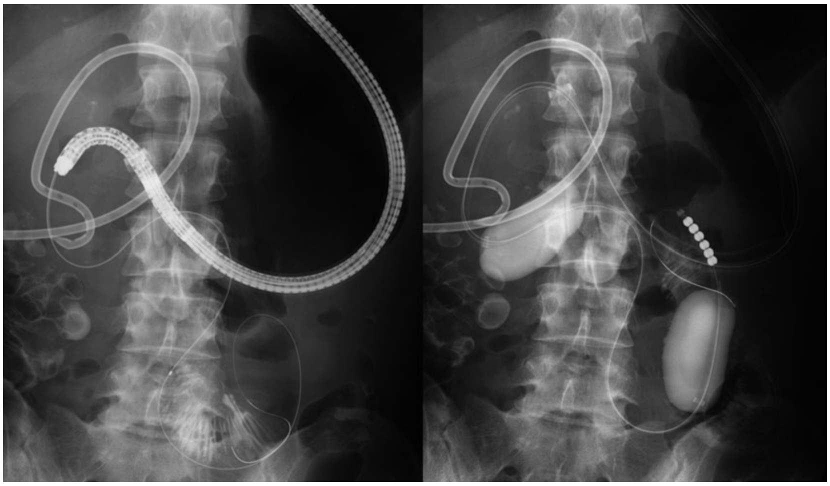

Figure 3 Endoscopic ultrasonography (EUS)-guided balloon-occluded gastrojejunostomy bypass (EPASS) procedure (double-balloon insertion). First, a guidewire is inserted with a catheter using a standard upper gastrointestinal (GI) endoscope (left). Then, a double-balloon catheter is advanced across the stomach over the wire and the balloons are inflated (right).

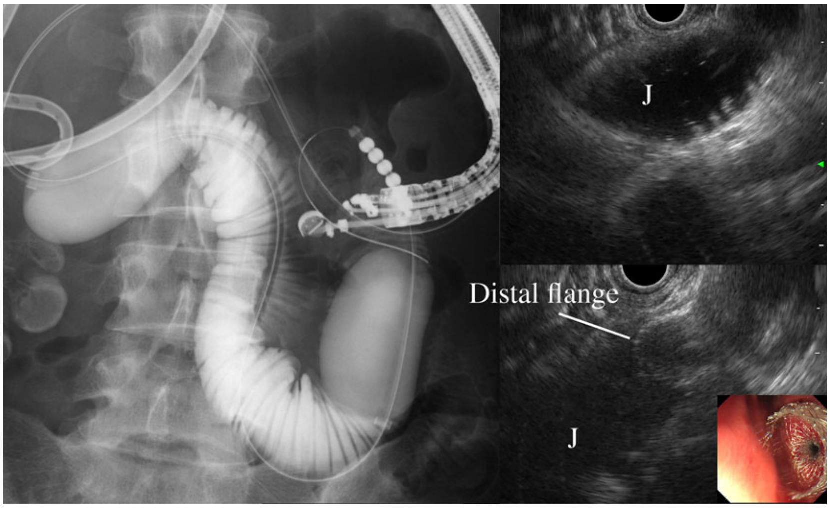

Figure 4 One-step (freestyle) endoscopic ultrasonography (EUS)-guided balloon-occluded gastrojejunostomy bypass (EPASS) procedure (stent placement). Fluoroscopic image shows distended jejunum using saline with contrast material between two balloons observed by EUS (left). EUS image shows distended jejunum (right upper) and deployed distal flange in the jejunum (right lower). Endoscopic image shows well-deployed proximal flange in the stomach (right lower corner). J, jejunum.

contrast material to hold the small intestine open. A sufficient quantity of saline with contrast material is introduced into the space between the two balloons to distend the small bowel lumen. An echoendoscope is advanced to the stomach to identify the distended duodenum or jejunum. Then, EPASS is divided into two procedures, namely one-step procedure (freestyle technique) and two-step procedure (standard technique). The former is carried out using direct electrocautery enhanced tip delivery system insertion without needle puncture, whereas the latter is a more standard procedure. It is carried out as follows: a 19-gauge FNA needle is used to puncture the duodenum or jejunum under EUS guidance. A guidewire is inserted through the 19-gauge needle. When an AXIOS™ stent[11] is used for EPASS, the 19-gauge needle is removed and the gastrojejunostomy tract is dilated over the wire using a 6-Fr electrocautery dilator and a 6-mm dilating balloon. The delivery system is advanced over the guidewire into the duodenum or jejunum. When the AXIOS-EC™ stent is used, the delivery system is directly advanced over the guidewire into the duodenum or jejunum while applying current (usually Autocut mode, 100 W, Effect 4). In case of one-step EPASS, electrocautery enhanced tip delivery system using 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.

Post-procedural strategy

Patients remain in hospital after the procedure and antibiotics are continued for at least 3 days. Liquid diet is begun 1 or 2 days later, and the diet is advanced as tolerated. Patients are discharged home when they demonstrate adequate tolerance to oral diet.

OUTCOMES OF EUS-GE

RELATIVELY LARGE CASE series including 10 and more cases showed that the technical success rate is approximately 90% regardless of technique used, although there were two retrospective studies (Table 3). In assisted technique except EPASS, retrieval or dilating balloon was frequently used to help the puncture in the duodenum and jejunum. In the EPASS procedure, the success rate of the one-step procedure was higher than that of the two-step procedure (100% *vs* 82%). Interestingly, almost all cases in which the stent was successfully placed showed clinical success (Fig. 5). Although there was no fatal case, adverse

Table 3 Outcomes of EUS-guided gastroenterostomy using LAMS for GOO ($n \geq 10$)

Author	Year	No. cases	Technique	Type of balloon	Study design	Single/ Multicenter	Technical success (%)	Clinical success (%)†	Adverse event	Fatal case	Convert to surgery
Khashab *et al.*[4]	2015	10	D: 1 B: 9	RB 4 DB 5	R	Multicenter	90	90	None	None	1‡
Itoi *et al.*[6]	2016	20	EPASS one-step: 9 two-step: 11	Double-balloon enteric tube	P	Single	100/82	90	Pneumoperitoneum 1	None	None
Tyberg *et al.*[5]	2016	26	D: 3 NOTES: 2 B: 13 USS: 5 NBD: 3	NA	R	Multicenter	92	85	Peritonitis 1 Bleeding 1 Pain 1	None	1‡

†Intention-to-treat analysis.
‡Possibly the same case.
B, balloon-assisted endoscopic ultrasonography (EUS)-gastroenterostomy; D, direct EUS-gastrojejunostomy; EPASS, EUS-guided double-balloon-occluded gastrojejunostomy bypass; NA, not applicable; NBD, nasobiliary drain; NOTES, natural orifice translumenal endoscopic surgery; P, prospective; R, retrospective; USS, ultraslim endoscope.

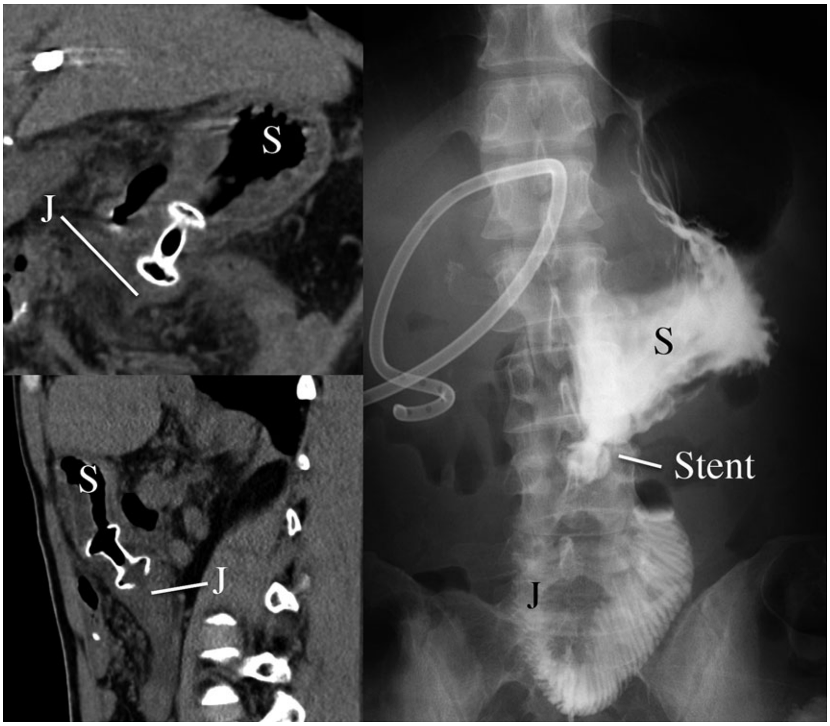

Figure 5 Stent imaging after endoscopic ultrasonography (EUS)-guided balloon-occluded gastrojejunostomy bypass (EPASS) procedure. Computed tomography shows well-placed stent connecting the stomach and the jejunum (left upper and lower). Gastrography shows well-flowing contrast material directly from the stomach to the jejunum (right). J, jejunum; S, stomach.

events were seen in several cases, but none was serious (peritonitis, bleeding). One failed case using balloon-assisted EUS-GE was converted to a laparoscopic gastrojejunostomy. In two failed cases using the EPASS procedure, there was clinical improvement with conservative treatment.

Recent comparative study between EUS-GE and endoscopic enteral stenting showed that EUS-GE may be ideal for malignant GOO with comparable effectiveness and safety to endoscopic enteral stenting while being associated with fewer symptom recurrences and requirements for re-intervention.[11]

FUTURE PERSPECTIVES OF EUS-GE

ALTHOUGH EUS -GUIDED GASTROJEJUNOSTOMY was first reported in the pig model, several studies[4–6] on EUS-GE revealed the feasibility of this technique with a high success rate when used clinically.[7–10] However, there are still major obstacles even using what is now considered an ideal LAMS (AXIOS-EC™). In an ideal world, EUS-GE would entail easy transgastric access of the LAMS into the collapsed and mobile duodenum or jejunum, without any preparation and no dedicated tools for EUS-GE except the LAMS. However, in order to access the duodenum and jejunum safely, the inflated balloon-assisted technique and double-balloon-occluded technique are mostly used for EUS-GE. A randomized trial between these two techniques should be carried out in the near future. Theoretically, however, it appears impossible to conduct secure puncture into the collapsed duodenum and jejunum unless some preparation to distend the small bowel (e.g. water-filling luminal technique) is conducted. However, even if a large amount of water is injected into the small bowel, the small bowel moves within the peritoneal cavity and becomes gradually collapsed owing to the flow of water to the colon by peristalsis even when anti-motility drugs are given. Thus, maintaining sufficient distention of the small bowel for secure puncture is thought to be difficult. Therefore, until clarification of the superiority of the balloon-assisted technique, if possible, the use of a double-balloon enteric tube may be preferable to trap fluid and distend the small bowel between the two balloons. In addition, this system is very useful as additional fluid can easily be injected for the distention of the small bowel when the small bowel collapses after needle puncture or bougie use. However, theoretically, complete GOO may preclude advancement of the guidewire and over-the-wire devices such as the double-balloon tube in the distal jejunum. In case of complete GOO, pre-dilation using a dilating balloon before inserting over-the-wire devices seems to be useful. Nonetheless, EUS-GE may be more suitable in patients with incomplete GOO than in complete GOO.

The AXIOS-EC™ stent seems an essential device for successful EUS-GE. In the EPASS procedure, one-step delivery system insertion without needle puncture resulted in 100% success.[6] In developing this technique, we realized that when multiple steps are used, failure can occur at each of these steps. For example, advancing the guidewire during exchange of devices leads to pushing the duodenum or jejunum away from the stomach. In fact, the success rate of two-step EPASS was 82%. Therefore, if the targeted duodenum and jejunum is sufficiently distended, the one-step procedure may be ideal. Finally, we believe the one-step approach enables carrying out the real one-step EPASS which appears to be safe, reliable and time-saving (mean procedure time: 25.5 min[6]) whereas the non-EPASS procedure took longer (mean procedure time: 96 min, range 45–152 min).[4]

Nowadays, we can choose three procedures except EUS-GE for the treatment of GOO (i.e. endoscopic enteral stenting, open surgical GJ and laparoscopic GJ). There are several advantages and disadvantages in each procedure (Table 4). EUS-GE may be superior to endoscopic enteral stenting regarding prolonged stent patency as a result of short length (1 cm) and the fully covered metal stent, although the anastomotic site is limited. In contrast, laparoscopic GJ seems to be inferior to EUS-GE in terms of procedure time and invasiveness (pain score etc.) and hospital stay. In particular, it may be unsuitable for malignant patients at end stage.

Limitations of EUS-GE include the small number of cases of a mostly retrospective nature and the lack of a control group. Furthermore, in the near future, long-term follow up to determine the optimal method of maintaining permanent patency should be evaluated. Additionally, the learning curve and endoscopic training of various types of EUS-GE appear to be a big concern. An appropriate training system using a dedicated training model should be established to disseminate this technique.

In conclusion, the present review revealed the feasibility of a novel EUS-GE using a LAMS. As a next step, clinical prospective trials with adequate sample size and, moreover, with a comparison between EUS-GE and duodenal metal

Table 4 Comparison of current techniques for gastric outlet obstruction

Procedure	Advantage	Disadvantage
EUS-guided gastroenterostomy	Bypass of tumors Short procedure time Potential prolonged stent Less painful procedure Short hospital stay	Need for special device Non-established difficult endoscopic procedure Limited portion of stent placement Inability in cases of complete obstruction Possible serious adverse events
Endoscopic enteral stenting	Short procedure time Established easy endoscopic procedure Broad indication regardless of various patient conditions Non-limited portion of stent placement Less painful procedure Short hospital stay	Stent migration Stent occlusion as a result of tumor ingrowth/overgrowth
Open surgical gastroenterostomy	Bypass of tumor Permanent large anastomosis Established surgical procedure	Most invasive procedure Longer hospital stay than endoscopic procedures Contraindicated in critically ill patients
Laparoscopic gastroenterostomy	Bypass of tumor Permanent large anastomosis Established surgical procedure Less invasive than open surgical gastroenterostomy	Invasive procedure Longer hospital stay than endoscopic procedures Contraindicated in critically ill patients

EUS, endoscopic ultrasonography.

stenting or surgical GE are warranted. However, until these outcomes are clarified, a multidisciplinary approach in patients with GOO should be considered not only by endoscopists but also by surgeons and interventional radiologists.

CONFLICTS OF INTEREST

AUTHORS DECLARE NO conflicts of interest for this article.

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