REVIEW

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CLINICAL ENDOSCOPY

Endoscopic stenting for malignant gastric outlet obstruction: focusing on comparison of endoscopic stenting and surgical gastrojejunostomy

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Malignant gastric outlet obstruction (GOO) is a condition characterized by blockage or narrowing where the stomach empties its contents into the small intestine due to primary malignant tumors or metastatic diseases. This condition leads to various symptoms such as nausea, vomiting, abdominal pain, and weight loss. To manage malignant GOO, different treatment options have been employed, including surgical gastrojejunostomy (SGJ), gastroduodenal stenting (GDS) using self-expandable metallic stent (SEMS), and endoscopic ultrasound-guided gastrojejunostomy (EUS-GJ). This review focuses on comparing the clinical outcomes of endoscopic stenting (GDS and EUS-GJ) with SGJ for malignant GOO. Studies have shown that GDS with SEMS provides comparable clinical outcomes and safety for the palliation of obstructive symptoms. The choice between covered and uncovered SEMS remains controversial, as different studies have reported varying results. EUS-GJ, performed via endoscopic ultrasound guidance, has shown promising efficacy and safety in managing malignant GOO, but further studies are needed to establish it as the primary treatment option. Comparative analyses suggest that GDS has higher recurrence and reintervention rates compared to EUS-GJ and SGJ, with similar overall procedural complications. However, bleeding rates were lower with GDS than with SGJ. Randomized controlled trials are required to determine the optimal treatment approach for malignant GOO.

Keywords: Endoscopic ultrasonography; Gastric outlet obstruction; Gastrointestinal endoscopy; Gastrojejunostomy; Self-expandable metallic stents

INTRODUCTION

Malignant gastric outlet obstruction (GOO) refers to a condition in which there is a blockage or narrowing at the point where the stomach empties its contents into the small intestine by primary malignant tumors or metastatic diseases. Symptoms caused by malignant GOO include nausea, vomiting, early satiety, abdominal pain or discomfort, loss of appetite, and weight loss. Dehydration, electrolyte imbalances, malnutrition, or gastroparesis can also be complicated.[1,2] To resolve and manage clinical problems complicated by malignant GOO, several treatment options have been applied clinically. Surgical gastrojejunostomy (SGJ) was initially applied for the resolution of malignant GOO. Then, gastroduodenal stenting (GDS) with self-expandable metallic stents (SEMS) was popular as an alternative option for malignant GOO. Recently, endoscopic ultrasound-guided gastrojejunostomy (EUS-GJ) was introduced with the rapid development of interventional endoscopic ultrasound.[3-5] Herein, we reviewed clinical outcomes of endoscopic stenting (ES) such as GDS and EUS-GJ and compared them with SGJ for the treatment of malignant GOO.

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THE CLASSIFICATION OF TREATMENT MODALITIES FOR PALLIATION OF MALIGNANT GOO

The treatment modalities for the resolution of symptomatic malignant GOO are shown in Figure 1. Palliative approaches for malignant GOO are divided into ES and SGJ. ES includes GDS and endoscopic gastrojejunostomy. GDS is the conventional endoscopic placement of SEMS at the obstruction site in malignant GOO. Endoscopic gastrojejunostomy has been performed in the following three ways: endoscopic ultrasound (EUS-GJ), forward-viewing endoscopy (endoscopic magnetic gastrojejunostomy), and the natural orifice transluminal endoscopic surgery (NOTES) approach. In the following sections, we will focus on GDS and SGJ, which are currently being actively implemented clinically; and EUS-GJ, which has been started relatively recently but is being tried by several groups.

GASTRODUODENAL STENTING

The SGJ, which involved creating a connection between the stomach and the jejunum, had been selected for a conventional treatment of malignant GOO. However, this procedure is invasive and carries a higher risk of complications.[6-10] Gastroduodenal stent placement using a SEMS (Fig. 2) has shown comparable clinical outcomes and safety for palliation of obstructive symptoms complicated by malignant GOO.[11-14] Initially, SEMS in the early developmental stages of the procedure were uncovered. The uncovered SEMS inevitably developed tumor ingrowth over time, which covered SEMS were developed to overcome. However, because the SEMS in the early developmental stages had high axial force with poor conformability, covered SEMS resulted in frequent stent migration.[15] The covered stents used in esophageal obstruction are full-covered types, but covered stents for malignant GOO are mostly partially covered and uncovered at both ends to reduce migration. The clinical studies about the efficacy of SEMS on malignant GOO are summarized in Table 1.[15-27] Previous studies reported stent malfunction due to stent migration in 0-8.3% of patients with malignant gastroduodenal obstruction with uncovered stents[16,19,24] and 8.8% to 28% of patients with malignant GOO with covered stents.[28-30] A meta-analysis of 61 articles analyzing the clinical results of

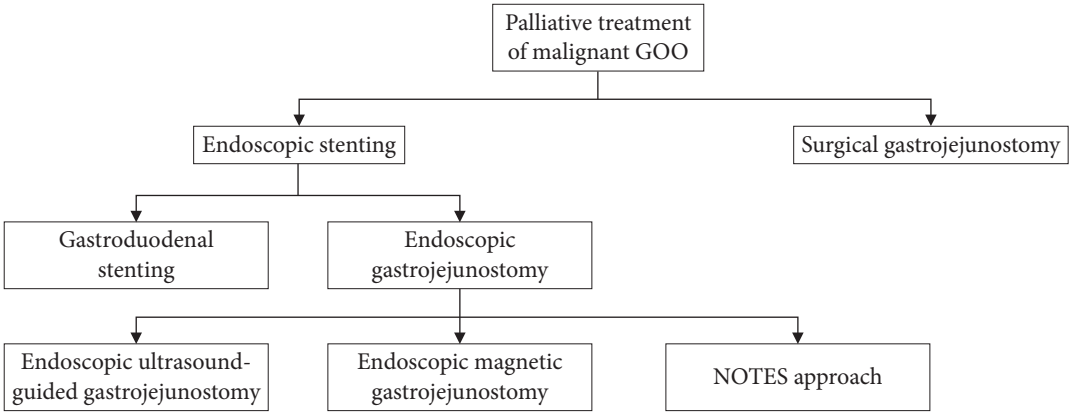

Fig. 1. The treatment modalities for palliation of malignant gastric outlet obstruction (GOO). NOTES, natural orifice transluminal endoscopic surgery.

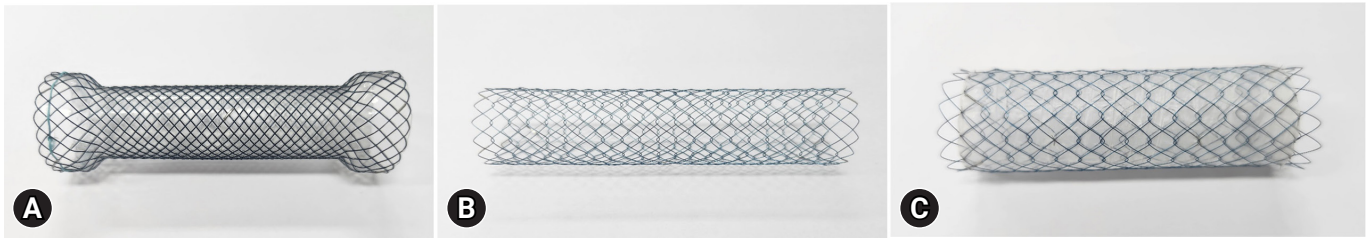

Fig. 2. Photographs of self-expanding metallic stents. Covered (A), uncovered (B), and triple-layer, covered (C) self-expanding metallic stents.

Table 1. Characteristics of studies about clinical efficacy of self-expandable metal stents on malignant gastric outlet obstruction

Study	Design/ centers	Country	No. of patients finally analyzed	Type of malignancy	C-SEMS	U-SEMS	Technical success (%)[a]	Clinical success (%)[a]	8-wk patency (%)[a]	Stent patency (wk)	Stent migration during follow-up (%)[a]	Restenosis during follow-up (ingrowth, overgrowth, stent compression) (%)[a]	Reintervention during follow-up (%)[a]	Major complications (%)[b]	Follow-up (wk)[a]
Kim et al. (2010)[16]	RCT/single center	Korea	80	GC	Niti-S pyloric or Niti-S ComVi pyloric stent (double layered)	Enteral Wallstent or Enteral WallFlex	100/100	95/90	61.3/61.1	NA	32.3/8.3	3.2/44.4	NA	2/0	14.5 (1–117)/ 14 (1–114)
Maetani et al. (2014)[17]	RCT/multicenter	Japan	62	GC, PC, BDC	Niti-S ComVi stent (triple layered)	Niti-S stent	100/100	87.1/93.5	NA	NA	6.5/3.3	0/19.4	3.3/19.4	3.2/3.2	10.4/13.3
Lim et al. (2014)[15]	RCT/multicenter	Korea	120	GC, PC, DC, AC, BDC, GBC	Niti-S ComVi pyloric stent (double layered)	Niti-S pyloric/ duodenal D-type stent	100/100	100/98.4	NA	13.6 (8–19)/13.1 (8.9–17.3)	13.6/0	6.8/21.3	22.0/21.3	0/0	14.0 (8–26)/14.0 (7–22)
Lee et al. (2015)[18]	RCT/multicenter	Korea	102	GC	WAVE SEMS with an anti-migration design (Bona stents)	U-SEMS (Bona stents)	98.0/96.1	94.1/86.2	72.5/62.7	NA	9.5/5.4	7.1/37.8	23.5/39.2	0/0	21.3 (±10)/ 20.1 (±9.5)
van Hooft et al. (2007)[19]	Retrospective/ multicenter	Netherlands, Italy, Germany	62	PC, GC, MD, BDC, GBC, AC, DC		WallFlex duodenal stent	97	85	NA	NA	1	1	NA	8	4.3
van Hooft et al. (2009)[20]	Prospective/ multicenter	Netherlands	51	PC, BDC, GBC, GC, DC, AC, MD		WallFlex duodenal stent	98	84	NA	43.8	2	12	14	10	8.9
Havemann et al. (2009)[21]	Prospective/ single center	Denmark	45	PC, GC, GyC, UC, HC, MD		Hanaro stents	91	63	NA	NA	7	14	14	4	17.3 (9–25.9)
Kim et al. (2011)[22]	Prospective/ multicenter	Korea	50	GC, PC, BDC, GBC	Niti-S ComVi pyloric stent		100	88	NA	13.1±8.0	10	18	28	0	15.7 (±9)
Isayama et al. (2012)[23]	Prospective/ multicenter	Japan	50	PC, GC, BDC, MD	Niti-S M-ComVi stent (triple layered)		100	90	NA	21.4±1.3	6	10	NA	4	20 (±2.8)
Sasaki et al. (2013)[24]	Retrospective/ multicenter	Japan	42	PC, GC, BDC, DC		WallFlex duodenal stent	100	83.3	NA	16.0 (3–18)	0	23.8	26.2	2.4	3.3 (1.8–6)
van den Berg et al. (2013)[25]	Prospective/ multicenter	Netherland	46	PC, BDC, GC, MD, DC, GBC		The Evolution enteral stents	89	72	NA	9.6	4	26	NA	6	12.4 (5–33.9)
Jung et al. (2016)[26]	Retrospective/ single center	Korea	220	PC, GC, BDC, GBC, DC, MD	Fully C-SEMSs, partially C-SEMSs[c]	Variable[c]	96.8	86.4	NA	NA	37.5/9.1/5.8[d]	12.5/22.1/26.7[d]	NA	0/0.5/0[d]	17.7 (8–32)
Hori et al. (2017)[27]	Retrospective/ multicenter	Japan	252	PC, GC, BDC, GBC	Ultraflex stent, Niti-S ComVi stent	WallFlex duodenal stent, Niti-S pyloric stent	99.2/100	82.5/88.1	NA	12.3/9	4.8/0.8	9.5/11.9	NA	7.9/3.2	12.4/9

Values are presented as median (range) or mean±standard deviation unless otherwise indicated.

C-SEMS, covered self-expanding metal stent; U-SEMS, uncovered self-expanding metal stent; RCT, randomized controlled trial; NA, not available; GC, gastric cancer; PC, pancreatic cancer; BDC, bile duct cancer; DC, duodenal cancer; AC, ampullary cancer; GBC, gallbladder cancer; MD, metastatic disease; GyC, gynecological cancer; UC, urological cancer; HC, hematological cancer.

[a]Former numbers indicate values of C-SEMS and later ones do those of U-SEMS. [b]Major complication is defined as adverse events caused by SEMS placement requiring additional interventions or hospitalization. [c]Niti-S stents (Taewoong Medical), Bona stents (Standard Sci-Tech), Hanaro stents (M.I. Tech Co. Ltd.), Boston stents (Boston Scientific), and S&G stents (S&G Biotech Inc.) were used. [d]The numbers separated by "/" indicate the value in order of fully covered SEMS, partially C-SEMS, and U-SEMS.

GDS for malignant GOO published from January 2015 to February 2021 showed that technical and clinical successes were 99.4% (95% confidence interval [CI], 98.9%–99.8%) and 88.9% (95% CI, 86.7%–90.9%). The recurrence rates were 28.7% (95% CI, 19.7%–38.6%), and the reintervention rate was 20.3% (95% CI, 16.9%–23.9%).[6]

THE COMPARISON OF CLINICAL EFFICACY AND SAFETY BETWEEN COVERED AND UNCOVERED SEMS

According to the results of a meta-analysis, which analyzed studies on the clinical performance and safety of covered and uncovered SEMS in malignant GOO, technical and clinical success were not statistically different between the two SEMS (odds ratio [OR], 0.69; 95% CI, 0.21–2.3 and OR ,1.1; 95% CI, 0.76–1.61, respectively).[31] Stent patency, defined as the time between stent deployment and stent dysfunction was higher in covered than in uncovered SEMS (hazard ratio, 0.68; 95% CI, 0.48–0.96). Covered SEMS were associated with higher stent migration (OR, 4.28; 95% CI, 2.79–6.57). Uncovered SEMS were associated with a higher rate of stent occlusion (OR, 0.34; 95% CI, 2.79–6.57). However, there were no differences in terms of overall adverse events, reintervention, and dysfunction rates. In addition, patient survival was similar in covered and uncovered stent groups (hazard ratio, 0.96; 95% CI, 0.75–1.23).[31]

Thus far, four randomized, controlled studies in which clinical efficacy and safety of endoscopic placement of covered vs. uncovered SEMS were sufficiently demonstrated, have been conducted worldwide, three in Korea and one in Japan.[15-18] In terms of clinical efficacy, the two randomized trials showed similar results in stent malfunction caused by stent migration and restenosis in covered and uncovered SEMS.[15,16] However, in the two other studies, the clinical outcomes of covered SEMS were better than those of uncovered SEMS.[17,18]

When looking at the results of these meta-analyses and comparative studies, it seems difficult to draw any conclusions about which type of stent should be chosen as a first option between covered and uncovered SEMS. However, we must consider the following several points. Firstly, it is highly likely that the performance of the stents used in previous studies was not the same. The manufacturing methods and stent designs are different in the various companies that produce SEMS and they could cause differences in the clinical performance of SEMS. Secondly, the causative diseases of malignant GOO were different in the prior studies. The patient cohorts of many studies consisted of various cancers, such as pancreatic, gastric, duodenal, bile duct, gallbladder, and metastatic cancers, and some conducted studies on patients with a single cancer type, such as gastric cancer.[16,32,33] Thirdly, the cancer progression and the clinical disease severity during the follow-up period were different among studies. These factors could affect the clinical outcome and prognosis of SEMS placement in malignant GOO. In addition, whether chemotherapy is administered can also affect the clinical outcomes of SEMS placement. Several retrospective studies have shown that chemotherapy is associated with prolonged uncovered stent patency in patients with malignant pyloric obstruction.[34-36] A long time-to-progression and first-line chemotherapy were substantial protective factors against re-stenosis.[37] Chemotherapy has been associated with stent migration.[15,35,36] In a study conducted by Lim et al.,[15] the rate of stent migration in the covered SEMS group was higher in the patients who underwent chemotherapy than in those who did not undergo chemotherapy. However, in most studies, it is difficult to find statistically significant results analyzing the influence of chemotherapy on SEMS placed endoscopically.

Innovations in the design of SEMS should be made to improve clinical efficacy in malignant GOO. Two of the above-mentioned randomized, controlled trials indicated a triple-layered design for covered SEMS; clinical outcomes in the covered SEMS group were superior to the uncovered SEMS group. This warrants attention. It is speculated that this innovative design substantially influenced the decrease in the rate of stent migration. The superiority of triple-layered, covered SEMS must be validated in more clinical prospective studies.

ENDOSCOPIC GASTROJEJUNOSTOMY

Since endoscopic gastrojejunostomy has advantages of both SGJ and endoscopic metal stent placement, such as a short length of anastomosis and less invasiveness, endoscopic gastrojejunostomy may be an ideal treatment for malignant GOO. Endoscopic approaches can be divided into two: (1) using flexible forward-view endoscopy, and (2) using endoscopic ultrasound (Fig. 3).

Using flexible forward-view endoscopy

Studies with animal models on endoscopic gastrojejunostomy began to be reported in the early 1990s and early 2000s.[38-40] Later, endoscopic magnetic gastrojejunostomy[41-43] and the

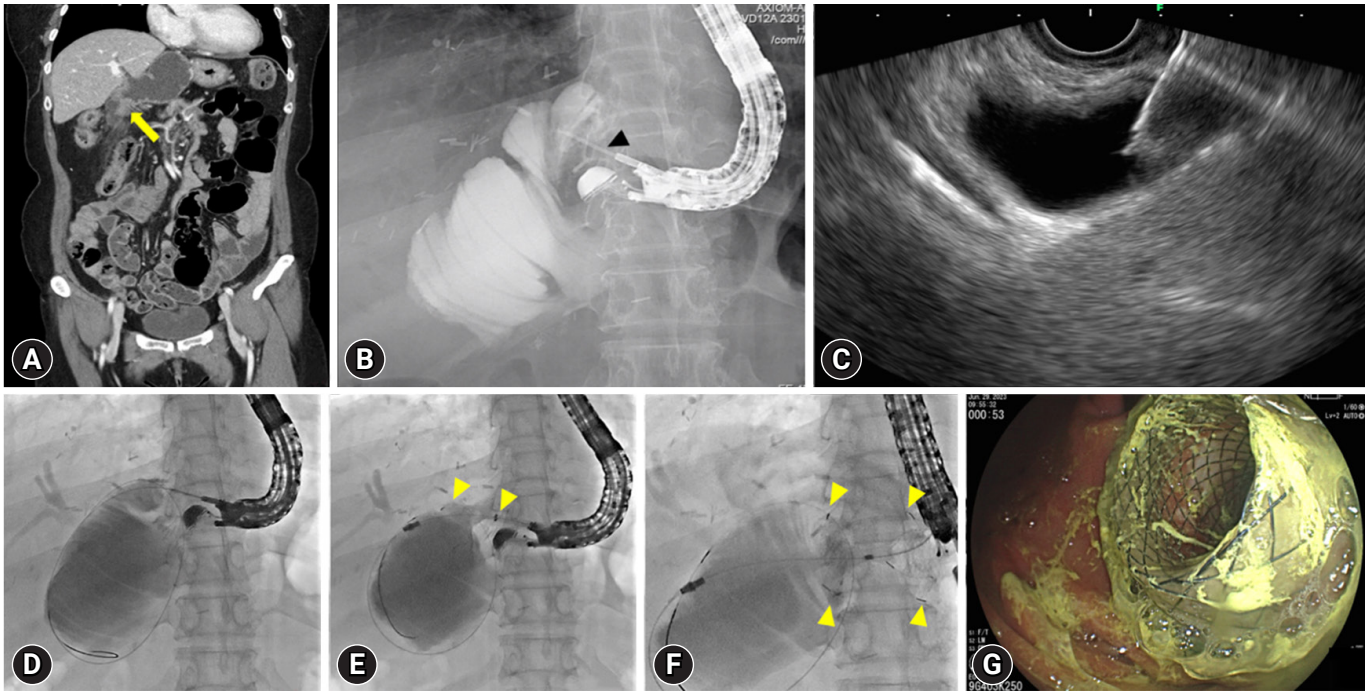

Fig. 3. An example of endoscopic ultrasound (EUS)-guided gastrojejunostomy in a patient with recurrent intraductal papillary neoplasm of the bile duct and long afferent loop stricture undergoing right anterior partial sectionectomy, S1 and radical bile duct resection, and subtotal gastrectomy with Billroth-II reconstruction. (A) A coronal image of the dilated afferent loop caused by mid afferent loop stricture (yellow arrow) on computed tomography scan. (B, C) A needle puncture (black arrowhead) on fluoroscopic and EUS view. (D) A guidewire insertion through the punctured needle into dilated afferent loop. (E) Stent (yellow arrowheads) deployment along the inserted guidewire. (F, G) Completed stent (yellow arrowheads) deployment on fluoroscopic and endoscopic view.

NOTES approach[44,45] were suggested. However, all of these were small-scale studies with insufficient progress to merit successful implementation in a clinical situation, for the following reasons. Firstly, flexible forward-view endoscopy is very difficult to perform with only a conventional endoscope. Secondly, in the case of the magnetic method, it takes approximately 10 days after magnet installation until a gastroenteric fistula is formed. Thirdly, the safety of the procedure has not been sufficiently proven. Therefore, the concept of endoscopic gastrojejunostomy has evolved into an approach using endoscopic ultrasound.

Using endoscopic ultrasound

Endoscopic ultrasound-guided drainage therapy has been consistently published since the early 2000s.[41] EUS-GJ is usually proceeded with the following steps. (1) The patient is placed under conscious sedation or general anesthesia to ensure comfort during the procedure. (2) An endoscope with an integrated ultrasound probe is inserted into the patient's mouth and guided down the esophagus into the stomach. (3) Under ultrasound guidance, a needle is advanced through the stomach wall and into the jejunum, creating a tract. (4) A guidewire is then threaded through the needle and into the jejunum. (5) Over the guidewire, a stent or a balloon catheter is placed to create a connection (anastomosis) between the stomach and the jejunum. (6) The stent is deployed, expanding and securing the connection. (7) The endoscope is withdrawn, and the procedure is completed.

Recent studies and case reports have shown comparable efficacy and safety of EUS-GJ in managing malignant GOO, contributing to its increasing adoption as a minimally invasive therapeutic option.[3,46-55] There have also been studies on ES in cases of both malignant biliary obstruction and GOO. The extent of GOO can be divided into three types: (1) invasion of only the duodenal bulb; (2) invasion to the second part of the duodenum, to the main papilla; and (3) invasion of the third part of the duodenum, without the involvement of the papilla. According to a study analyzing the results of 11 studies examining the treatment results of endoscopic treatment in patients

with both malignant biliary and GOO, stenting was performed on the GOO site in 10 studies, and EUS-GJ was used to treat malignant GOO in one study.[56] Endoscopic ultrasound-guided biliary drainage (EUS-BD) therapies were performed at the same time or within seven days. The clinical outcomes of EUS-BD were very good (a mean technical success of 96.4%; 95% CI, 92.2%–99.0%) and a mean clinical success of 85.0% (95% CI, 68.0%–96.3%). Clinical success of duodenal stenting and EUS-GJ for malignant GOO was 90% and 100%, respectively.[56] Therefore, when malignant biliary obstruction and malignant GOO occur at the same time, GOO is not a problem at all even if it is solved by conventional ES or relatively recently introduced EUS-GJ. However, it is still too early to say that EUS-GJ can be applied as a primary treatment of choice for malignant GOO. A randomized trial comparing the method with conventional SEMS placement should be conducted to verify the efficacy and safety of EUS-GJ.

COMPARISON OF CLINICAL OUTCOMES OF GDS, EUS-GJ, AND SGJ

In a meta-analysis comparing the clinical results of GDS, EUS-GJ, and SGJ in the studies published between January 2015 and February 2021, the technical success was lowest in EUS-GJ (95.3% [95% CI, 89.3%–98.9%] in EUS-GJ, 99.4 % [95% CI, 98.9%–99.8%] in GDS, and 99.9% [95% CI, 99.5%–100%] in SGJ, p=0.0048).[6] In addition, the recurrence and reintervention rates of GDS were higher than those of EUS-GJ and SGJ; the recurrence rates were 28.7% (95% CI, 19.7%–38.6%) in GDS, 4.0% (95% CI, 0%–15.0%) in EUS-GJ, and 16.9% (95% CI, 11.6%–23.0%) in SGJ, respectively (p=0.0036), and the reintervention rates were 20.3% (95% CI, 16.9%–23.9%) in GDS, 11.2% (95% CI, 4.9%–19.6%) in EUS-GJ, and 12.6% (95% CI, 6.6%–20.1%) in SGJ, respectively (p=0.041).

In terms of safety, overall procedural complications were similar (GDS, 18.7% vs. EUS-GE, 21.9% vs. surgical GJ, 23.8%; p=0.32). Although estimated bleeding rates were similar between GDS and EUS-GJ (1.7% [95% CI, 0.9%–2.7%] vs. 2.9% [95% CI, 0.2%–8.6%], p=0.999), the bleeding rate for GDS was lower than that for SGJ (5.2% [95% CI, 3.2%–7.5%], p=0.0033 for pairwise comparison).[6]

There have only been small reports on the comparison between SGJ and GDS.[8,9,11,57-59] In a multicenter-based, randomized, controlled trial performed by Jeurnink et al.,[11] SGJ was associated with better long-term outcomes. In the study, the majority of enrolled patients had pancreatic cancer and GDS was compared with bypass surgery. Approximately half of the 77 initially enrolled patients refused to participate in the randomization, which was described as a limitation of the study.

SELECTION OF TREATMENT MODALITIES OF GDS, EUS-GJ, AND SGJ IN MALIGNANT GOO

A multidisciplinary, team-based decision-making process including gastroenterologists, surgeons, and oncologists is important to select the most appropriate and personalized treatment option for each patient with malignant GOO. The team has to assess the individual patient's overall health status, tumor characteristics, and potential risks and benefits of each treatment option.

GDS is advantageous in several aspects. It is a minimally invasive procedure, avoiding the need for open surgery. It is associated with shorter procedure time, reduced hospital stay, and faster recovery compared to SGJ. SEMS can be easily removed or exchanged if needed. GDS carries a lower risk of complications compared to SGJ.[60,61] GDS can preclude the potential risks associated with open surgery, such as general anesthesia, surgical wound infections, postoperative pain, and longer hospital stay.

However, GDS is not always feasible and is preferred to SGJ. If the sites of GOO show extensive or complex obstruction or an attempt to place a SEMS is unsuccessful, in these cases, SGJ may be preferred. Tumor-related factors should also be considered. If the tumor is bulky, invasive, or associated with a high risk of tumor ingrowth, SGJ could provide more durable relief of obstruction compared to ES. Finally, consideration of clinical factors such as patient preferences for SGJ, life expectancy, anticipated treatment course, and quality of life could inform the decision of SGJ over GDS.

According to a recent guideline released by the American Society for Gastrointestinal Endoscopy, GDS is preferentially recommended in patients who are poor surgical candidates with short life expectancy (<6 months) and want early resumption of oral diet and discharge from the facility.[62] Conversely, SGJ is preferentially recommended in patients with a life expectancy of >6 months and a good performance status.[62]

More clinical data are required on the circumstances in which EUS-GJ is preferentially selected for patients with malignant GOO. If the procedure is successful, the rates of restenosis and reintervention are lower than those of GDS. However, there is still doubt about the feasibility and safety of the procedure.

More randomized clinical trials are needed to validate the feasibility and safety of EUS-GJ.

CONCLUSIONS

Since the early 2000s, ES has shown excellent clinical outcomes and safety, affirming that it can replace surgical bypass. In terms of the difficulty of the endoscopic procedure, ES can be performed if the gastrointestinal endoscopist is familiar with the operation of conventional endoscopic devices, such that clinical implementation of the procedure has succeeded worldwide. More recently, EUS-GJ has shown remarkable clinical results, although only a few studies have been reported.[63,64] However, there are still procedural difficulties to be solved and safety issues to determine. Ultimately, non-inferiority compared to conventional endoscopic stent treatment should be demonstrated in a randomized, prospective clinical study, such that the endoscopic ultrasound-based approach can be applied more often in clinical situations. Although ES has optimistic clinical outcomes, there are some potential future directions for ES. Innovation in stent designs has to be attempted to enhance clinical efficacy and reduce complications. Research on anti-migration mechanisms, drug elution to the surface of SEMS in techniques to prevent tumor ingrowth, and modifications of stent design to promote better luminal patency should be done. Advanced endoscopic technology may lead to the development of more minimally invasive approaches for ES. Robotic-assisted endoscopic platforms or endoscopic suturing devices may have a crucial role in improving clinical outcomes and widening the indications of endoscopy while reducing invasiveness. To prove the possibility of these innovative approaches, prospective and randomized clinical trials are warranted.

Conflicts of Interest

The authors have no potential conflicts of interest.

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Author Contributions

Conceptualization: CGK; Data curation: SGL; Formal analysis: SGL; Investigation: SGL; Supervision: CGK; Writing–original draft: SGL; Writing–review & editing: CGK.

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