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ORIGINAL ARTICLE

How I do it. Pancreatojejunostomy: surgical tips to mitigate the severity of postoperative pancreatic fistulas after open or minimally invasive pancreatoduodenectomy

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Abstract
Pancreatoduodenectomy is the most appropriate technique for the treatment of periampullary tumors. In the past, this procedure was associated with high mortality and morbidity, but with improvements in patient selection, anesthesia, and surgical technique, mortality has decreased to less than 5%. However, morbidity remains increased due to various complications such as delayed gastric emptying, bleeding, abdominal collections, and abscesses, most of which are related to the pancreatojejunostomy leak. Clinically relevant postoperative pancreatic fistula is the most dangerous and is related to other complications including mortality. The incidence of postoperative pancreatic fistula ranges from 5–30%. Various techniques have been developed to reduce the severity of pancreatic fistulas, from the use of an isolated jejunal loop for pancreatojejunostomy to binding and invagination anastomoses. Even total pancreatectomy has been considered to avoid pancreatic fistula, but the late effects of this procedure are unacceptable, especially in relatively young patients. Recent studies on the main techniques of pancreatojejunostomy concluded that duct-to-mucosa anastomosis is advisable, but no technique eliminates the risk of pancreatic fistula. The purpose of this study is to highlight technical details and tips that may reduce the severity of pancreatic fistula after pancreatojejunostomy during open or minimally invasive pancreatoduodenectomy.

Keywords Pancreatojejunostomy · Pancreatoduodenectomy · Complications · Robotic Surgery · Minimally invasive · Technique

Introduction

Pancreatoduodenectomy is the most appropriate technique for the treatment of periampullary tumors. In the past, this procedure was associated with high mortality and morbidity, but with improvements in patient selection, anesthesia, and surgical technique, mortality has decreased to less than 5% [1]. However, morbidity remains increased due to various complications, such as delayed gastric emptying, bleeding, abdominal collections, and abscesses, most of which are related to the pancreatojejunostomy leak [2]. Clinically relevant postoperative pancreatic fistula is the most dangerous and is related to other complications including mortality. The incidence of postoperative pancreatic fistula ranges from 5% to 30% [3]. Various techniques have been developed to reduce the severity of pancreatic fistulas, from the use of an isolated jejunal loop for pancreatojejunostomy [4] to binding and invagination anastomoses [5, 6]. Even total pancreatectomy has been considered to avoid pancreatic fistula, but the late effects of this procedure are unacceptable, especially in relatively young patients [7–9]. Recent studies on the main techniques of pancreatojejunostomy concluded that duct-to-mucosa anastomosis is advisable [10], but no technique eliminates the risk of pancreatic fistula [11]. The aim of this study is to highlight technical details and tips that may reduce the severity of pancreatic fistula after pancreatojejunostomy during open or minimally invasive pancreatoduodenectomy based on our experience and the literature.

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Preoperative assessment and anticipation of surgical risk

Assessment of anatomic variation is very important. The right hepatic artery may arise from the superior mesenteric artery and run parallel to the bile duct or even retroportal. In an open procedure, we can feel the pulse of the artery, but in a minimally invasive approach, preoperative mapping of the great vessels is essential to avoid accidental transection. Failure to consider this fact may result in inadvertent injury to this artery, leading to ischemia of the right liver. In some situations, the common hepatic artery has an anomalous origin, and its accidental ligation can have very serious or even fatal consequences [12]. Even more rarely, a common hepato-mesenteric trunk [13] may be present, and its preoperative identification is of paramount importance, as inadvertent ligation may lead to total hepatic ischemia and death.

Assessment of the vascular anatomy of the celiac and mesenteric arteries during preoperative pancreatic surgery is also of utmost importance to avoid anastomotic leaks, catastrophic complications, or even death [14]. In addition, surgeons must check the flow of the celiac artery before ligating the gastroduodenal artery in every case using the Bull test [15].

The presence of a ligamentum arcuatum with compression of the celiac trunk or arteriosclerotic stenosis of the celiac trunk can be diagnosed preoperatively or intraoperatively with the Bull test. In this situation, revascularization of the celiac trunk is critical for maintaining perfusion of the liver, pancreas, spleen, and stomach. The Bull test may also reveal stenosis of the common hepatic artery without celiac stenosis (Fig. 1). Fortunately, a much rarer situation is stenosis of the superior mesenteric artery, in which ligation of the connections with the celiac trunk (in the setting of pancreaticoduodenectomy) results in acute intestinal ischemia [16].

Venous variations that may complicate surgical technique are extremely rare and include anomalies of the porto-mesenteric venous axis. Prepancreatic preduodenal portal vein is a rare congenital variant of the portal vein system that has been reported in only 17 patients [17].

Fig. 1 CT sagittal view of a celiac axis stenosis

Preoperative procedures including neoadjuvant treatment

Many patients are referred to our department after biliary stenting and tumor biopsy. These two procedures increase the morbidity of pancreatoduodenectomy, because they lead to increased postoperative infection (contamination of the bile duct often with pathogens resistant to conventional antibiotic therapy). The use of broad-spectrum antibiotics may be necessary to reduce the incidence of infection and even anastomotic dehiscence (some bacterial pathogens produce collagenase) [18]. Biopsy may also lead to pancreatitis and local hemorrhage, which can be seen on imaging and may alter the timing of surgical intervention. These complications can make it difficult to identify surgical margins, especially in minimally invasive procedures.

Neoadjuvant chemotherapy for borderline resectable disease has been increasingly used over the past decade and is associated with an increased risk of major intraoperative bleeding [19]. However, preoperative chemoradiation may be associated with a reduction in the incidence of pancreatic leaks and leak-related morbidity and mortality, but may increase the difficulty of the procedure [20].

Peroperative clinical management

Administration of corticosteroids in the perioperative period in patients with small duct and soft pancreas reduces the severity of acute pancreatitis and, consequently, the severity of pancreatic fistula [21, 22]. Hydrocortisone is administered on admission and repeated every 12 h for 48 h.

Prophylactic administration of octreotide showed no protective effect on the rate of postoperative pancreatic fistula [23]. In fact, a previous study has shown that prophylactic administration of octreotide may also be harmful [24].

Regarding the use of antibiotic therapy, the previous studies have reported conflicting results of prolonged antibiotic prophylaxis for infectious complications after pancreatoduodenectomy. Preoperative biliary instrumentation and the presence of ampullary malignancy are highly associated

with contaminated bile, with approximately 95% of these patients having positive bile cultures [25]. In a recent systematic review and meta-analysis, the authors noted that fewer organ/space infections occur, and prolonged antibiotic prophylaxis should be administered [25]. The duration of antibiotic prophylaxis ranged from 5 to 10 days, although the optimal period has not yet been determined.

Wherever possible, epidural analgesia is used and maintained until the third/fourth postoperative day, depending on the patient's needs. This reduces the use of opioids and facilitates resumption of bowel motility. In a recent study with multivariate analyses, epidural analgesia was significantly associated with fewer postoperative surgical complications after pancreatoduodenectomy [26].

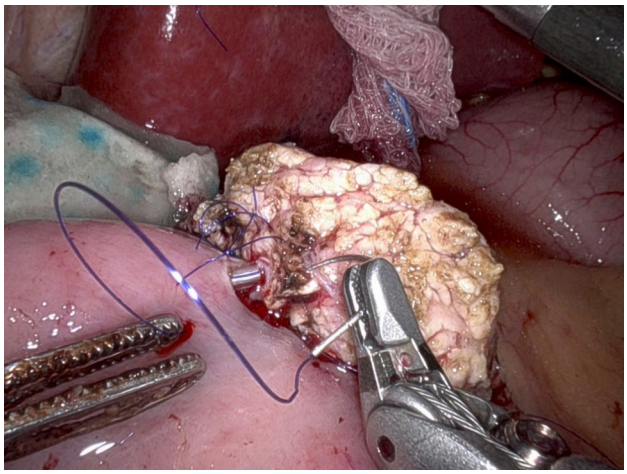

Fig. 2 Intraoperative view of robotic pancreatojejunostomy

Pancreatojejunostomy technique

There are several described techniques of pancreatojejunostomy, including invagination and duct-to-mucosa techniques. The main technique used by our team is an end-to-side double-layer duct-to-mucosa pancreatojejunostomy. To perform a safe and reliable anastomosis, the following considerations should be considered.

First, perfusion of the pancreatic stump should be assessed immediately after removal of the surgical specimen. Several authors consider hypoperfusion of the pancreatic remnant to be an important factor in the development of postoperative pancreatitis and pancreatic fistula [14, 15]. The vascularization of the pancreatic stump should be assessed during the procedure. Recently, the use of intraoperative fluorescence imaging after administration of indocyanine green during robotic PD has been proposed to assess pancreatic vascularization [27]. In open surgery, this assessment may be more difficult and depend on the surgeon's experience.

Second, the consistency of the pancreas and the size of the pancreatic duct may influence the anastomosis. If the pancreas has a firm, indurated consistency and the duct is dilated and centralized, a duct-to-mucosa running 5-0 absorbable suture is performed, followed by a second layer of interrupted 4-0 Prolene sutures that include the pancreatic capsule and the seromuscular layer of the jejunum. The use of a stent in the pancreatic duct is not necessary in this situation. This is the situation in which we have the lowest rate of postoperative pancreatic fistula (4.3%—data not published). On the other hand, if the pancreas is soft and the pancreatic duct is less than 3 mm, the duct-to-mucosa should be made in separate stitches and the use of a pancreatic stent is advisable. In cases where the robotic platform is used, the duct-to-mucosa anastomosis can be safely performed with a running suture thanks to the 3D magnified view (Fig. 2). Indeed, the dexterity of the robot allow to easy perform anastomosis. In a recent worldwide review of 2597 robotic PDs, excellent results of the technique were reported [28]. Since 2018, all our minimally invasive pancreatoduodenectomies have been performed robotically.

External drainage can significantly reduce the amount of extravasated pancreatic juice when a fistula occurs. A recent meta-analysis showed a significantly lower rate of clinically relevant postoperative pancreatic fistula compared with treatment without stents [29, 30]. In another study examining perioperative measures to reduce pancreatic fistulas after pancreatoduodenectomy, external drainage of the pancreatic duct was the only measure associated with a reduction in pancreatic fistulas [31]. We only use this external drainage technique for open procedures, as it is difficult to exteriorize the pancreatic stent correctly. While reviewing the literature for this manuscript, we came across an ingenious technique

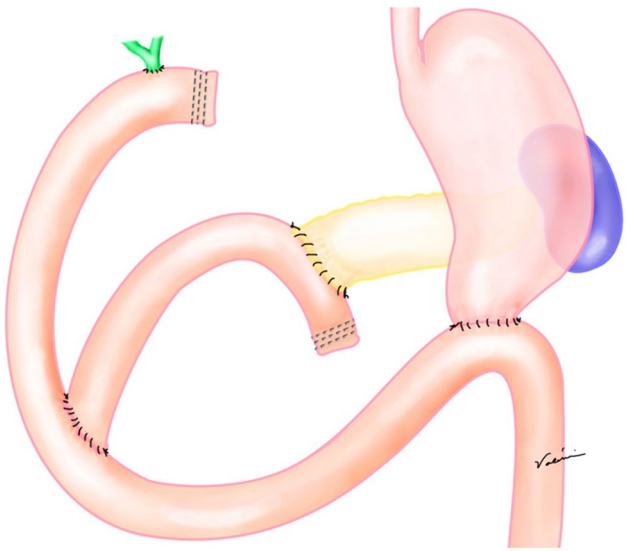

Fig. 3 Schematic representation of the isolated jejunal loop for pancreatojejunostomy

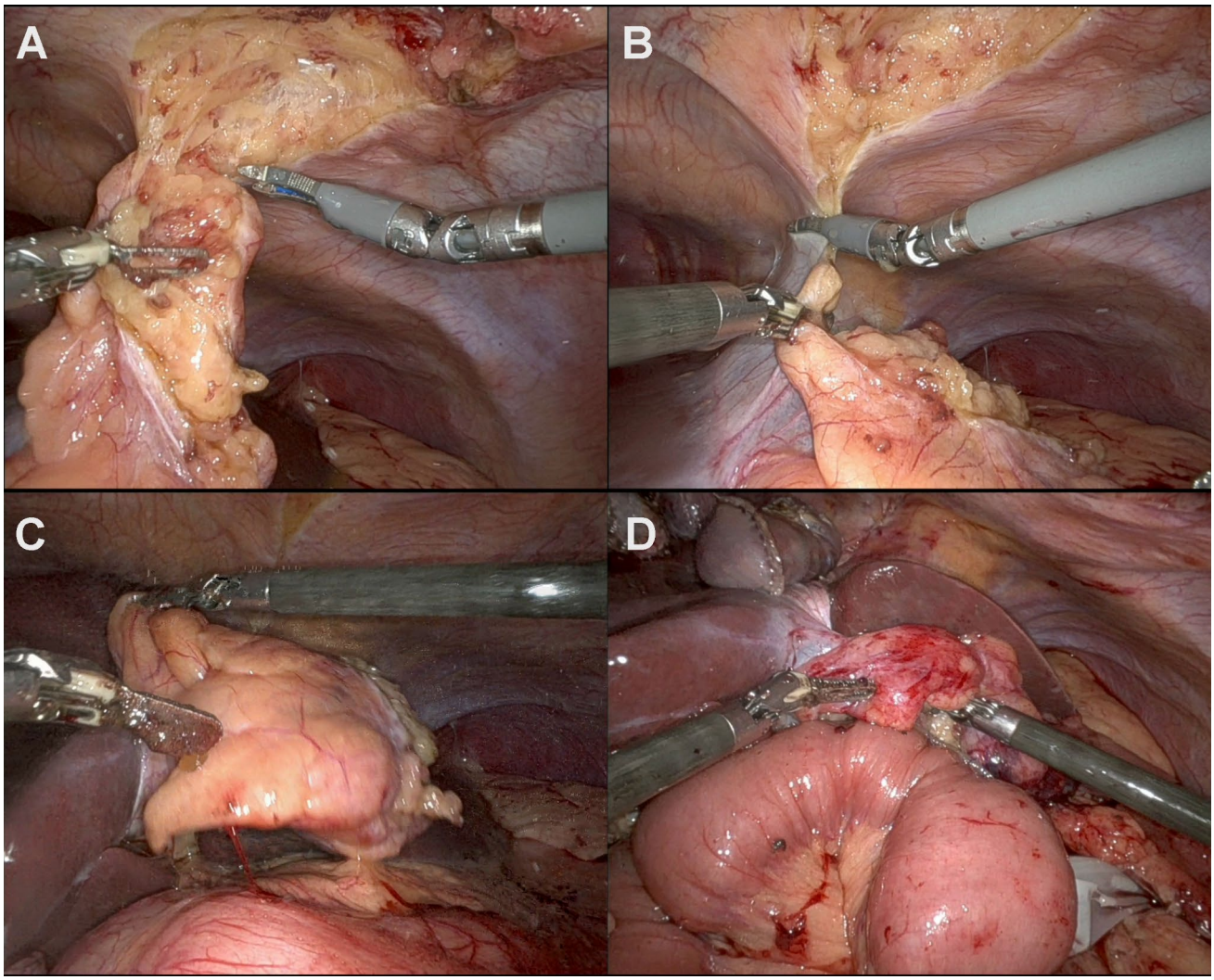

Fig. 4 Intraoperative view of creation and use of a flap from the preperitoneal fat together with the teres and falciform ligaments to protect the pancreatojejunostomy and greater vessels. **A** Teres ligament is already divided and part of the preperitoneal fat is being harvested. **B** Falciform ligament is included in the flap. **C** Intraoperative view of the flap. **D** Flap is used to wrap the greater vessels and the pancreatojejunostomy

for performing external drainage during minimally invasive PD, which we have not yet used [32].

Internal stents are useful in keeping a thin pancreatic duct open but do not reduce the severity of pancreatic fistula. However, displacement and/or obstruction of the drain is not uncommon. We have patients in whom the internal stents are still present many years after the procedure. Even if they are asymptomatic, they can be a cause of future complications. Since we have been using robots exclusively for minimally invasive PD, we have abandoned the use of internal stents, as the quality of the anastomosis between the duct and the mucosa is very good. If the duct is posterior and eccentric, seromuscular sutures must be placed well posteriorly to anteriorize the duct. This is true for ducts of any size and any consistency of the pancreas. In the rare cases in which the pancreatic duct cannot be found, the invagination technique should be used.

Third, the use of an isolated jejunal loop for pancreatojejunostomy has been the subject of several publications. Recently, this type of reconstruction was shown not to decrease the incidence of pancreatic fistulas but to reduce the severity of this complication [33]. A recent report also showed that isolated jejunal loop for pancreatojejunostomy (Fig. 3) in soft pancreas and small pancreatic duct reduces the severity of pancreatic fistulas [34]. In a prospective randomized study, an isolated jejunal loop for pancreatojejunal anastomosis reduced the severity of pancreatic fistula [35]. This technique is also indicated in very young patients with low-grade malignant disease, because a single jejunal loop causes reflux of pancreatic juice into the biliary tree. In

patients with expected long-term survival, this reflux could lead to malignant degeneration of the biliary epithelium [36, 37]. This technique may also be recommended for less-experienced surgeon that may struggle with a higher severity of pancreatic fistula [34].

Finally, the use of the omental flap, ligamentum falciforme, or ligamentum teres has recently been recommended to avoid or reduce the risk of postoperative fistula or extraluminal hemorrhage [38, 39]. We used the falciform ligament and the teres ligament with some of the preperitoneal fat to wrap the regional vessels and the pancreatojejunostomy to reduce the risk of postoperative complications (Fig. 4).

Abdominal drainage

A randomized, prospective, multicenter trial of pancreaticoduodenectomy with and without routine intraperitoneal drainage had to be discontinued because of an increase in mortality from 3% to 12% in patients undergoing PD without intraperitoneal drainage. Since then, the use of abdominal drainage has not been questioned [40]. The type, location, and number of drains may vary according to surgeon preference and experience, and there has been no study on this topic. Also, no clear evidence of the superiority of active versus passive drainage has ever been found [41]. The use of a double drainage, one for the biliary anastomosis and another for the pancreatic anastomosis, appears to reduce the incidence of abdominal collections and the need for postoperative intervention [4]. We always use two drains, one with negative pressure near the hepaticojejunostomy and exteriorized in the right flank (or through trocar incision in the right flank). The second drainage is a double lumen drain with passive drainage near the pancreaticojejunostomy, which is placed in the left flank (or through a trocar incision in the left flank). The removal of the drain depends on the amylase level in the fluid on the first and third postoperative day, as previously described [42].

Conclusions

Mortality after pancreatoduodenectomy has decreased in recent decades, reflecting technical improvements and probably the regionalization of this procedure in large and specialized centers [43]. However, increased mortality has been reported in high-risk [44] and low-income patients [45]. In contrast to high-volume and highly specialized centers with low mortality as reported by Cameron, mortality in nationwide studies representing the real world can be as high as 10% [46, 47].

Therefore, it is conceivable that many small centers have higher complications and mortality because of technical problems, most of which are related to pancreatojejunostomy. Because no type of pancreatojejunostomy is superior to another [29], it is possible that some technical details applied to all types of anastomoses could reduce or mitigate the severity of anastomotic leakage. In patients with an enlarged pancreatic duct in a fibrotic pancreas, no or few complications occur with almost all techniques in experienced centers [1, 2]. However, in less-experienced centers with a high-risk pancreas, as described above, increased morbidity and mortality are observed, even when pancreatojejunostomy is performed with a technique considered good. Therefore, surgical tips as we have described to mitigate the severity of postoperative pancreatic fistulas after pancreatoduodenectomy are welcome in pancreatic surgery.

Data availability All data referred to this manuscript is available upon request to the authors.

Declarations

Ethical Standards, conflicts of interest, Research involving human participants and/or animals, and Informed consent Authors have no conflict of interest or disclosures.

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