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TOPIC HIGHLIGHT

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Reconstruction after pancreatoduodenectomy: Pancreatojejunostomy *vs* pancreatogastrostomy

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Abstract

Pancreatic surgeons try to find the best technique for reconstruction after pancreatoduodenectomy (PD) in order to decrease postoperative complications, mainly pancreatic fistulas (PF). In this work, we compare the two most frequent techniques of reconstruction after PD, pancreatojejunostomy (PJ) and pancreatogastrostomy (PG), in order to determine which of the two is better. A systematic review of the literature was performed, including major meta-analysis articles, clinical randomized trials, systematic reviews, and retrospective studies. A total of 64 articles were finally included. PJ and PG are usually responsible for most of the postoperative morbidity, mainly due to the onset of PF, being considered a major trigger of life-threatening complications such as intra-abdominal abscess and hemorrhagia. The included systematic reviews reported a significant difference only in the incidence of intraabdominal collections favouring PG. PF, delayed gastric emptying and mortality were not different. Although there was heterogeneity between these studies, all were conducted in specialized centers by highly experienced surgeons, and the surgical care was likely to be similar for all the studies. The disadvantages of PG include an increased incidence of delayed gastric emptying and of main pancreatic duct obstruction due to overgrowth by the gastric mucosa. Exocrine function appears to be worse after PG than after PJ, resulting in severe atrophic changes in the remnant pancreas. Depending on the type of PJ or PG used, the PF rate and other complications can also be different. The best method to deal with the pancreatic stump after PD remains questionable. The choice of method of pancreatic anastomosis could be based on individual experience and on the surgeon's preference and adherence to basic principles such as good exposure and visualization. In conclusion, up to now none of the techniques can be considered superior or be recommended as standard for reconstruction after PD.

Key words: Pancreatoduodenectomy; Pancreatojejunostomy; Pancreatogastrostomy; Pancreatic fistula; Pancreatic cancer; Surgical technique

Core tip: Pancreatoduodenectomy is a technique with a high rate of morbidity and mortality. Surgeons try to find the best technique of reconstruction in order to decrease postoperative complications. We compare the two most frequent techniques of reconstruction after pancreatoduodenectomy, namely pancreatojejunostomy and pancreatogastrostomy, to determine which of the two is better. We offer a systematic review of the main papers published with all the pros and cons of each technique. The best method to deal with the pancreatic stump after pancreatoduodenectomy remains questionable. The choice of method of pancreatic anastomosis could be based on individual experience and on the surgeon's preference and adherence to basic principles, such as good exposure and visualization.

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INTRODUCTION

Pancreatic surgeons try to find the best technique of reconstruction after pancreatoduodenectomy (PD) in order to decrease the frequency and seriousness of postoperative complications, mainly pancreatic fistulas (PF)[1].

The aim of this work was to compare the two most frequent techniques of reconstruction after PD, pancreatojejunostomy (PJ) and pancreatogastrostomy (PG) in order to determine which of the two is better.

PANCREATOJEJUNOSTOMY

Whipple's technique was described in 1935 and initially involved a two-time excision, performing bypass pathways before resection of the surgical specimen[2]. This name is reserved today to the resection of the pancreatic head and accompanying biliodigestive structures: gastric antrum, duodenal frame, first jejunal loop, gallbladder in continuity with the cystic duct and distal common bile duct.

After excision, reconstruction is needed. There are several ways but the best known is described by Child in 1943[3], consisting of successive drainage of the pancreas, bile duct and stomach in the first jejunal loop and still prevails today. This circuit is simple and ensures a rapid mixture of bile and pancreatic secretions.

More generally, to prevent backflow of one anastomosis to another, this type of reconstruction must follow these rules: (1) PJ is proximal to hepaticojejunostomy, which is proximal to gastrojejunostomy; (2) the distance between each small bowel anastomosis is ideally of at least 30-40 cm to limit food reflux into the biliary and pancreatic anastomosis; and (3) the anastomosis must be isoperistaltic. The first jejunal loop is usually mobile enough to place it in the supramesocolic compartment and allow these three anastomoses.

PJ is usually responsible for most of the postoperative morbidity[4], which currently remains high[5,6], mainly due to the onset of PF, being considered a major trigger of life-threatening complications such as intra-abdominal abscess and hemorrhagia[7]. Because of this, we have described several types of anastomoses, all aimed to reduce the rate of occurrence of the feared fistula.

Types of pancreatojejunostomies

Reconstruction methods between the pancreas and the small remnant include various forms ranging from end-to-side anastomosis, termino-terminal anastomosis or pancreatic intussusception in the jejunum. Of these, the most used are the invagination and duct-to-mucosa anastomosis without stenting the main pancreatic duct (MPD).

End-to-side PJ: This anastomosis has two variants which are: (1) direct anastomosis in a single plane, consisting of an anastomosis in a single plane between the upper and lower pancreatic edges and the longitudinal gap (3-4 cm) in the jejunum; and (2) duct-to-mucosa anastomosis, which is the most frequently used. The jejunal loop is placed with the fornix on the left, and in a slight clockwise rotation so that its antimesenteric edge is in contact with the pancreatic sectional area. A seromuscular longitudinal incision must be performed with length equal to the sectional area of the pancreas. The jejunal mucosa is incised on a limited basis against the MPD. The backplane of the seromuscular end-to-side anastomosis begins with a continuous suture from outside to inside in the pancreas (avoiding excessive pressure to prevent tearing) and then from inside to outside in the jejunum. The suture is started at the upper edge of the sectional area, ending in the lower part. Then, interrupted suture is performed taking the MPD wall and the mucosa of the jejunum to face the MPD. The anterior plan begins with a continuous suture that follows the same principles as the backplane. This suture is completed with a second angled stitch.

Both techniques were studied in a prospective randomized trial by Bassi *et al*[8] in which it was concluded that the rate of PF was lower after duct-to-mucosa anastomosis.

PJ by invagination: This anastomosis is acceptable when the remaining pancreas is thin and can enter the jejunum[9-11]. The principle of intussusception is to coat the entire bed of the pancreatic section with the wall of the jejunum to suppress PF that may come from the secondary conduits sectioned on the periphery of the bed or are exposed by a parenchymal necrosis due to the sutures which pass through the capsule.

There are three types of PJ by invagination: (1) classic end-to-end anastomosis. It is an end-to-end PJ performed with "U" stitches. Next, the pancreas is inserted into the jejunum and tied. This technique has not been evaluated in a randomized clinical trial; and (2) end-to-end anastomosis with invagination by Peng *et al*[12] (binding). Described by Peng *et al*[12] in 2002, the technique includes three modifications: (1) the jejunum is everted on itself to make a first anastomosis between the jejunal mucosa and the pancreas; (2) to improve cohesion between the pancreas and jejunum, the jejunal mucosa covering the pancreas along 2-3 cm is initially destroyed by chemical or thermal means to create an adhesion zone; and (3) a ligature is applied around the covered area after the procedure when the jejunum is properly arranged on the pancreas.

The results of this anastomosis were excellent in a randomized clinical trial conducted by the promoter of this technique[13], but so far have not been confirmed in two prospective studies in 2010[14,15]. More recently, a prospective, but not randomized, study showed that the

method described by Peng is safe but is not associated with a lower frequency of PF, morbidity or mortality in comparison with the duct-to-mucosa anastomosis[16]. End-to-side anastomosis with invagination by Grobmyer *et al*[17]. This anastomosis consisted of making a muco-mucosa anastomosis by a jejunal incision in the antimesenteric border of the small intestine and whose size is equivalent to the MPD, associating an invagination of the pancreatic bed in the seromuscular layer of the jejunum. For this, the side walls of the jejunum are fixed to the pancreatic capsule in order to cover the bed section.

This anastomosis has been successful in two comparable, retrospective series[17,18] and in a clinical randomized trial[19].

Comparing both types of anastomosis, duct-to-mucosa and invagination, the duct-to-mucosa anastomosis was initially described as safer and with a significantly lower rate of fistula[20,21]. Subsequently, in 2003 a prospective randomized trial[8] found PF in 14% of patients: 13% in the group with duct-to-mucosa anastomosis and 15% in the group with anastomosis by invagination, although the difference was not significant. A randomized prospective study in 2009[19] concluded that the invagination method significantly decreased the rate of PF *vs* duct-to-mucosa anastomosis (12% *vs* 24%, $P = 0.04$) in the pancreas with both soft and hard texture.

Anastomotic variants

Several alternatives to the above techniques have been described, all aiming to reduce the occurrence of a fistula and its consequences: (1) PJ with stent. The principle of stenting anastomosis is to derive the flow of pancreatic secretions with the aid of a catheter inserted in the MPD. We distinguish between lost drainage and externalized drainage (or internal-external drainage): Anastomosis with internal drainage consists of introducing a catheter with a diameter equivalent to the MPD during the anastomosis. Then the catheter migrates spontaneously (in a few days or weeks) to the jejunum and is evacuated by natural means. The effectiveness of this procedure has only been evaluated in a single randomized clinical and was negative[22]. This procedure seems especially useful to prevent stenosis of the pancreatic duct during anastomosis. Anastomosis with external drainage consists of introducing a catheter in the MPD then externalizing it through the intestinal wall (covering it or not according to Witzel's technique) and then through the abdominal wall. The drain is left without pinching for the first postoperative days (usually 10-14 d), then can be clamped once healing is achieved, so that the pancreatic secretion passes. It is removed 4-6 wk after surgery. Comparing the presence of external or internal drainage, a study by Tani *et al*[23] in 2010 concluded that there was no significant difference between the implementation of internal or external drainage, and concurred with a meta-analysis in which it was stated that internal drainage does not affect the development of fistulas and is not useful in a soft pancreas[24]. Comparing the use of external drainage or use of none, there is a study which states that the range of PF between external drainage or no drainage is similar, with no decrease in the rate (11.5% *vs* 14.8%; $P = 0.725$) with the use of external drainage[25]. A meta-analysis of randomized controlled trials most recently by Hong *et al*[26] concluded that the application of external drainage after pancreatoduodenectomy can decrease the incidence of pancreatic leakage compared with the use of any drainage. This technique is discussed in a different section.

PANCREATOGASTROSTOMY

PJ, and variations thereof, has been the technique most frequently used, although PG is a good alternative. In 1934, Tripodi performed a PG in a dog, and reported adequate pancreatic secretion postoperatively[27]. The first PG in humans was performed in 1944[28]. Since then, several series with around 3800 patients have been published[29-31], and their outcomes have been compared in some papers with those of PJ to determine the best reconstructive technique.

Types of pancreatogastrostomies

Basically, three types of PG have been described: (1) in classic duct-to-mucosa anastomosis the pancreatic stump is sutured to the seromuscular layer of the gastric wall, while the MPD is sutured to the full-thickness stomach[32], with or without a lost pancreatic stent; (2) in pancreatic stump intussusception into the stomach, the distance between the surface of the stump and the suture is longer, thus decreasing the risk of a fistula between the stitches that cross the pancreatic capsule. Suturing can be performed from the posterior gastric surface or from the inside of the gastric cavity through an anterior gastrostomy[33]. Transverse gastrotomy seems to be associated with a higher incidence of delayed gastric emptying[34,35] compared with a longitudinal incision[32,36]; and (3) in the exteriorized pancreatic stent, the tube introduced into the pancreatic duct passes through the anterior gastric wall and the abdominal wall. Drainage may be closed 10–14 d later and removed 4-6 wk after surgery.

Alternative procedures include a binding or purse string suture around the anastomosis in the gastric wall[37], with complete stitches traversing the anterior and posterior surface of the pancreatic stump associated with a duct-to-mucosa anastomosis[38] or a "gastric partition" where the PG is performed[39]. An aspirating nasogastric tube is always recommended. At any rate, there are no studies showing the superiority of any of these techniques.

Definition of pancreatic fistula

The most frequent complications after PD are delayed gastric emptying, PF, postoperative bleeding and intra-abdominal abscess[40-43]. Although mortality has dramatically decreased from higher than 20% in the 1980s to less than 5% nowadays[40,44-47], morbidity remains around 40%-50%[48,49]. Differences in the definitions of these complications have led to a consensus of the International Study Group for Pancreatic Surgery (ISGPS) in 2006.

PF appears in 3%-30% of patients[1,41,50,51]. It must be suspected when the amylase content of drained fluid is more than 3 times the normal value in the third postoperative day. ISGPS classifies fistulas as: (1) grade A (patient is stable, has a transient fistula and no collections in computed tomography); (2) grade B (patient needs parenteral nutrition, antibiotics and somatostatin and has peripancreatic collections that can be percutaneously drained); and (3) grade C (patient needs to be under intensive care, have percutaneous drainage of the collections or surgery to repair the leakage, to change from PJ to PG or to do a total pancreatectomy)[43,52].

Advantages of pancreatogastrostomy over pancreatojejunostomy

The technique of PG has several potential advantages over PJ. It can be performed easily, because the posterior wall of the stomach lies immediately anterior to the mobilized pancreatic remnant and is usually wider than the transected pancreas. The posterior wall of the stomach is thick and highly vascularized compared with the jejunum. PG anastomosis is then located at a certain distance away from the major blood vessels, which are skeletonized during the resection phase of the tumor and the lymph nodes. If a PF occurs after PG, the major vessels are less prone to being damaged by activated proteolytic enzymes of the pancreas[53].

In PG, the pancreatic exocrine secretions enter the potentially acidic gastric environment, precluding digestive damage of the pancreatoenteric anastomosis by activated proteolytic enzymes. In PJ, the activation of pancreatic exocrine secretions can occur more easily in the presence of intestinal enterokinase and bile. These factors can easily cause digestive damage to the anastomosis and the major vessels in the presence of abundant proteolytic enzymes escaping from the fistula[35].

PG avoids the long jejunal loop where pancreatobiliary secretions accumulate during the early postoperative period and reduces the number of anastomoses in a single loop of retained jejunum, which potentially decreases the likelihood of loop kinking[53]. Postoperative gastric decompression can result in removal of gastric and pancreatic secretions. It also avoids tension on the anastomosis. A nasogastric tube can be used as drainage if a fistula occurs after PG, thereby avoiding potentially invasive procedures[53].

The decreased morbidity of intra-abdominal complications for PG may be the result of the aforementioned theoretical advantages.

Comparison of both techniques

To compare both techniques of reconstruction, five randomized trials[39,52,54-56] and several meta-analysis and systematic reviews[16,22,53,57-64] have been published in the recent years. Systematic reviews included 553 patients and found a significant difference only in the incidence of intraabdominal collections favoring PG (OR = 0.46; 95%CI: 0.26-0.79; P = 0.005). PF, delayed gastric emptying and mortality were not different. The recent paper by Topal *et al*[56] included 329 patients and showed a lower incidence of PF after PG (OR = 2.86; 95%CI: 1.38-6.17; P = 0.02). Although there was heterogeneity between these studies, all were conducted in specialized centers by highly experienced surgeons and the surgical care was likely to be similar for all the studies.

It is generally accepted that, compared with a fibrotic pancreatic remnant, a soft and fragile pancreatic stump frequently results in a high rate of pancreatic anastomosis leakage[59]. Among the conditions which can lead to PF, pancreatic texture, pancreatic stump blood supply, pancreatic duct size and pancreatic juice output are important factors[43,52].

Disadvantages of PG have been identified, including an increased incidence of delayed gastric emptying and of MPD obstruction due to overgrowth by the gastric mucosa. Available data on hormone levels indicate that the exocrine function appears to be worse after PG than after PJ, resulting in severe atrophic changes in the remnant pancreas[60].

Other factors such as presenting symptoms, preoperative blood parameters, the presence of comorbid illness and preoperative biliary drainage that may influence the frequency or type of morbidity, were not usually considered. Furthermore, the definition of PF also varied between these articles, with only two studies[39,56] applying the ISGPF criteria. Also, none of the papers considered stratification of the patients by MPD diameter, which also seems to correlate strongly with pancreatic texture[53].

The reported technique for PD was variable. From the article published by Fernández-Cruz *et al*[39], with 100% of patients having a pylorus-preserving modification (PPPD) and no patient with the classic Whipple procedure, to that by Topal *et al*[56], with 61% and 39% of patients having the respective procedures. There were also variations of the PJ technique that could be associated with differences in the PF rate. Three randomized trials show a lack of uniform technique[52,54,55]. A duct-to-mucosa technique was used as the standard in one trial[52] and at the surgeon's discretion in another two trials[55,56]; end-to-end PJ was used in two trials at the surgeon's discretion[54,55]; and a duct-to-mucosa PJ with an internal stent was used in only one trial[39].

The techniques of PG were also different in the five randomized trials[39,52,54-56]. In one paper[54], the pancreatic anastomosis used the classical technique first described, two randomized trials used the second technique[52,56] and in another trial the details of PG anastomosis were not mentioned[55]. The lack of a uniform technique for PG raises the same controversy as for PJ, since different operative procedures could reasonably lead to different complications.

A new technique, PPPD with gastric partition was described only in the study by Fernández-Cruz *et al*[39]. Although this technique was associated with lower rates of postoperative fistula than PJ, this surgical technique is not easy to reproduce and might not always be possible for oncological reasons[56]. This complexity may explain why gastric partitioning with preservation of the pylorus and

the gastro-epiploic arcade, together with the placement of a pancreatic stent through the anastomosis, is still not implemented in most centers.

Ways to decrease complications

Use of occlusive substances: Neoprene injection[61] in the MPD to occlude the duct thus neutralizing exocrine pancreatic secretion is an option that has not reduced the rate of PF according to a randomized clinical trial[62]. Another recent randomized trial evaluated the effect of topical fibrin glue applied externally to all anastomoses after PD. The conclusions of this study are that fibrin glue application does not reduce the incidence of anastomotic leaks[62].

Use of somatostatin: Somatostatin and somatostatin analogues (octreotide) was used in all patients in the studies by Bassi *et al*[52], Topal *et al*[56] and at the surgeon's discretion in the study by Duffas *et al*[55]. However, somatostatin was not used prophylactically in any patients in the studies by Yeo *et al*[54] and Fernández-Cruz *et al*[39]. Prophylactic use of somatostatin and octreotide in pancreatic surgery remains controversial and several meta-analyses came to contradictory conclusions. A more recent meta-analysis of randomized trials on the effectiveness of somatostatin analogues for pancreatic surgery[63] concluded that somatostatin analogues reduce postoperative complications but do not reduce perioperative mortality, and they do shorten hospital stay in patients undergoing pancreatic surgery for malignancy. For this reason, adequately powered trials with a low risk of bias are necessary.

Although some long-term outcomes show that exocrine function after PG is decreased compared with PJ, available data on hormone levels indicate that endocrine function appears to be similar. Despite these results, the benefits resulting from a reduction in occurrence of postoperative PF are higher[35].

Wrapping: Use of the omentum or falciform ligament to wrap local retroperitoneal vessels in pancreaticojejunal anastomosis. Its use in the West is limited. It is used for two purposes: (1) to avoid the autolytic effect and proteolytic activity of pancreatic juice and infected fluids on surrounding organs, especially the abdominal vessels. This is intended to reduce the postoperative bleeding rate; and (2) to reduce the rate of PF by avoiding complications arising from it.

Wrapping is not exempt from complications such as panniculitis, intestinal obstruction, necrosis of the omentum, and intrabadominal abscess. In some patients over or under size, it cannot be used.

The falciform ligament shares a percentage of the features we have discussed for the omentum, but it is smaller and shorter so it can be used to cover vascular structures but it is hard to wrap a PJ. A great advantage is that no complications have been associated with its use.

The literature on wrapping in oncologic pancreatic surgery is rare, and usually consists of retrospective studies with a low level of evidence,and studies mixing different types of pancreatic surgery and various wrapping techniques. It seems that wrapping slightly decreases postoperative bleeding and PF, and when this occurs is less severe than when not using wrapping. However, a prospective randomized trial is needed to let us know if we can use the technique more generally[64].

Use of stents

Only in one randomized trial are stents used[39]. The benefit of an internal or external stent across pancreaticoenteric anastomosis remains controversial. Two prospective randomized trials have reached different conclusions on the benefit of stenting in reducing the PF rate[22,50]. Winter *et al*[22] found that the use of a short internal stent did not reduce the frequency or the severity of pancreatic fistula after PJ. In their study the technique of PJ anastomosis was not standardized. Poon *et al*[50] used an end-to-side, duct-to-mucosa anastomosis, and the patients were randomized to have either an external stent inserted across the anastomosis to drain the pancreatic duct or no stent. This trial showed a reduction in the incidence of PF from 20% in the non-stented group to 6.7% in the stented group.

CONCLUSION

The best method to deal with the pancreatic stump after PD remains in question even. The choice of method of pancreatic anastomosis could be based on individual experience and on the surgeon's preference and adherence to basic principles such as good exposure and visualization. It is important to suture placement without choking the MPD to not produce a watertight anastomosis and preservation of the blood supply. In conclusion, up to now none of the techniques can be considered as superior and recommended as standard for reconstruction after PD. Future large-scale, high-quality, multicenter trials are required to clarify the issues of reconstruction following PD.

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