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Treatment of choice for malignant gastric outlet obstruction: More than clearing the road

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Abstract

In this editorial, we comment on the in-press article in the *World Journal of Gastrointestinal Endoscopy* concerning the treatment of malignant gastric outlet obstruction (mGOO). The original theory of treatment involves bypassing the obstruction or reenabling the patency of the passage. Conventional surgical gastroenterostomy provides long-term relief of symptoms in selected patients, with substantial morbidity and a considerable rate of delayed gastric emptying. Endoscopic stenting was introduced as an alternative minimally invasive procedure with less procedural morbidity and rapid clinical improvement; however, it presented a high rate of long-term recurrence. Therefore, challenges remain in the treatment of mGOO patients to improve clinical outcomes. Endoscopic ultrasound-guided gastroenterostomy has recently emerged as a promising method because of the combined effects of surgery and endoscopy, whereas stomach-partitioning gastrojejunostomy has been reported as a modified surgical procedure to reduce the rate of delayed gastric emptying. In decision-making regarding the treatment of choice, it should be taken into account that mGOO might be accompanied by a variety of pathological conditions, including cancer cachexia, anorexia, malabsorption, and *etc.*, all of which can also lead to the characteristic symptoms and poor nutritional status of mGOO. The treatment plan should consider comprehensive aspects of patients to achieve practical improvements in prognosis and the quality of life.

Key Words: Malignant gastric outlet obstruction; Surgical gastroenterostomy; Endoscopic stenting; Endoscopic ultrasound-guided gastroenterostomy; Stomach-partitioning gastrojejunostomy; Anorexia-cachexia syndrome

Core Tip: The original idea for malignant gastric outlet obstruction (mGOO) treatment involves bypassing the obstruction *via* surgical gastroenterostomy or reopening the passage *via* endoscopic stenting. Substantial morbidity and only partial relief from conventional procedures have prompted modified procedures, such as endoscopic ultrasound-guided gastroenterostomy and stomach-partitioning gastrojejunostomy, for which there is limited evidence for synthesis. Notably, mGOO is usually accompanied by a variety of pathological conditions that can result in presentations similar to or the same as those of mGOO. A multidisciplinary approach should be adopted for decision-making in treatment plans.

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INTRODUCTION

Gastric outlet obstruction (GOO) is a mechanical obstruction caused by pyloric and/or duodenal stenosis. Peptic ulcer disease was historically the primary cause of GOO; however, malignancies currently account for 50% to 80% of cases because of increased use of acid suppression therapy. Malignant GOO (mGOO) results primarily from gastrointestinal and periampullary cancers[1]. Among them, pancreatic cancer is the most common cause of mGOO in Western countries, whereas gastric cancer is the leading cause of mGOO in Asia[2]. The incidence of mGOO reportedly ranges from 15% to 20% in patients with pancreatic cancer[3].

As a late complication of advanced malignancies, mGOO is believed to aggravate symptoms such as nausea, vomiting, abdominal pain, and weight loss and exacerbate poor nutritional status. Thus, mGOO significantly affects patient survival because therapeutic treatment is compromised[4].

The treatment of patients with mGOO has long been discussed in terms of the adoption of distinct procedures, with significant progress made in techniques in recent years. In the current issue of the *World Journal of Gastrointestinal Endoscopy*, Vilas-Boas *et al*[5] suggested in their mini-review that studies should focus on improving quality-adjusted survival instead of technical success while evaluating mGOO treatment modalities. In this editorial, we provide a review on the development of various mGOO treatment methods and noteworthy points in the evaluation of mGOO treatment modalities.

PRIMARY THEORY

As patients with mGOO mostly present with nausea, vomiting, dehydration, and malnutrition, the primary theory is to address the obstruction by creating a new gastrointestinal pathway or reenabling the passage of food and liquid. Therefore, traditional treatment for GOO has long been surgical gastroenterostomy (SGE)[6-8] or endoscopic enteral stenting[9-11].

SGE was first proposed decades ago as the classical treatment for mGOO when the anastomosis is positioned on the anterior or posterior side of the stomach. With the exact position away from the tumor location, an antecolic or a retrocolic side-to-side gastrojejunostomy is performed[12]. The procedure was reported to yield long-lasting relief of GOO symptoms in up to 72% of patients by reestablishing the continuity of food passage; however, SGE is associated with substantial postoperative morbidity that leads to prolonged hospitalization and delayed chemotherapy[13]. Patients with mGOO are usually elderly and have advanced malignancies, as well as other medical illnesses, and surgery morbidity rates are higher than 70% in the early period[14]. In recent years, with extensively developed techniques and surgical skills, the associated morbidity (13%-55%) and mortality (2%-36%) rates have still been considerable[13,15,16].

As most patients with mGOO have a limited survival period, surgical complications that preclude normal activities outside the hospital account for a significant fraction of their remaining lifetime. Treatment that shortens the hospital stay and has lower morbidity and mortality rates is preferable.

In 1992, Topazian *et al*[17] reported the first use of a self-expandable metallic stent for treating mGOO. During the procedure, a covered or uncovered self-expanding metal stent is sent across the stricture over the wire or through the endoscope. With the worldwide application and development of this procedure in the following years, endoscopic stenting (ES) has been proven to be a less invasive effective modality for treating malignant GOO, with reduced morbidity and shorter hospital stays than those of SGE, especially for patients who may not be surgical candidates[18]. The ESMO and Korean clinical practice guidelines for pancreatic cancer both favor ES over gastrojejunostomy to treat mGOO, as ES has a lower complication rate and results in shorter hospitalization than does gastrojejunostomy[19,20].

However, tissue ingrowth and/or overgrowth over time may result in stent occlusion and recurrent mGOO, which explains the higher rates of long-term luminal obstruction. Recently, Reijm *et al*[21] reported the clinical outcomes of duodenal stent placement for the palliation of mGOO symptoms in a series of patients over a period of 20 years, with the

data showing that more than half of the patients (59%) experienced recurrent mGOO after a median time of 28 days. Other complications of endoscopic treatment are stent migration, hemorrhage and perforation, all of which require multiple endoscopic or surgical reinterventions[13,16,22,23]. Tamura *et al*[24] reported a propensity score-matched analysis in 2023 with a mean follow-up period of 129.2 days. Although the short-term outcomes were significantly more favorable in the matched ES group than in the SGE-matched group, long-term adverse events were rated as high as 25.5% in the matched ES group, and Kaplan–Meier analysis revealed that overall survival after the procedure was significantly longer in the matched SGE group than in the matched ES group. Therefore, although ES has been proposed as an alternative to SGE owing to rapid clinical improvement, its major drawback is a high rate of stent malfunction, which requires frequent reinterventions, especially in patients with prolonged survival of more than 6–12 months[11,18,25–28]. As mGOO generally portends a poor prognosis[29], avoiding repeated interventions and/or hospitalizations might be highly important for patients with advanced malignancy and a limited lifetime expectancy.

In light of these concerns, life expectancy was proposed as a criterion for decision-making. The NCCN guidelines for treating pancreatic cancer and gastric cancer advocate for gastrojejunostomy over ES for patients who are fit for surgery and have an overall survival expectancy of more than 3–6 months[30,31]. The American Gastroenterological Association (AGA) recommends that surgical gastrojejunostomy should be considered for patients with GOO that have a life expectancy greater than 2 months, who are surgically fit and have good functional status. Enteral stenting can be reserved for patients with a limited life expectancy[32].

MODIFIED PROCEDURES

When palliative surgical gastrojejunostomy has been accepted as the standard treatment for patients with a prolonged survival expectancy, postoperative adverse events occurred in up to 82.9% of SGE patients, even according to the latest report by Martinet *et al*[33]. To achieve tangible improvement in quality of life during the limited survival period, it is necessary to make technical progress in the treatment of mGOO.

Endoscopic ultrasound-guided gastroenterostomy (EUS-GE) for mGOO was first reported by Khashab *et al*[34] in 2015. They developed a novel EUS-guided technique for creating an anastomosis between the stomach and an adjacent jejunal loop *via* the placement of a lumen-apposing metal stent to achieve adequate positioning and deployment of the stent, as determined by endoscopy and radiology. The procedure is believed to combine the minimal invasiveness of an endoscopic procedure and the long-lasting effect of SGE[35–40]. It could also be used to treat patients in whom ES failed in the first place[36]. According to two recent meta-analyses, EUS-GE has a technical success rate higher than 90% and a clinical success rate of up to 90%[41,42]. A multicenter comparative study reported this year revealed that EUS-GE provided a long-term clinical success rate (91.1%) and a technical success rate (87.5%) comparable to those of SGE for GOO[33]. A few months later, Cobb *et al*[43] reported a systematic review of the long-term effectiveness of endoscopic gastrojejunostomy upon mGOO and found that EUS-GE had an overall complication rate of 10.5% and a rate of symptom recurrence of 5.9% at up to 5 months of follow-up. The results indicated that EUS-GE may provide additional benefits, as the procedure could be applied in patients who are not SGE candidates.

Nevertheless, a learning curve of 12 to 25 procedures has been reported for EUS-GE because the procedure requires advanced endoscopic skills and techniques[44,45]. Thus, the AGA recommends, with caution, that EUS-GE should be considered on the basis of local experience[32]. Given that EUS-GE has been applied in clinical practice for less than a decade and that the procedure requires advanced endoscopic experience, comparative studies of EUS-GE and other treatments for GOO are limited, with some conflicting results[42,46–49]. To date, there are no consistent guidelines recommending this technique over other methods for the treatment of malignant GOO[50].

As progress in the technique might lead to impressions of clinical procedures, some inherent issues should not be overlooked. Long-term clinical experience and many previous studies have indicated that conventional side-to-side gastrojejunostomy may provide only partial palliation in numerous patients, as the retention of food may still remain after surgery because of impaired gastric emptying[51,52] or because the gastric contents always preferentially flow to the pylorus rather than the anastomosis[53]. In fact, the rate of delayed gastric emptying (DGE) after conventional gastrojejunostomy can reach 50%, as reported in the literature[54,55]. As this results in poor quality of life, the efficacy of conventional gastrojejunostomy for palliation has been questioned.

The technique of stomach partitioning was originally described by Devine[56] in 1925 for the treatment of duodenal ulcers and was later applied in the treatment of unresectable distal gastric cancer by Maingot[57]. The original method completely separates the distal stomach from the proximal body, and an anastomosis is made between the proximal stomach and the adjacent jejunum; therefore, food emptying directly through the anastomosis passage is ensured. The disadvantage of this procedure is that the distal gastric remnant is left to a practically confined compartment and exposed to the risk of potential bleeding from the tumor; thus, decompression of the gastric antrum may be necessary in some cases. In light of this concern, Kaminishi *et al*[58] reported partial stomach-partitioning gastrojejunostomy (PGJ) in 1997, also called the modified Devine[56] exclusion method, which separates the lower part of the stomach and performs anastomosis between the jejunum and the proximal part of the stomach while maintaining a tunnel that is 2–3 cm in diameter along the lesser curvature. The PGJ procedure divides the stomach, which is conducive to food emptying and effectively reduces food stimulation of the tumor to lower the risk for gastric remnant rupture. The additional advantage is the retention of the possibility of postoperative endoscopic cancer surveillance and intervention or access to bile ducts [58,59]. In recent years, promising outcomes of PGJ, compared with those of conventional gastrojejunostomy, have been reported in terms of lower rates of DGE and enhanced postoperative recovery[53,59–61].

A network meta-analysis reported this year suggested that PGJ and EUS-GE were more advantageous than conventional gastrojejunostomy and ES in terms of combined safety and efficacy[62]. Nonetheless, the unpopularity of PGJ has resulted in limited supporting evidence; therefore, this procedure has rarely been performed to date because of the lack of evidence from prospective studies and RCTs[60]. Most recently, a propensity score-matched cohort study reported by Hai *et al*[63] compared the long-term outcomes between stomach-partitioning and conventional gastrojejunostomy. They failed to demonstrate differences in the incidence of mGOO recurrence and survival outcomes between the two groups, whereas earlier retrospective studies reported that the SPGJ approach improved survival in patients with mGOO by increasing the tolerance of chemotherapy[64]. Further controlled studies with longer follow-up periods are needed to address this debate.

BENEFIT AS EXPECTED OR NOT

Malnutrition is a common and principal problem among advanced cancer patients and negatively impacts their quality of life and clinical outcomes. mGOO increases the difficulty of oral intake, which can lead to severe malnutrition. Therefore, mGOO treatment was believed to be crucial for cancer patients by removing the obstruction so that patients can tolerate oral nutrition to improve their nutritional status and quality of life or receive radiochemotherapy[65,66]. However, nausea and vomiting have long been reported in 30%–45% of patients with pancreatic cancer, whereas actual gastric outflow obstruction occurs in only 5% of patients at the time of diagnosis[8]. There is growing recognition that the etiology of impaired nutritional status is multifactorial and includes anorexia, elevated resting energy expenditure, gastric/biliary obstruction, malabsorption, treatment side effects, tumor cytokines, *etc*[67]. It takes much more than addressing GOO to improve the nutritional status of advanced cancer patients.

mGOO usually occurs in patients with advanced malignancies, who may experience anorexia-cachexia syndrome, which is accompanied by a variety of symptoms, including intestinal malabsorption, nausea, anorexia and depression[68–70]. The typical mGOO symptoms are similar to those of anorexia-cachexia syndrome, including early satiety, nausea, postprandial vomiting, weight loss, and poor nutritional status[71]. In light of this concern, questions regarding the treatment of GOO were raised as early as the previous century, and further prospective studies may be needed to determine whether any true palliation of symptoms can be achieved in patients treated for obstruction[14]. Cachexia is accompanied by a set of functional and behavioral disorders, such as anorexia and depression[70]. Anorexia, a key component of cancer cachexia syndrome, is characterized by a diminished desire to eat[70,72]. While depression in cancer patients can exacerbate appetite and reduce food intake[73], it is associated with increased morbidity, including anorexia and anxiety, which further aggravates reduced food intake and impairs patients' quality of life[74,75]. These aspects of anorexia-cachexia syndrome continue to exist after the treatment of GOO, which might hinder the evaluation of the effectiveness of the treatment procedure. Moreover, how many patients benefit from GOO treatment in terms of the characteristic presentations of GOO; *i.e.*, nausea and vomiting, which are both common symptoms in advanced cancer patients and severely affect their quality of life, remains to be determined. Nausea and vomiting can be multifactorial in origin that include elevated intracranial pressure, infections, opioid use, ascites, hepatomegaly, dyspepsia or gastritis, and malignant bowel obstruction[76]. Therefore, addressing all these intricately linked conditions in treatment plan selection is critical for patients with GOO to improve their clinical outcomes, manage their disease more effectively, and enhance their quality of life.

CONCLUSION

The outcome of mGOO treatment in advanced cancer patients can be influenced by a variety of factors. Classical treatment procedures include surgical gastrojejunostomy and ES, which have either considerable perioperative morbidity or high long-term recurrence rates. As patients with GOO have a median survival of only 2–10 months, doctors face intense challenges when selecting treatment modalities. Compared with conventional procedures, the recent introduction of EUS-GE and PGJ has resulted in promising outcomes, with limited evidence for synthesis. Moreover, mGOO may be merely one of the multiple factors underlying typical presentations, such as nausea and vomiting, as well as malnutrition. As most guidelines suggest, a multidisciplinary approach should be adopted to help patients decide on the choice of treatment, with implications for health care resource optimization. To date, most of the data have been derived from retrospective and heterogeneous studies that were prone to selection and detection bias. Future prospective studies and randomized controlled trials could provide stronger evidence for clinical decision-making.

FOOTNOTES

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