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Review Article

Strategies for pancreatic anastomosis after pancreaticoduodenectomy: What really matters?

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ABSTRACT

Background: The postoperative pancreatic fistula rate remains approximately 10–20% even in institutions treating a high-volume of pancreatic cases. The best strategy to restore the continuity between the pancreatic remnant and the digestive tract is still in debate.
Data sources: Studies were identified by searching PubMed for studies published between January 1934 (when pancreaticogastrostomy was technically feasible) and December 2016. The following search terms were used: "duct-to-mucosa", "invagination", "pancreaticojejunostomy", "pancreaticogastrostomy," and "pancreaticoduodenectomy". The search was limited to English publications.
Results: Many technical methods have been developed and optimized to restore pancreaticoenteric continuity, including pancreaticojejunostomy, pancreaticogastrostomy, and stented drainage of the pancreatic duct, among other modifications. Researchers have also attempted to decrease the postoperative pancreatic fistula after pancreaticoduodenectomy by using fibrin glue and somatostatin analogues. However, no significant decrease in postoperative pancreatic fistula has been observed in most of these studies, and only an external pancreatic duct stent has been found to decrease the leakage rate of pancreatic anastomosis after pancreaticojejunostomy.
Conclusion: Pancreatic surgeons should choose a suitable technique according to the characteristics of individual cases.

Introduction

Presently, pancreaticoduodenectomy is regarded as the standard surgical procedure for patients with malignant and premalignant tumors in the pancreatic head and periampullary region. Recently, given the continuous improvements in surgical technique and advancements in perioperative management, the mortality rate associated with pancreaticoduodenectomy has decreased to less than 5% in high-volume centers [1–3]. However, surgical morbidity after pancreaticoduodenectomy remains high (40–50%) even in large series. In most series, the three leading causes of morbidity after pancreaticoduodenectomy are postoperative pancreatic fistula (POPF), delayed gastric emptying, and wound infection. Among them, POPF is the most frequent major complication of alimentary tract reconstruction after pancreaticoduodenectomy and may lead to other complications, such as intraabdominal abscess, intraabdominal hemorrhage, reoperation, and even death [4,5]. Pancreatic anastomosis after pancreaticoduodenectomy remains the "Achilles' heel" of this surgical procedure. Therefore, many diverse strategies have been proposed to diminish POPF rates, including technical modifications. To date, more than 50 types of pancreatic and digestive tract reconstruction techniques have been reported [6]. However, the POPF rate remains approximately 10–20% even in high-volume pancreatic centers [3,7]. Recently, numerous randomized studies and meta-analyses and systematic reviews have addressed the outcome of different reconstruction strategies. Nevertheless, the best strategy to restore the continuity between the pancreatic remnant and the digestive tract is still in debate. The present review was to investigate the key factors of affecting the outcomes during pancreatic reconstruction and compare the main pancreatic anastomosis technique.

Multiple pancreaticojejunostomy

For many years, multiple pancreaticojejunostomy techniques have been used to connect the pancreatic remnant with the

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jejunum to restore pancreatic juice drainage during pancreaticoduodenectomy; these techniques include duct-to-mucosa sutures, invaginated pancreaticojejunostomy, binding pancreaticojejunostomy and other modified techniques. To date, numerous observational clinical studies or randomized controlled trials (RCTs) have sought to determine the best method to perform the pancreaticojejunostomy.

The duct-to-mucosa and invagination methods are well-established classic anastomotic methods that have conventionally been used for pancreaticojejunostomy, and there has been a long-standing debate as to which technique is better. To date, numerous studies have been conducted to address this topic. Some retrospective studies [6–8] have demonstrated that duct-to-mucosa pancreaticojejunostomy has a lower rate of POPF in patients with a dilated pancreatic duct or hard pancreas, whereas the invagination pancreaticojejunostomy technique is more applicable in patients with a normal soft pancreas. However, among the seven RCTs [9–15], only one prospective randomized study [13] has reported a lower POPF rate in the duct-to-mucosa pancreaticojejunostomy group than in the invagination pancreaticojejunostomy group. In further stratified analyses, the advantage was not evident in patients with a soft pancreatic stump. Two meta-analyses [16,17] including some of these RCTs have reported no significant differences in the POPF rate between the two anastomotic methods. In addition, duct-to-mucosa pancreaticojejunostomy is not superior to invagination pancreaticojejunostomy in terms of mortality, morbidity and reoperation rates in patients with pancreaticoduodenectomy.

Because all the methods to connect the pancreas with the jejunum via suture may result in pancreatic fistula, a special technique termed "binding pancreaticojejunostomy" has been designed by Peng et al. [18]. In this novel method, the jejunum is sealed to the pancreatic stump, in contrast to the use of multiple anchoring sutures. Three retrospective studies and one randomized comparative trial using this technique have been published [18–21]. One of these studies has compared the new "binding" pancreaticojejunostomy ($n = 106$) with conventional end-to-end anastomosis ($n = 111$). Three years follow-up showed that patients in "binding" group had no POPF, while 7.2% of the patients in conventional group had POPF ($P < 0.05$) [21]. However, in two additional prospective studies in European populations, this promising outcome was not repeatable [22,23]. Notably, the binding method is a worthwhile procedure to decrease the POPF rate in cases with a soft pancreas texture with a normal main pancreatic duct.

Previously, pancreaticojejunostomy and hepaticojejunostomy have been rebuilt on the same intestinal loop, thus allowing pancreatic juice to be activated easily by biliary secretion and potentially increasing the incidence and severity of POPF. On the basis of this theory, isolated Roux loop pancreaticojejunostomy was first described in 1976 by Machado et al. [24]. However, as compared with conventional duct-to-mucosa pancreaticojejunostomy or pancreaticogastrostomy, isolated Roux loop pancreaticojejunostomy is not associated with a lower rate of POPF. The only advantage of isolated Roux loop pancreaticojejunostomy is a lower incidence of postoperative steatorrhea [25].

Pancreaticogastrostomy

Regardless of the various modifications used in pancreaticojejunostomy, numerous large studies have described the pancreatic fistula rate of greater than 10%. Pancreaticogastrostomy has been proposed as an alternative to the more commonly used pancreaticojejunostomy. Pancreaticogastrostomy was shown to be technically feasible in 1934 [26]. Almost all retrospective studies have suggested a decrease in morbidity, mainly in terms of POPF, with pancreaticogastrostomy. To date, nine completed RCTs have compared pancreaticogastrostomy and pancreaticojejunostomy in terms of POPF and other complications. Mixed results have been reported among these RCTs [25,27–34]. Four single-center [25,27,28,31] and two multicenter prospective RCTs [29,34] have reported similar POPF rates between the two types of pancreatic anastomosis: 22%, 12.3%, 13%, 10%, 16% and 20% for pancreaticogastrostomy versus 20%, 11.1%, 16%, 12%, 20% and 22% for pancreaticojejunostomy, respectively. In contrast, the other two multicenter [32,33] and one single-center prospective RCTs [30] have reported that pancreaticogastrostomy is more efficient than pancreaticojejunostomy in decreasing the incidence of POPF. Therefore, numerous meta-analyses, including these RCTs, have been conducted to summarize the currently available evidence on pancreaticogastrostomy versus pancreaticojejunostomy [35–41]. In most of these meta-analyses, pancreaticogastrostomy appears to be superior to pancreaticojejunostomy in decreasing the incidence of POPF and intraabdominal fluid collection. However, the number of patients with premalignant disease, such as intraductal papillary mucinous neoplasm, neuroendocrine tumor, and solid pseudopapillary tumor, has increased. Generally, these patients exhibit longer survival time. Therefore, it is worthwhile to focus more on the postoperative function of the pancreatic remnant. Although pancreaticogastrostomy offers an advantage over pancreaticojejunostomy in decreasing POPF, pancreaticogastrostomy appears to be associated with an important functional disadvantage over the long-term, namely, an increased incidence of pancreatic exocrine insufficiency. For example, patients who undergo pancreaticoduodenectomy with pancreaticogastrostomy are more likely to develop steatorrhea than their counterparts [42]. Patients administered pancreatic enzyme within one year after surgery have been found to be more prevalent among patients receiving pancreaticogastrostomy (75.8% versus 38.5%, $P < 0.001$). The main reason for this finding is intragastric inactivation and disintegration of the pancreatic lipase by gastric acid. Among the pancreatic enzymes, lipase is the most important enzyme for relief from symptomatic steatorrhea and the most labile to gastric acid. Lipase is less resistant to gastric disintegration than trypsin or chymotrypsin [43].

Other modifications or supplements

Pancreaticojejunostomy and pancreaticogastrostomy are the two classic methods of reconstruction. Although numerous trials have been conducted to compare efficiency between the two methods, no consensus has been reached regarding the best method to reduce pancreatic fistula. In addition, various technical modifications, such as placement of an internal or external stent, reinforcement of anastomosis with fibrin glue, and octreotide application, have been used to decrease the incidence and severity of POPF.

Stented anastomosis

Theoretically, a stent may help divert the pancreatic juice away from the anastomosis and also facilitate more precise sutures for duct-to-mucosa anastomosis, especially in cases with small pancreatic ducts. In addition, a stent can provide inner support to the anastomosis. An internal or external stent across pancreaticojejunostomy anastomosis is widely used by many surgeons, but the benefits remain controversial because of the scarcity of data from RCTs. Two RCTs demonstrated that an internal pancreatic duct stent does not decrease the frequency or the severity of POPFs [44,45]. In the randomized comparative study by Winter et al. [44] the trial was stopped early given the real possibility that pancreatic stents might be causing harm. According to the only meta-analysis, [46] which has also included five observational clinical studies, the use of an internal pancreatic duct stent does