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MINIREVIEWS

Treatment of gastric outlet obstruction that results from unresectable gastric cancer: Current evidence

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Abstract

Malignant gastric outlet obstruction (GOO) is a common condition that results from locally advanced malignancies in the upper gastrointestinal tract, such as pancreatic, gastric, and other carcinomas. Two types of procedures for malignant GOO, namely, gastrojejunostomy (GJ) with laparotomy or a laparoscopic approach and endoscopic stenting (ES), are currently available. Although numerous previous reports have clarified the benefits and drawbacks of each procedure, whether GJ or ES should be used in patients with GOO that results from gastric cancer who may have a longer life expectancy than patients with other malignancies has not been determined. In this review, which focuses on gastric cancer-induced GOO, we analyzed the two systematic reviews and a meta-analysis that compared GJ and ES and outlined the current status of GOO treatment. We also provide an updated review that includes laparoscopic GJ. Various data from 13 studies in one review and 6 studies in another review were analyzed. Although the main results of the present review indicated that both GJ and ES were efficacious treatments in patients with GOO that resulted from gastric cancer, current evidence suggests that GJ may be the preferable procedure given its good performance status and improved prognosis in gastric cancer patients.

Key words: Gastric outlet obstruction; Gastrojejunostomy; Endoscopic stenting; Gastric cancer; Review

Core tip: Both gastrojejunostomy (GJ) and endoscopic stenting (ES) are effective treatments in patients with gastric outlet obstruction that results from gastric cancer. The advantages of GJ include fewer late complications and a long patency, whereas the advantages of ES include better short-term outcomes, including the length of the hospital stay. Although no large-scale randomized clinical trials have compared the safety and efficacy of the two procedures, this present literature review

indicates the superiority of GJ compared with ES given its good performance status and improved prognosis in gastric cancer patients as well as the widespread use of the less invasive laparoscopic GJ procedure.

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INTRODUCTION

Malignant gastric outlet obstruction (GOO) is a clinical symptom of advanced malignancies in the upper gastrointestinal tract, most commonly pancreatic and gastric malignancies. Other causes include lymphomas, ampullary carcinomas, biliary tract cancers, and metastases[1-3]. Associated symptoms, including nausea, vomiting, reflux, malnutrition, dehydration, and abdominal distention, reduce patient quality of life (QOL), and patients with malignant GOO often present with a poor condition and performance status (PS)[4]. Furthermore, palliative treatment is important and required for patients with unresectable primary malignancies or metastatic lesions.

Treatments for malignant GOO include gastrojejunostomy (GJ), which is traditionally adopted, and palliative endoscopic stenting (ES), which is considered less invasive with a faster improvement of oral intake compared with GJ[5]. Recently, the use of palliative ES has increased[6]. In addition, various types of stents are now available, and the procedure has been established and advocated[7-11]. However, the disadvantages of ES include a high rate of stent re-obstruction and migration as late complications, and pleural treatment is required with some frequency[2].

Many comparative trials of GJ and ES in patients with malignant GOO have been performed to evaluate the safety, feasibility, costs, and patient QOL. However, to date, the available data regarding "gastric cancer" patients with GOO who could theoretically have a longer life expectancy than patients with other malignancies are not sufficient to definitively conclude the comparative benefits and limitations of GJ and ES. In this review, we outline the current status of GJ and ES treatment for malignant GOO, especially in gastric cancer, and provide a future perspective.

STUDY STRATEGY

Data source and search strategy

An increasing number of studies regarding ES, including novel devices, has been reported during the past decade, especially in the most recent five years; thus, the outcome of GJ should be compared with recent ES. Literature searches of the electronic PubMed and Embase databases were performed. The searches were limited to articles published from January 2010 to December 2014 in English as well as human- and clinical trial-related articles to identify objective articles from January 2010 to December 2014. The following terms were utilized: "Gastric outlet obstruction", "GOO", "gastric cancer", and "gastric carcinoma". The abstracts were reviewed, and articles not related to the specific content were excluded. Duplicate references and repeated articles were also excluded. All articles considered eligible were selected, and the final selection was based on the full research papers.

Study selection

We included review articles, studies that reported randomized and controlled trials or experimental studies, and case studies. Articles were first screened and selected based on the titles. The full text was obtained for 45 articles.

MALIGNANT GOO THAT RESULTS FROM OF GASTRIC CANCER

Despite a decrease in the incidence of gastric cancer over previous decades, gastric cancer remains the fourth most common malignant disease and the second main cause of cancer-related death worldwide[12]. To date, the curative resection ratio for newly diagnosed gastric cancer is approximately 50%, and 20% to 30% of patients with gastric cancer present with stage IV disease[13,14].

Malignant GOO is a common condition among locally advanced gastric cancer patients and can lead to significant morbidity, including nausea, vomiting, abdominal pain, dehydration, malnutrition, and weight loss. Not surprisingly, these clinical symptoms have a negative impact on QOL[15]. To avoid the disastrous consequences of malignant GOO, appropriate treatment is indispensable, which enables not only an amelioration of the patient's QOL but also the commencement of chemotherapy, including essential oral agents, such as S1 or capecitabine[16]. These treatments are included in the first-line regimen for unresectable gastric cancer recommended in the Japanese gastric cancer treatment guidelines[17].

GJ is traditionally the palliative treatment of choice for patients with malignant unresectable GOO, whereas the palliative endoscopic treatment of GOO with endoluminal self-expanding metallic stents has only recently become available. Both treatments have benefits and limitations associated with prognosis; thus, it is important to determine the optimal treatment approach. Although GOO may occur with other malignancies, such as pancreatic periampullary carcinoma, lymphoma, and metastases to the duodenum of jejunum[1-3], GOO in gastric cancer should be considered separately. First,

gastric cancer has a longer life expectancy than other biological malignancies, and more chemotherapy agents have been developed for this malignancy compared with other diseases[18-20]. Second, GOO that results from gastric cancer has a reduced possibility of co-occurring with an obstruction of the bile duct compared with biliopancreatic malignancies. Several studies have reported a median overall survival of 13 mo for unresectable or recurrent gastric carcinoma[21], which is longer than pancreatic cancer (6.7-8.5 mo)[22].

Therefore, the decision regarding whether to select GJ or ES should depend on the condition and PS of patients. Furthermore, prior to any procedure, information regarding the benefits and drawbacks of GJ and ES is necessary for well-informed consent.

TREATMENTS FOR GASTRIC OUTLET OBSTRUCTION

GJ

Traditionally, GOO caused by malignancy is treated with a palliative "open" GJ (OGJ), which is surgically performed[23]. Although this modality has a favorable outcome and relieves many symptoms derived from GOO, it results in some morbidity and mortality given the poor condition of these patients[1,24]. Several recent studies have reported the effectiveness of "laparoscopic" GJ (LGJ) with regard to safety, feasibility, and invasiveness; however, its role has not been clarified[25,26]. Jeurnink *et al*[5] reported that LGJ appears to be more favorable regarding tolerable oral administration, the duration of the hospital stay, and the complication ratio compared with OGJ. However, no significant differences were identified between the two approaches[27]. Navarra *et al*[28] also published a randomized controlled trial (RCT) that compared LGJ and OGJ (n = 12 patients each). LGJ resulted in significantly less intra-operative blood loss, a shorter time to tolerating solid food intake, and a reduced rate of complications; however, no significant difference was identified in the postoperative hospital stay[28]. In contrast, older retrospective studies have reported benefits with regard to intra-operative blood loss and hospital stay as well as a high conversion rate to OGJ[29,30]. Different outcomes of LGJ have been reported, and this variation can be explained by the small sample sizes and low power. However, no clinical trials with sufficient power have demonstrated the effectiveness of LGJ compared with OGJ, and LGJ is now the preferred standard for malignant GOO treatment[31].

ES

Endoscopic treatment of GOO with endoluminal self-expanding metallic stents was first described by Topazian *et al*[6] in the early 1990s. Over the previous decade, experiences and reports of the use of ES have increased. In addition, various types of upper gastrointestinal stents have become available, and well-established ES procedures have been advocated and performed[32]. Recently, several articles have reported that patients who present with GOO with a long life expectancy should undergo ES given its safety, minimal invasiveness, and cost-effectiveness[33]. Self-expandable metallic stents (SEMSs) are the standard devices for recanalization of an obstructed digestive lumen. However, some SEMSs exhibit re-occlusion because of tumor in growth through openings between the stent wire filaments or stent migration as late major complications[34]. Covered SEMSs prevent ingrowth through the mesh wall, and they are advantageous compared with uncovered SEMSs in esophageal cancer[35]. However, in malignant colorectal obstruction, covered stents do not exhibit an advantage compared with uncovered stents due to high migration rates[36]. Several studies have also suggested that covered stents are associated with more frequent re-intervention despite approximately similar outcomes and complications in malignant GOO. Therefore, with regard to ES for GOO, the effectiveness and complications of covered and uncovered SEMSs in patients with GOO have recently been highlighted. Kim *et al*[37] reported a prospective RCT of covered *vs* uncovered stents for the palliation of GOO in gastric cancer patients and concluded that the overall stent patency did not differ between the two groups; moreover, frequent migration of the covered SEMSs offsets its advantages in the prevention of re-stenosis. Maetani *et al*[38] also reported similar results in a multicenter randomized trial in Japan, *i.e.*, no significant difference in the stent patency between triple-layered covered and uncovered metallic stents for the palliation of malignant GOO; however, the use of a triple-layered covered SEMS was associated with less frequent stent dysfunction more than 4 wk after the initial stent. Regardless of the stent configuration, covered or uncovered, the ES procedure for GOO caused by malignancy is considered safe and efficacious.

RECENT SYSTEMATIC REVIEW AND COMPARATIVE RESEARCH OF TREATMENTS FOR GOO THAT RESULTS FROM GASTRIC CANCER

Two systematic reviews

Two systematic reviews and a meta-analysis that compared GJ and ES have been published since 2010. In review 1 in 2010, Ly *et al*[27] performed a comprehensive search of the literature for the period from 1990 to 2008 using Medline, EMBASE, Google Scholar, ISI Proceedings, the Cochrane Library, and online registers of CCTs but not PubMed. This review included only clinical studies that directly compared GJ and ES for the palliative treatment of GOO, which included randomized clinical trials (RCTs) and prospective and retrospective cohort comparison studies. Thirteen studies were analyzed, including 10 retrospective cohort comparison studies[1,26,39-46], 1 prospective study[41], and 2 RCTs[25,47]. In review 2 in

Table 1 Characteristics and main results of two reviews

Review	Year	Study type			Primary tumor			Procedure		Favorable group regarding several variables			
		Retro	Pro	RCT	Stomach	Pancreas	Others	GJ	ES	Toleration of oral intake[1]	Time to oral intake[2] (d)	Hospital stay[3] (d)	Complication
1	2010	10	1	2	94 (18.3%)	240 (46.7%)	180 (35.0%)	255 (LGJ 37)	244	ES	ES (2.0 d)	ES (9.4 d)	GJ is approximately equal to ES
2	2012	0	3	3	55 (28.6%)	86 (44.8%)	51 (26.6%)	92 (LGJ 0)	74	GJ (not-RCT)	ES (2.1-5.0 d)	ES (2.5-7.0 d)	Major: GJ is approximately equal to ES Minor: ES

[1]Patients were more likely to tolerate oral intake following ES than GJ in Review 1; however, Review 2 reported the opposite results. The difference was only significant in the non-RCT group; [2]The mean time from the procedure to initiate oral intake was 7 d (Review 1) and 3.6 d (Review 2) less for ES compared with GJ; [3]The mean length of hospital stay was reduced by 12 d (Review 1) and 7.5 d (Review 2) for ES compared with GJ. Retro: Retrospective; Pro: Prospective; RCT: Randomized controlled trial; GJ: Gastrojejunostomy; ES: Endoscopic stenting; LGJ: Laparoscopic GJ.

2012, Zheng *et al*[48] searched the PubMed, Embase, Chinese Biomedical Database, and Cochrane Library for all studies between 1996 and 2010. The inclusion criteria were as follows: controlled clinical trials (CCTs) and RCTs; analyses of "both" GJ (OGJ and LGJ) and ES; any sample size; full paper; and not a duplicate report. Six studies remained in the final analysis, including three RCTs[25,47,49] and three CCTs[41,50,51]. Both reviews included the same two studies. One study was a RCT reported by Mehta *et al*[25] in 2006, and the other study was a CCT reported by Johnsson *et al*[41] in 2004.

Table 1 provides the characteristics of the comparative data and main results for GJ and ES in the two reviews with regard to the study type, primary tumor site, number of procedures, and favorable procedure group with better results regarding: (1) the number of patients who tolerated oral intake; (2) time to oral intake (days); (3) length of hospital stay (days); and (4) complications. Ninety-four (18.2%) of 514 patients and 55 (28.6%) of 192 patients with GOO that resulted from "gastric cancer" were included. Technical success was only documented in Review 2, and GJ exhibited greater technical success than ES [odds ratio (OR) = 0.10, 95%CI: 0.02-0.47, I^2 = 0%, P = 0.0039] according to a meta-analysis. However, the significant difference remained only in the non-RCT group. Nevertheless, both GJ and ES demonstrated satisfactory results regarding technical success (success rates of 99% to 100% and 8% to 100%, respectively). The ability to tolerate oral intake after palliative treatments for GOO is one of the most important endpoints and was documented as a "clinical success" in Review 2. With regard to the ability to tolerate oral intake, 11 studies included in Review 1 reported more favorable results following ES compared with GJ. Although no significant difference was identified in the two studies included in Review 2, one study reported that ES was associated with greater clinical success than GJ (P = 0.007). Regarding the time to oral intake after the palliative procedure, all reported data in both reviews indicated that ES had clear merits compared with GJ. The average time from the procedure to the initiation of oral intake was approximately 3 d less for ES compared with GJ. Several studies have evaluated the length of hospital stay and medical costs. All studies reported a significantly reduced hospital stay for patients who underwent ES compared with GJ (mean difference of 12 d). One RCT and one CCT demonstrated reduced total medical costs and hospital stay costs with ES compared with GJ. In summary, approximately all studies indicated that ES has advantages compared with GJ. However, cost should not be the main factor in decisions regarding procedures for malignant GOO patients because the costs per day for patients who consumed at least a soft diet were quite similar between both procedures. Better long-term clinical outcomes after GJ compared with ES were noted in the major prospective randomized SUSTENT study, which was included in Review 2[52].

Both reviews indicated that there are no significant differences in the major complication rates between GJ and ES (OR = 1.04, 95%CI: 0.47-2.29, P = 0.93 according to meta-analysis data in Review 1; OR = 3.76, 95%CI: 0.57-24.72, P = 0.17 in Review 2). The detailed major medical complications that result from GJ were reported as respiratory tract infections, myocardial infarction, and acute renal failure, whereas the complications of ES were procedure-related, including stent failure migration and obstruction. Although minor complications were described only in Review 2, they were less likely the result of ES compared with GJ (OR = 0.28, 95%CI: 0.10-0.83, P = 0.02). Regarding morality, both reviews indicated similar conclusions indicating no differences between the two treatments (OR = 0.58, 95%CI: 0.18-1.86, P = 0.36).

The length of survival was estimated in both reviews. Despite the inclusion of both randomized and non-RCT, no significant difference was identified between GJ and ES (mean difference 26 d; 95%CI: 69.03-16.40 d, P = 0.23 in Review 1).

Table 2 Patient demographics and main results in two reviews

Ref.	Study type	Procedure		Performance status		Comparison between GJ and ES regarding several variables				
		GJ	ES	GJ	ES	Toleration of oral intake	GOO recurrence	Time to oral intake	Hospital stay	Complication
Fiori *et al*[53]	Prospective	9 (LGJ 0)	9	NR	NR	GJ is approximately equal to ES	GJ (0%) < ES (33%)[a]	GJ (6.3 d) ES (3.1 d)	GJ (10 d) ES (4.8 d)	GJ: SSI, bleeding, ventral hernia ES: Stent dislocation, re-obstruction
No *et al*[54]	Retrospective	41 (LGJ 9)	72	0-1[1]: 68.3% 2[1]: 31.7%	0-1[1]: 59.7% 2[1]: 40.3%	GJ (95.1%) is approximately equal to ES (87.5%)	GJ (12.2%) < ES (44.4%)[a]	GJ (16 d) > ES (10 d)[a]	GJ (18 d) > ES (16 d)[3]	GJ is approximately equal to ES
Keränen *et al*[55]	Retrospective	21 (LGJ 0)	50	I-II[2]: 90.5% III-IV[2]: 9.5%	I-II[2]: 58% III-IV[2]: 42%	GJ (81%) is approximately equal to ES (88%)	GJ (9.5%) ES (24%)	GJ (4 d) > ES (1 d)[a]	GJ (8 d) > ES (3 d)[a]	GJ (10%) ES (26%)

[1]ECOG performance status; [2]WHO score; [3]Not significant; [a]$P < 0.05$. GJ: Gastrojejunostomy; ES: Endoscopic stenting; LGJ: Laparoscopic GJ; NR: Not reported; ECOG: Eastern Cooperative Oncology Group; WHO: World Health Organization.

DISCUSSION

Comparative studies between GJ and ES for malignant GOO that results from gastric cancer

One non-randomized prospective study[53] and two retrospective studies[54,55] are available regarding malignant GOO caused by limited unresectable or metastatic gastric cancer. Table 2 provides patient demographics and the main results of three studies with regard to study type, number of procedures, PS, and the favorable procedure group with better results regarding: (1) the number of patients who tolerated oral intake; (2) time to oral intake (d); (3) length of hospital stay (d); and (4) complications.

In a prospective study of 18 patients (9 OGJ and 9 ES treatment)[53], ES had more favorable results regarding the mean time to resume oral feeding (3.1 d) and mean length of hospital stay (4.8 d) compared with GJ (6.3 d and 10 d, respectively). Regarding the late results, such as the recurrence of GOO, late complications due to the procedure, overall survival, and patient satisfaction, no significant differences were identified between OGJ and ES. Recurrent symptoms of GOO were evident only in ES (n = 3 patients, 33%) due to stent migration and obstruction of the stent by food. Both procedures resulted in sufficient patient satisfaction.

In their retrospective study, No *et al*[54] concluded that GJ is preferable to ES for the palliation of GOO that results from gastric cancer in patients with a good PS, especially Eastern Cooperative Oncology Group (ECOG) 0 to 1. In this study, 72 ES and 41 GJ (32 OGJ and 9 LGJ) patients were compared regarding patient demographics, early outcomes and adverse events, late adverse events, patency duration, and survival. The two groups did not differ in most characteristics with the exception of sex (more men in the GJ group). The technical success rates in both groups were excellent (ES: 95.8% *vs* GJ: 97.6%); however, three technical failures were noted in the ES group. However, the time to oral intake was significantly less in the ES group compared with the GJ group (liquid diet: ES 2 d *vs* GJ 5 d, solid diet: ES 10 d *vs* GJ 16 d). Regarding adverse events, a higher rate of late adverse events was identified in the ES group compared with the GJ group (44.4% *vs* 12.2%, $P < 0.01$), whereas early adverse events were not significantly different between the two groups. The adverse events in the ES group were not significantly different according to the stent type (P = 0.158). Similarly, the number of re-interventions was significantly greater in the ES group compared with the GJ group (31 (43%) *vs* 4 (5.5%), respectively, $P < 0.001$). Regarding the patency duration, the median duration of both the first stent patency and total stent patency, including the patency achieved by an additional stent, was 210 d shorter in the ES group compared with the GJ group (P = 0.001, P = 0.044, respectively). The interesting finding in this previous study was the analysis according to PS (ECOG status). Patients in the GJ group exhibited significantly longer overall survival compared with the ES group, but only for ECOG 0 to 1.

Keränen *et al*[55] compared three palliative methods, including 50 ES, 26 palliative resections of the stomach (PR), and 21 GJ. All palliative surgeries were performed with laparotomy. Patients with ES presented with the poorest general condition among all groups in terms of the pre-procedure albumin level, PS, and amount of oral intake; thus, the ES group exhibited the worst survival. The main results regarding the palliation of GOO symptoms demonstrated that ES resulted in a faster improvement of oral intake, relief of GOO symptoms, and reduced hospital stay compared with GJ. The authors advocated considering how the clinical condition before treatment affects survival in malignant GOO that results from gastric cancer when determining the type of palliative procedures. Furthermore, the authors indicated that the study had several limitations. The study was non-randomized, retrospective, and

had a certain degree of defective follow-up data, which led to selection bias between the treatment groups. However, this retrospective study reported the time between ES treatment and re-obstruction; however, this information was described only in context, not in tables or figures. The median time to re-obstruction after ES was 95 d; thus, most patients had died before re-obstruction occurred. Therefore, re-obstruction of the stent is not a major problem for patients with a poor prognosis (< 3 mo), even in patients with gastric cancer and particularly in patients with pancreatic cancer or other malignancies with a worse prognosis.

In summary, the main findings of comparative studies between GJ and ES that focused on gastric cancer patients were similar to the findings of other RCTs, CCTs, and retrospective studies of patients with GOO that resulted from malignancies other than gastric carcinoma. In addition, no articles have referred to precise cost performance or compared LGJ and ES. Compared with GJ, ES is preferred for the rapid improvement of oral intake, relief of GOO symptoms, and reduced hospital stay, whereas the occurrence of late complications, such as stent obstruction or migration, is higher. The differences compared with other malignant GOOs are patient survival after GJ or ES and patient PS. The median survival durations in these three articles were 283, 189 to 293, and 50 to 241 d. Thus, the potential survival of GOO patients with gastric cancer may be increased by approximately 2 or 3 mo. Because several studies have reported that GJ is preferable for patients with a longer life expectancy[49], GJ should be selected more frequently in clinical practice for good PS patients with GOO that results from gastric cancer.

CONCLUSION

Both GJ and ES are effective treatments in patients with GOO that results from gastric cancer. GJ exhibits better long-term outcomes with regard to fewer late complications and long patency, whereas ES exhibits better short-term outcomes, including the length of the hospital stay. Although no large-scale studies or RCTs have compared the safety and efficacy of the two procedures, literature reviews suggest that GJ may be the preferable procedure because of the good PS and long prognosis of gastric cancer patients.

However, the bypass procedure is currently performed laparoscopically (LGJ), and various novel devices in the ES field can minimize stent obstruction or migration. Therefore, to determine the more preferable procedure in patients with GOO that results from gastric cancer, a prospective RCT of LGJ and ES with current devices specialized for gastric cancer patients is warranted.

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