



# Current State of Endoscopic Management for Malignant Gastric Outlet Obstruction

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## Editorial

The most common etiology of distal gastric and duodenal obstruction (here collectively referred to as gastric outlet obstruction, or GOO) has changed from benign peptic ulcer disease to malignancies over the past few decades [1]. Tumors of pancreas, stomach, duodenum, and biliary system, as well as metastatic malignancies can cause malignant GOO, with pancreatic adenocarcinoma (in the United States) and distal gastric cancer (in Asia) remaining relatively common causes [1,2]. Malignant GOO is a severely debilitating complication of malignancy that leads to significant suffering by causing nausea, vomiting, and abdominal pain, and prevents adequate oral intake [3]. Standard palliative options in patients with unresectable disease include endoscopic placement of Self-Expanding Metal Stents (SEMS), and surgical bypass procedures such as gastrojejunostomy. Surgical gastrojejunostomy for palliation of GOO carries a high risk of morbidity and mortality in this patient population, with risk of mortality reported to be as high as 10% [4]. Furthermore, previous studies have shown that palliative SEMS placement is more cost-effective and leads to faster resolution of symptoms and shorter hospital stay compared to surgical bypass [5,6]. However, surgical gastrojejunostomy can potentially lead to better long-term relief of obstructive symptoms or at least fewer re interventions especially in patients with longer predicted survival [7]. Endoscopic treatment of malignant GOO through placement of SEMS is associated with a very high technical success rate during the index procedure as well as high rate of short-term clinical success. In a prospective multicenter trial observational study a total of 108 adult patients with malignant GOO underwent placement of uncovered duodenal SEMS [8]. The authors reported a technical success rate of 99%, with only one patient having an unsuccessful deployment of the duodenal stent (it was deployed too distally) leading to successful deployment of a second stent during the same procedure. Similarly, stent patency was reported to be 95% at 14 days. Longer follow up in this study showed stent patency rates of 82% and 63% at three and six months, respectively. In a different multicenter small randomized clinical trial from Netherlands a total of 39 patients with malignant GOO were randomized to either laparoscopic gastrojejunostomy (n=18) or duodenal stenting with SEMS (n=21) [7]. Although oral intake improved more quickly after stenting as compared to surgical bypass, the authors reported a trend towards decreased oral intake starting at one month among patients in the stent group leading to a statistically significant worse food intake in this group at two months compared to gastrojejunostomy group. However, this study showed no difference between groups in terms of quality of life, patient satisfaction, or nausea symptoms. Seven patients in the stent group (33%) needed re interventions compared to 2 patients in the gastrojejunostomy group (11%,  $p < 0.01$ ) over more than six months of follow up. An earlier systematic review of the literature included data from 1046 duodenal stents and 297 gastrojejunostomy procedures [9]. Similar to the results mentioned above this study found comparable rates of technical success between the two methods and higher rates of short term clinical success and shorter length of stay with stenting, but stenting as associated higher rate of recurrent obstructive symptoms necessitating re intervention (18% over mean survival of 3.5 months). In summary, the evidence accumulated over more than 20 years has established duodenal SEMSs as part of standard of management for malignant GOO, leading to prompt palliation of obstructive symptoms in almost all patients, while its long-term clinical success remains somewhat limited by need for re intervention due to recurrent obstructive symptoms in 20% to more than 40% of the patients as reported in different studies. Recurrent obstructive symptoms can happen due to stent migration, more distal bowel obstruction due to additional metastasis or malignant peritoneal involvement, or food impaction in the stent, but in the majority of patients it happens due to progression of disease and tumor in-growth causing obstruction of the stent [8]. Careful consideration of the type of SEMS, as well as appropriate patient selection and following dietary recommendations after stenting can help to significantly decrease the rate of recurrent obstructive symptoms due to stent migration,

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multilevel malignant bowel obstruction and food impaction. Currently uncovered SEMS rather than fully or partially covered stents are the standard of treatment for managing malignant GOO as they have been shown to have lower rate of migration, and allow for better outflow of bile [10-12]. In addition, obtaining cross-sectional abdominal imaging to rule out multilevel malignant bowel obstruction or extensive peritoneal involvement and assess impending biliary obstruction has become a standard part of pre-procedural evaluation. However, none of these measures decreases the rate of stent obstruction due to tumor in-growth, especially considering the increasing survival times of patients with malignant GOO due to locally advanced or metastatic malignancies in the modern era of combination chemotherapy. Recent developments in EUS-guided endoscopic procedures has introduced EUS-guided endoscopic gastroenterostomy (EUS-GE) as a novel palliative procedure in this population, combining less morbidity, lower cost, prompt resolution of symptoms, and shorter hospital stay associated with less-invasive endoscopic procedures with the potential to significantly decrease the need for re intervention due to tumor in-growth over longer periods of time. Availability of Lumen Apposing Metal Stents (LAMS) has been a major development by facilitating safe creation of endoscopic enteral bypass between stomach and loops of small bowel, usually jejunum, under US and fluoroscopic guidance leading to very high rates of technical success. In the first case series reported in United States in 2015 a total of ten patients with GOO (three with malignant GOO) underwent attempted EUS-GE with LAMS with technical success in nine patients (90%) and no procedure related adverse events. The authors reported 100% clinical success defined as solid oral intake and there was no recurrence of symptoms during an average follow up of five months [13]. A subsequent multicenter case series reported attempted EUS-GE in 26 patients with a similarly high technical success rate of 92%, and clinical success rate of 85% for initiation of oral diet [14]. A retrospective study of 30 consecutive patients who underwent EUS-GE for malignant GOO compared their outcomes to 52 patients who had enteral stenting for the same reason. Authors did not find a significant difference in technical or clinical success rates or rate and severity of adverse events between the two groups, but patients in the EUS-GE group had a significantly lower rate of symptom recurrence and need for re intervention (4%, one patient, due to food impaction in the stent) compared to enteral stenting (29%, six patients with tumor in-growth and two patients with food impaction) over up to six months of follow up [15]. Three patients in EUS-GE group (10%) had severe adverse events with stents miss deployed in the peritoneal cavity, two of which were retrieved endoscopically during the index procedure without any further complications and one needed surgery. In a separate report, the authors retrospectively compared the same 30 EUS-GE procedures to 63 cases of surgical gastrojejunostomy for malignant GOO and reported similar clinical success rates and recurrence of GOO between the two groups, but a trend for lower rate of adverse events for EUS-GE (16%) compared to surgical bypass (25 [16]. A separate multicenter case series comparing EUS-GE and laparoscopic gastrojejunostomy showed the same results with similar success rates between the groups but lower risk of adverse events in EUS-GE group compared to surgical bypass [17]. Although none of these studies evaluated the efficacy and safety profile of EUS-GE in a randomized trial, they have shown consistently high rates of technical and clinical success for EUS-GE compared to both enteral stenting and surgical bypass, with a significantly lower rate of recurrence and need for re intervention compared to enteral stenting, and a trend for lower rates of adverse

events compared to surgical bypass. Malignant GOO is a common and debilitating complication of various primary and metastatic cancers leading to significant suffering due to obstructive symptoms and pain, severely decreased or inability to tolerate oral intake, and subsequent inability to receive palliative chemotherapy. Until recently, surgical bypass and enteral stenting have been the only palliative options in these patients. Although enteral stenting has been associated with lower cost and morbidity compared to surgical bypass, its use has been limited by a significant rate of recurrence of GOO and need for re intervention due to progression of disease and tumor in-growth, especially as patients survive longer with modern combination chemotherapy regimens. EUS-guided endoscopic gastroenterostomy is a novel endoscopic procedure to create an enteral bypass between stomach and loops of small bowel distal to the site of obstruction using lumen apposing stents. The available evidence suggests that EUS-GE can combine a minimally invasive endoscopic approach with the durability of surgical bypass by eliminating the risk of tumor in-growth in the stent. With increasing familiarity of therapeutic endoscopists with the use of lumen apposing stents and EUS techniques, EUS-GE should be considered part of standard palliative options in patients with malignant GOO.

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