Laparoscopic gastrojejunostomy for gastric outlet obstruction in patients with unresectable hepatopancreatobiliary cancers: A personal series and systematic review of the literature

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Abstract

The major symptoms of advanced hepatopancreatobiliary cancer are biliary obstruction, pain and gastric outlet obstruction (GOO). For obstructive jaundice, surgical treatment should be considered in recurrent stent complications. The role of surgery for pain relief is marginal nowadays. On the last, there is no consensus for treatment of malignant GOO. Endoscopic duodenal stents are associated with shorter length of stay and faster relief to oral intake with more recurrent symptoms. Surgical gastrojejunostomy shows better long-term results and lower re-intervention rates, but there are limited data about laparoscopic approach. We performed a systematic review of the literature, according PRISMA guidelines, to search for articles on laparoscopic gastrojejunostomy for malignant GOO. We also report our personal series, from 2009 to 2017. A review of the literature suggests that there is no standardized surgical technique either standardized outcomes to report. Most of the studies are case series, so level of evidence is low. Decision-making must consider medical condition, nutritional status, quality of life and life expectancy. Evaluation of
the patient and multidisciplinary expertise are required to select appropriate approach. Given the limited studies and the difficulty to perform prospective controlled trials, no study can answer all the complexities of malignant GOO and more outcome data is needed.

Key words: Duodenal obstruction; Gastrojejunostomy; Gastroenteroscopy; Gastric outlet obstruction; Gastric bypass; Laparoscopy; Laparoscopic surgery; Systematic review

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Core tip: Both non-operative endoscopic approach and surgical treatment are available for palliative treatment of gastric outlet obstruction due to advanced hepatopancreatic-biliary cancer. Stent is usually preferred in patients with poor general condition or short life expectancy. Laparoscopic gastrojejunostomy is a feasible, safe and efficient technical option. Given the limited studies, we performed a systematic review of laparoscopic gastrojejunostomy in patients with advanced hepatopancreatic-biliary malignancy. Clinical prospective trials comparing different approaches with adequate sample size are warranted.

INTRODUCTION

Obstructive jaundice, gastric outlet obstruction (GOO) and tumor-associated pain are the major symptoms of advanced hepatobiliary-pancreatic (HPB) cancer. Usually these cancers are not resected because of infiltration of local structures or disseminated disease. Today, these complications can be managed with endoscopic stenting and percutaneous treatment, which have lower rates of associated morbidity; thus, surgical strategies have decreased.

Around 70% of cases of advanced HPB cancer present obstructive jaundice[1,2], which is the most common symptom[3-5]. To resolve jaundice in unresectable or metastatic patients, endoscopic or percutaneous biliary stent is accepted as the gold standard[6]. Surgical treatment of biliary obstruction should be considered in persistent stent-problems, such as recurrent cholangitis or recurrent obstructive jaundice[6]; however laparoscopic surgery for biliary bypass is not a standard procedure[4,7]. Furthermore, the role of surgical pain relief in these patients seems to be marginal nowadays[6].

Finally, there is no consensus about the role of surgery in the management of malignant GOO. This clinical syndrome is characterized by abdominal pain, weight loss, nausea and vomiting, due to the mechanical obstruction, and may be caused by gastric, duodenal, HPB or extraluminal diseases; therefore, the treatment depends on underlying cause[8]. In recent decades, 50%-80% of cases have been attributed to malignancy. GOO may develop in up to 20% of patients with advanced HPB disease[4,9-14]. The aim of GOO treatment is to reestablish oral intake by restoring gastrointestinal continuity.

Decision-making with regard to palliative treatment of malignant GOO due to advanced HPB cancer has become more complex in recent years. Traditionally, open gastrojejunostomy (OGJ) was the only option[11,15]. In the 1990s, endoscopic duodenal stents were introduced. In the last few years, laparoscopic gastrojejunostomy (LGJ) has emerged as a feasible and safe option that offers improved morbidity and mortality rates compared with the open surgical approach[3]. As can be seen, then, several options are available and there is no current gold standard[9].

The literature on GOO focus on gastric disease and mixes different causes with different prognoses. This means that, the level of evidence in patients with HPB malignant diseases is low and data on the laparoscopic approach to GJ for malignant GOO due to advanced HPB cancers are limited.

Our aim in this paper is to review various aspects of the management of malignant GOO due to advanced HPB cancer. Focusing on the laparoscopic approach for gastroenteroanastomosis, we perform a systematic review of the literature and a retrospective review of our personal series of laparoscopic GJ for the treatment of malignant GOO due to advanced HPB cancer.

ROLE OF PROPHYLACTIC GASTROJEJUNOSTOMY

A cancer may be found to be unresectable during preoperative staging examinations. Only some 20% of HPB neoplasms are found to be resectable[16-18]. Despite the indications of preoperative staging radiological and endoscopic images, between 8% and 33% of patients are found to be unresectable on laparotomy[19]. This means that surgeons may be encounter this situation intraoperatively and must decide whether to perform prophylactic GJ. This decision should be based on the probability of GOO; between 10%-15% of patients develop GOO at a later stage[3,11,20].

Gurusamy et al[2] report no differences in overall survival, postoperative morbidity and mortality, quality of life (QOL) or length of stay (LOS). This Cochrane review included two RCTs assessing the role of prophylactic GJ in unresectable periampullary cancer[21,22]. The authors reported a long-term GOO incidence of 27.8% in patients with advanced HPB cancer who did not undergo...
prophylactic GJ and concluded that prophylactic GJ may not be necessary in all patients with advanced HPB malignancy undergoing laparotomy[2].

**PALLIATIVE TREATMENT OF GOO**

Physicians may also find a patient with uncontrolled vomiting and a diagnosis of advanced HPB malignancy. Palliative treatment should be offered to relieve the symptoms of GOO and ultimately to improve patient QOL. Palliative treatment is mandatory when the vomiting is uncontrolled.

**Stent vs palliative surgery**

Traditionally, GJ was the only option for the treatment of malignant GOO[11,15,15]. Since 1992, several studies have described the use, safety and efficacy of self-expandable metallic stents (SEMS)[10,23-33]. Thus, several options are currently available and there is no established gold standard.

The literature on palliative GJ show good functional outcomes and symptoms relief in up to 70% of patients and reduced re-intervention rates, but it is associated with postoperative complications, such as delayed gastric emptying (DGE)[8,12,14,34,35]. For its part, palliative endoscopic treatment is a well-established procedure today and is considered a valid alternative for avoiding surgery. The endoscopic approach is associated with shorter length of stay (LOS), faster initial relief and shorter time to oral intake, but also with greater symptom recurrences and risk of stent migration[8,12-14,36,39].

The current literature mixes together different etiologies, and even includes benign causes such as superior mesenteric artery syndrome, peptic ulcer stenosis, chronic pancreatitis or annular pancreas, different grades of GOO, and prophylactic and palliative treatments[40-44]. Kohan et al[45] report the results of surgical palliative treatment for pancreatic cancer; but they mixed elective bypass for the treatment of symptomatic malignant GOO together with and prophylactic GJ in advanced HPB cancer patients undergoing surgery for biliary obstruction.

Table 1 shows the results of previous systematic reviews and meta-analysis comparing endoscopic duodenal stent vs GJ for the treatment of malignant GOO, including both gastric and advanced HPB cancers and other metastatic cancers. Minata et al[8], Nagaraja et al[13] and Ly et al[38] have demonstrated shorter LOS and faster oral intake with endoscopic palliative treatment, but lower re-intervention rates with OGJ. No differences in survival or major complications were found. Nagaraja et al[13] concluded that the endoscopic approach minimizes pain, hospitalization, and physiologic stress to the patient, which are the main goals of palliation.

Decisions regarding the best therapeutic strategy for individual patients with malignant GOO due to advanced HPB cancer should be based on the performance and medical condition, the extent of the cancer, the prognosis, their quality of life and expectancy, and the availability and likely success of each treatment option[36,46,47].

Depending on the medical condition, one of the main factors to consider is nutritional status; thus, hypoalbuminemia is considered as a risk factor for GJ whether the disease is benign or malignant[48]. Surgeons should correct this situation if surgical palliation is the aim and at least 1-2 wk of nutritional treatment should be considered in order to decrease the risk of postoperative complications[48]. According Sasaki et al[49], poor performance status should be considered as additional risk factor.

With regard to the extent of the cancer, the presence of carcinomatosis with ascites has been reported as an independent predictive factor for poor clinical success of stent placement, without any differences in stent patency[50].

The choice of palliative GJ or endoscopic enteral stent should consider the life expectancy of patients and the likelihood of recurrent GOO after stenting. As regards the prognosis of malignant disease, in the SUSTENT study, Jeurnink et al[12], concluded that palliative GJ is the treatment of choice in patients expected to live two months or longer, whereas stent is preferable for patients with a life expectancy below this figure. This conclusion is based on the finding that surgery was more effective than endoscopic stent after a follow-up of two months[12]. Recurrent obstruction due to tumor ingrowth into stent or stent migration has been reported in 17%-27% of patients with endoscopic stent[51]. Severe complications associated with stenting include bleeding and perforation and have been reported in 1.2% of cases[51]. Comparing stent types, migration rates are higher with covered stents than with uncovered ones; in contrast, uncovered stenting has higher obstruction rates[11,52,53]. In addition, some patients may suffer combined obstructive jaundice and GOO. There are several options for treatment, but biliary endoscopic stenting can pose a challenge if a duodenal stent is in place[54]; patients with stent for biliary obstruction who subsequently have an endoscopic enteral stent are at an increased risk of biliary stent dysfunction[55]. Another option is endoscopic double stenting, a combination of biliary and duodenal stent placement, where different approaches could make it possible[56].

**Laparoscopic GJ for malignant GOO**

Wilson et al[57] published the first report of LGJ in two patients with malignant GOO due to advanced HPB cancer. Today, LGJ is a feasible option, and presents improved morbidity and mortality rates compared with the open surgical approach[58].

In 2007, Siddiqui et al[58] designed a model for patients with malignant GOO and performed a decision analysis. They concluded that endoscopic enteral stent
The outcomes and surgical techniques of LGJ for malignant GOO are displayed in Tables 2 and 3. Most studies were case series, five were cohort studies, two case/control studies and only two studies were randomized controlled trials (RCT). The studies included different etiologies for GOO, among them benign disease and only nine publications recorded patients with advanced HPB malignancy who had undergone laparoscopic palliative GJ, excluding case reports or reports of prophylactic GJ.

The articles were included or rejected based on the information in the title and summary, and in case of doubt, after reading the complete article.

Figure 1 presents a flowchart of systematic review of patients with advanced HPB malignancy who had undergone laparoscopic palliative GJ. The initial search yielded, 160 articles, but only 21 (13.12%) met the search criteria.

Table 1 Systematic review and meta-analysis: Stents vs gastrojejunostomy

| Ref.          | Type of study | GJ studies                  | Surgery                          | Endoscopic stent                  | No differences          |
|---------------|---------------|-----------------------------|----------------------------------|-----------------------------------|-------------------------|
| Minata et al., 2016 | Systematic review | LGJ (Mehta 2006, Jeurnink 2010) | Lower re-intervention rate        | Covered: Higher migration         | Technical success       |
|               |               | OGJ (Jeurnink 2010, Fiori 2013) |                                  | Uncovered: Higher                |                          |
|               |               |                             |                                  | obstruction                      |                          |
| Nagaraja et al., 2014 | Meta-analysis | Laparoscopic GJ (Mittal 2004, Mehta 2006, Jeurnink 2007, Jeurnink 2010) | More major complications          | More likely to tolerate oral intake |                          |
| Ly et al., 2010 | Systematic review | Open GJ (Jeurnink 2007, El-Shabrawi 2006, Mehta 2006, Espinal 2006, Mejia 2006, del Piano 2005, Maetani 2005, Fiori 2004, Mittal 2004, Maetani 2004, Johnsson 2004, Wong 2002, Yim 2001) | More likely to tolerate oral diet earlier | Shorter LOS | Technical and clinical outcomes |
|               |               | Laparoscopic GJ (Jeurnink 2007, Mehta 2006, Mittal 2004) |                                  |                                  | Survival 30 d-mortality |
|               |               |                             |                                  |                                  | Major complications     |

LOS: Length of stay; GJ: Gastrojejunostomy.

Figure 1 Flowchart.

was a optimal strategy, associated with a 72% success rate and the lowest 1-mo mortality rate (2.1%), one of the drawbacks was recurrent duodenal obstruction, found in up to 25%. They reported a 69% success rate after LGJ (overall 1-mo mortality 2.5% and a cost increase of $10340), and 63% success after open GJ with higher 1-mo mortality (4.5%) and more expensive treatment (a cost increase of $12191).

Given the limited number of controlled trials of the laparoscopic approach in palliative GJ, data available are insufficient to perform an analysis comparing LGJ with OGJ or endoscopic stent.

We therefore performed a systematic literature review, in accordance with the PRISMA guidelines, on patients with advanced HPB malignancy who had undergone laparoscopic palliative GJ up to February 2018. The search items were the following MESH terms: [(Gastric outlet obstruction) OR (Gastric Outlet Obstructions) OR (Obstruction, Gastric Outlet) OR (Obstructions, Gastric Outlet) OR (Outlet Obstruction, Gastric) OR (Outlet Obstructions, Gastric) OR (Duodenal obstruction) OR (Duodenal Obstructions) OR (Obstruction, Duodenal) OR (Obstructions, Duodenal)] AND [(Gastric bypass) OR (Bypass, Gastric) OR (Gastrojejunostomy) OR (Gastrojejunostomies) OR (Gastroenterostomy) OR (Gastroenterostomies)] AND [(Laparoscopy) OR (Laparoscopies) OR (Surgical Procedures, Laparoscopic) OR (Laparoscopic Surgical Procedure) OR (Procedure, Laparoscopic Surgical) OR (Procedures, Laparoscopic Surgical) OR (Surgery, Laparoscopic) OR (Laparoscopic Surgical Procedures) OR (Laparoscopic Surgery) OR (Laparoscopic Surgeries) OR (Surgeries, Laparoscopic) OR (Surgical Procedure, Laparoscopic)]. Eligibility criteria were any type of article that included patients with advanced HPB malignancy who had undergone laparoscopic palliative GJ, excluding case reports or reports of prophylactic GJ.

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The results displayed in Table 2, show that there are no standardized outcomes for reporting results after...
## Table 2 Systematic review of laparoscopic gastrojejunostomy for gastric obstruction due to advanced hepatobiliary cancer

| Ref.                        | n     | Type of study                  | HPB Etiology | Biliary obstruction | Operating time | Perioperative morbidity | Time to initiate intake | Time to solid food | LOS Duration of food intake | Comment                                             |
|-----------------------------|-------|--------------------------------|--------------|--------------------|-----------------|------------------------|------------------------|---------------------|--------------------------|---------------------------------------|
| Jeurnink et al [60], 2007   | 95    | Cohort: GJ (42) vs duodenal stent (53) | All patients (laparoscopy: 10) | GJ: 17 previous treatment | ND              | ND                     | ND                     | ND                  | ND                       | ND                                               |
| Hamade et al [4], 2005      | 21    | Cohort: laparoscopic GJ/CJ/GJ+CJ | All patients | 5 biliary bypass, 8 GJ+biliary bypass | gastric bypass 75 min, GJ+CJ 130 min | ND              | ND                     | ND                     | ND                  | ND                       | ND                                               |
| Kazanjian et al [3], 2004   | 9     | Case series: LGJ               | All patients | ND                 | ND              | 2 reconversions, 1 leak, 1 sepsis, 1 DGE | ND                     | ND                  | ND                       | ND                                               |
| Alam et al [3], 2003        | 8     | Case series: LGJ               | All patients | ND                 | ND              | 1 pneumonia, 1 Cholangitis | ND                     | ND                  | ND                       | ND                                               |
| Kuriansky et al [3], 2000   | 12    | Case series: LGJ+biliary bypass | All patients | 12 CCJ             | 89.16 min (35-150) | 2 wound infection, 1 pneumonia, 2 DGE, 1 reintervention (bleeding) | ND                     | ND                  | ND                       | ND                                               |
| Casaccia et al [3], 1999    | 6     | Case series: LGJ               | All patients | 4 ES: 2 Laparoscopic CCJ | 82 min (60-135) | 1 Bleeding (transfusion) | ND                     | ND                  | ND                       | ND                                               |
| Casaccia et al [3], 1998    | 5     | Case series: LGJ               | All patients | 4 ES: 1 Laparoscopic CCJ | ND              | 1 Bleeding (transfusion) | ND                     | ND                  | ND                       | ND                                               |
| Rhodes et al [3], 1995      | 16    | Case series: laparoscopic CCJ ± GJ (5GJ, 3 both, 9CCJ) | All patients | ND                 | 75 min | 1 DGE, 1 ictus | ND                     | ND                  | ND                       | ND Results of the entire data series           |
| Wilson et al [3], 1992      | 2     | Case series: LGJ               | All patients | ND                 | 120 min | None | 2d | 3 d, 4 d | 4-5 d | 1 patient until death | ND                                               |
| Zhang et al [3], 2011       | 28    | Case series: LGJ for benign/malignant disease | ND          | 7 HPB malignancy | ND              | 2 reinterventions (anastomotic leak, trocar site hemorrhage), 2 bleeding controlled by endoscopy, 1 ileus, 5 DGE | 3d | 5 d | 8 d (2-83) | ND Results of the entire data series           |
| Guzman et al [3], 2009      | 20    | Cohort: LGJ AND OGJ | Laparoscopy: 8 HPB malignancy | ND | 116 min | 2 DGE | ND | 7 d | 8 d | ND                  |
| Navarra et al [3], 2006     | 24    | RCT: 12 LGJ vs 12 OGJ | Laparoscopy: 5 HPB malignancy | ND | 150 min | None | ND | 4.08 d | 11 d | ND                  |
Regression of malignant GOO due to advanced HPB cancer, excluding prophylactic GJ and OGJ. All patients had histological diagnosis of HPB cancer. For this purpose, the Mambrino XXI® electronic medical history was used.

Our results are shown in Table 4. All GJ were performed by the same surgeon using the same approach (IP, antecolic and stapler plus manual suture).

Three patients had previous biliary stent, and another patient needed a percutaneous biliary stent after laparoscopic GJ due to obstructive jaundice. The clinical success rate was 100%, with all patients maintaining oral intake until death. The median time from surgery to hospital discharge was 12 d (range 5-13), excluding hospital stay prior surgery attributable to GOO. One patient died due to sepsis caused by a hepatic abscess on postoperative (PO) day 78, and another died due to carcinomatosis and tumor progression on PO day 82. Median overall-survival was 214.67 d.

**Personal series: palliative laparoscopic gastrojejunostomy**

We also performed a retrospective study at the Department of General Surgery and Digestive of the University Hospital of Guadalajara. The period analyzed was January 2009-March 2018. We included all consecutive patients who underwent laparoscopic palliative GJ for malignant GOO due to advanced HPB cancer, excluding prophylactic GJ and OGJ. All patients had histological diagnosis of HPB cancer. For this purpose, the Mambrino XXI® electronic medical history was used.

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**Other surgical options for malignant GOO**

Several surgical procedures for GJ have been reported since Devine et al’s first description in 1925, which introduced a procedure consisting of transection of the stomach and anastomosis between the jejunal loop and the proximal stump of the stomach.[73] But GJ may be not fully effective due to of DGE or tumor bleeding;
so a modified Devine procedure has been developed, in which the stomach is partially divided into proximal and distal parts, and the proximal part of the stomach is anastomosed to the proximal part of the jejunum[74,75]. This technique, stomach-partitioning GJ (SP-GJ), minimizes contact between food and the tumor and allows endoscopic examination[74]. The first laparoscopic approach for SP-GJ was described by Matsumoto et al.[76] in 2005. This surgical technique is associated with lower incidence of bleeding and delayed gastric emptying, with no increase in anastomotic leakage[74-78].

Other surgical approaches reported in the literature for the management of malignant GOO include natural orifice transumbilical surgery[79] or a laparoscopic-assisted approach for a circular mechanical GJ, in which the proximal jejunum is exteriorized by laparoscopy via an epigastic trocar-site incision[80].

**Novel endoscopic approaches for malignant GOO**

EUS-gastroenteroanastomosis (EUS-GE) was first described by Fritscher-Ravens et al.[81,82] in 2002. It is produced by anatomical puncture from the stomach into the third part of the duodenum (EUS-guided gastroduodenostomy), or into the jejunum (EUS-guided gastrojejunostomy) or ileum (EUS-guided gastrojejunostomy). Depending on the tumoral involvement, gastric or jejunal endoscopes can be used. A circular mechanical GJ is created either with a stapling device or by suturing. The technical feasibility of EUS-GE has been confirmed in 15 patients reported by Fritscher-Ravens et al.[82,83]. The procedure was well tolerated and no major complications were described.
gastrojejunostomy[83].

This new EUS technique involves the placement of a lumen-apposing metal stent (LAMS). Data regarding its use are limited[84-87]. In 2017, Pérez-Miranda et al[87] reported the results of a multicenter cohort study comparing EUS-GJ and LGJ. All patients in the EUS-GJ group had symptomatic GOO, compared with only 34% of patients in LGJ group. The clinical success rates in the two groups were 84% vs 90%, LOS was 9.4 d vs 8.9 d and adverse events were 12% vs 41%, with the EUS-GJ group presenting better results in all cases. This is a new EUS technique and it should be reserved for use at experienced centers.

**CONCLUSION**

Palliative treatment of GOO due to advanced HPB cancer may improve QOL and resolve symptoms. Both a non-operative endoscopic approach and surgical treatment are available (Table 5) and an estimation of probable survival is essential for the choice of treatment. Evaluation of the patient and multidisciplinary expertise are required to select the appropriate approach.

Stent is usually preferred in patients with poor general condition or short life expectancy. LGJ is a feasible, safe and efficient technical option. Given the limited studies and the difficulty of performing prospective controlled trials due to patient heterogeneity, no study can cover all the complexities of malignant GOO and more outcome data are needed. Prospective clinical trials with adequate sample sizes comparing different approaches size are warranted.

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