REVIEW

Reconstruction Method After Pancreaticoduodenectomy. Idea to Prevent Serious Complications

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ABSTRACT

Pancreatic fistula after pancreaticoduodenectomy represents a critical trigger of potentially life-threatening complications and is also associated with markedly prolonged hospitalization. Many arguments have been proposed for the method to anastomosis the pancreatic stump with the gastrointestinal tract, such as invagination *vs.* duct-to-mucosa, Billroth I (Imanaga) *vs.* Billroth II (Whipple and/or Child) or pancreaticogastrostomy *vs.* pancreaticojejunostomy. Although the best method for dealing with the pancreatic stump after pancreaticoduodenectomy remains in question, recent reports described the invagination method to decrease the rate of pancreatic fistula significantly compared to the duct-to-mucosa anastomosis. In Billroth I reconstruction, more frequent anastomotic failure has been reported, and disadvantages of pancreaticogastrostomy have been identified, including an increased incidence of delayed gastric emptying and of pancreatic duct obstruction due to overgrowth by the gastric mucosa. We review recent several safety trials and methods of treating the pancreatic stump after pancreaticoduodenectomy, and demonstrate an operative procedure with its advantage of the novel reconstruction method due to our experiences.

INTRODUCTION

The indications for pancreaticoduodenectomy have expanded to encompass a broad spectrum of periampullary tumors including both malignant and benign lesions, chronic pancreatitis, and, occasionally, trauma. During the last decade, although the rate of operative mortality significantly decreased after pancreaticoduodenectomy, the incidence of post-operative morbidity still remains high [1, 2]. The occurrence of pancreatic fistula is a critical trigger of life-threatening complications such as intra-abdominal abscess and hemorrhage [3], which is also potentially associated with markedly prolonged hospitalization. Most of the large pancreaticoduodenectomy series have reported rates of pancreatic fistula of over 10% [4, 5, 6, 7]. Risk factors for pancreatic fistula depend upon: 1) general patient factors, including age [8], sex [9], diabetes mellitus [10] and nutrition [11]; 2) disease-related factors, including pancreatic duct size [4], pancreatic texture [12], and pathology; and 3) procedure-related factors, including blood loss [13], operative time [14], and anastomotic method [15]. Among these risk factors, the most important might be the texture of the remnant pancreas [16]. Indeed, despite an occurrence rate of pancreatic fistula of 5% in cases of hard pancreatic tissue, the rate rises to nearly 20% in cases of soft pancreatic texture [5, 6, 7]. The risk of developing a pancreatic fistula is significantly associated with the final histopathological diagnosis of the resected specimen, with lower risk in adenocarcinoma and higher risk in cystic neoplasms or disease originating from the bile duct [17]. This is also because pancreatic malignancy usually causes main pancreatic duct dilatation and occurs in chronic pancreatitis; therefore, a fibrotic hard remnant pancreas and enlarged duct are easily anastomosed, whereas a soft pancreas remains at risk of pancreatic fistula due to its fragility and its secretion of a large amount of pancreatic juice [18].

Surgical technique might be one improvable aspect of pancreaticoduodenectomy that can reduce the pancreatic leakage rate; it is critical in the management of the pancreatic remnant because of the various methods used by surgeons. Methods of reconstruction used between the remnant pancreas and the intestine include end-to-side, with or without duct-to-mucosa anastomosis, end-to-end invagination styles, and arguably, anastomosis of the remnant pancreas with the stomach is also another method. Here, we review several safety trials and certain methods of treating the pancreatic stump after pancreaticoduodenectomy.

Received September 8th, 2011 - Accepted October 26th, 2011

Key words Pancreatic Fistula; Pancreaticoduodenectomy; Pancreaticojejunostomy; Reconstructive Surgical Procedures

Abbreviations ISGPF: International Study Group on Pancreatic Fistula

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COMPARISON OF SURGICAL METHODS

Definition of Pancreatic Fistula

The diagnosis of pancreatic fistula is suspected on the basis of many clinical or biochemical findings. In 2005, pancreatic fistula has been defined by the International Study Group on Pancreatic Fistula Definition (ISGPF) defined pancreatic fistula [19]. A broad definition begins with the criteria of the volume of drainage fluid output on or after postoperative day 3, with amylase content greater than 3 times for serum level. In addition, pancreatic fistula was classified according to three clinical grades: grade A, pancreatic fistula with no clinical impact; grade B, pancreatic fistula that requires specific treatment and a change in management or adjustment in the clinical pathway; and grade C, pancreatic fistula that requires a major change in clinical management or deviation from the normal clinical pathway. Since the initiation of clinical grading of pancreatic fistula as defined by the ISGPF, several authors, as shown in this review, have evaluated pancreatic fistula according to this classification. Several recent studies that have characterized pancreatic anastomotic failure after pancreatico-duodenectomy according to the ISGPF definition demonstrated operative complications-related ratios of grade B to C pancreatic fistula of 6.9-15% [20, 21, 22, 23].

Pancreaticojejunostomy

There are two widely used methods to accomplish an end-to-side pancreaticojejunostomy after pancreatico-duodenectomy: invagination pancreaticojejunostomy (or dunking the pancreatic remnant into the jejunum) or duct-to-mucosa pancreaticojejunostomy. Continuous duct-to-mucosa anastomosis is described as being safer and as having a significantly lower leakage rate [24, 25]. According to one prospective randomized trial [15], pancreatic fistulas were detected in 14% of patients; 13% in the duct-to-mucosa group and 15% in the invagination group, and the difference was not significant. In a more recent trial [18], the overall rate of pancreatic fistula was 17.8%, and the invagination method significantly decreased the rate of pancreatic fistula *versus* the duct-to-mucosa anastomosis (12% *vs.* 24%; P=0.04). In addition, in an analysis of the occurrence of pancreatic fistula in pancreatico-jejunostomy, 40% originated from the parenchyma or a small side-branch duct and appeared to be as common as that with duct-to-mucosa anastomosis [26]. In particular, with a soft pancreas, no pancreatic duct dilatation is usually detected; thus, duct-to-mucosa anastomosis might be difficult. However, with the invagination method, when covering the pancreas with the outer layer of intestine (Figure 1), fragile pancreatic tissue is often torn during suturing.

Pancreaticogastrostomy

Since several retrospective studies reported that pancreaticogastrostomy reduces the occurrence of pancreatic fistula after pancreaticoduodenectomy [27], there has been a trend toward increasing use of this type of anastomosis. In pancreaticogastrostomy, the anastomosis is made with the thick and richly vascular gastric wall, and it suppresses activation of proteolytic enzymes. Enterokinase in particular is required to convert trypsinogen to trypsin, the active form, and it is present in the mucosa of the small intestine but not in the gastric mucosa. This activation also requires a neutral pH. Therefore, even if leakage does occur, it does not lead to life-threatening complications because the pancreatic enzymes are hardly activated. Through use of this concept, the pancreatic fistula rate was reported to decrease clearly from 22% to 11%, and especially so in grade-C pancreatic fistula, where the rate dropped significantly from 6.7% to 1.4% [12]. However, this indicated pancreatic fistula rate itself is still high, and the results of a prospective randomized trial comparing pancreaticogastrostomy with pancreaticojejunostomy showed that the overall incidence of pancreatic fistula was 11.7%, and the condition occurred with similar frequency after pancreaticojejunostomy (11.1%) and after pancreatico-gastrostomy (12.3%) [28]. Length of postoperative hospital stay also did not differ between the two procedures. Because the objective safety of pancreaticogastrostomy was not supported by the data from these prospective studies and meta-analysis [29], the best method for dealing with the pancreatic stump after pancreaticoduodenectomy remains in question. In addition, disadvantages of pancreaticogastrostomy have been identified, including an increased incidence of delayed gastric emptying and of pancreatic duct obstruction due to overgrowth by the gastric mucosa. Available data on hormone levels indicate that endocrine function appears to be equal, but exocrine function appears to be worse after pancreatico-gastrostomy than after pancreaticojejunostomy,

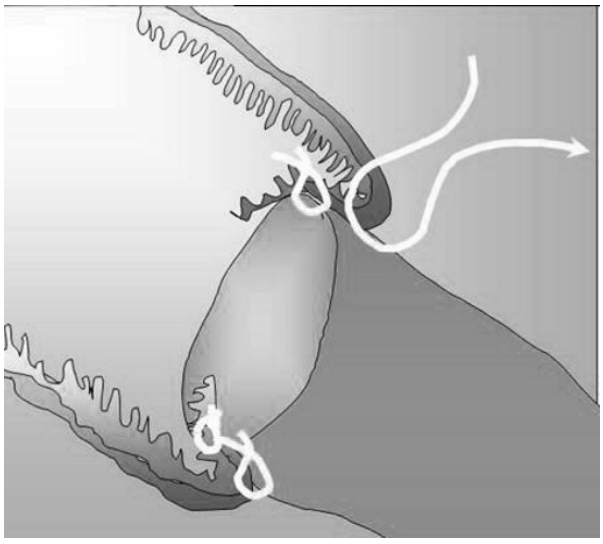

Figure 1. Problem in invagination method. Fragile pancreatic tissue is often torn during suturing when covering the pancreas with the outer layer of intestine (white arrow) with the invagination method.

resulting in severe atrophic changes in the remnant pancreas [30].

Reconstruction Types

Theoretically, there are several physiological and technical advantages of pancreaticojejunostomy. Mainly, two types of reconstruction procedures are performed with pancreaticojejunostomy: Billroth I (Imanaga method), comprising gastrojejunostomy, pancreaticojejunostomy, and choledochojejunostomy, and Billroth II (Whipple and/or Child method), comprising pancreaticojejunostomy or choledocho-jejunostomy and gastrojejunostomy. Billroth I reconstruction was most commonly performed, but more frequent anastomotic failure has been reported because the angularity of the jejunal loop might be related to these problems [31]. According to a report on the Billroth II method [25], use of the long isolated jejunal loop is associated with significantly lower pancreatic leakage rate and postoperative morbidity compared with the use of a short isolated jejunal loop (4.34% *vs*. 14.2% and 27.5% *vs*. 50.7%, respectively), and its overall mortality rate is 1.5%.

REDUCING PROBLEMS WITH THE PANCREAS STUMP ANASTOMOSIS

Because an adequate blood supply to the stump of the pancreas is critical to wound healing, the next step leading to a successful anastomosis [11], postoperative infusion planning must be supported. Although the use of somatostatin analogue was focused on to prevent pancreatic fistula in the past, its use is still not accepted by general consensus [32]. The use of early postoperative enteral nutrition has been demonstrated to reduce the incidence of pancreatic fistula after pancreaticoduodenectomy [33].

Many surgeons have placed a stent across the pancreaticoenterostomy, and a stent may be useful for diversion of pancreatic juice from the pancreatic anastomotic site, decompression of the remnant pancreas, and patency of the main pancreatic duct. Reported findings show no significant difference between internal and external stenting [34], whereas placement of drainage tube was associated with a clearly lower rate of pancreatic fistula compared with non-stented patients [6]. Due to the concern about length of hospital stay, shorter postoperative length of stay is not only considered a predictor of the use of less-invasive surgical procedures but also forces evaluation of the necessity of wound treatment or external drainage tube placement. A recent comparison study between non-stent and external stent use showed no improvement of these factors [35], and potential complications associated with stent removal were also recognized. Placement of a stent may be critical to reduce postoperative complications, but which is best, the internal or external type, is still being argued.

As consideration for replaced intra-abdominal (out of intestine) drainage tube removal, a randomized trial showed that early drain removal (on postoperative day 3) was associated with a decreased rate of pancreatic fistula (P=0.0001) and abdominal complications (P=0.002) compared with standard removal (postoperative day 5 or beyond) [36].

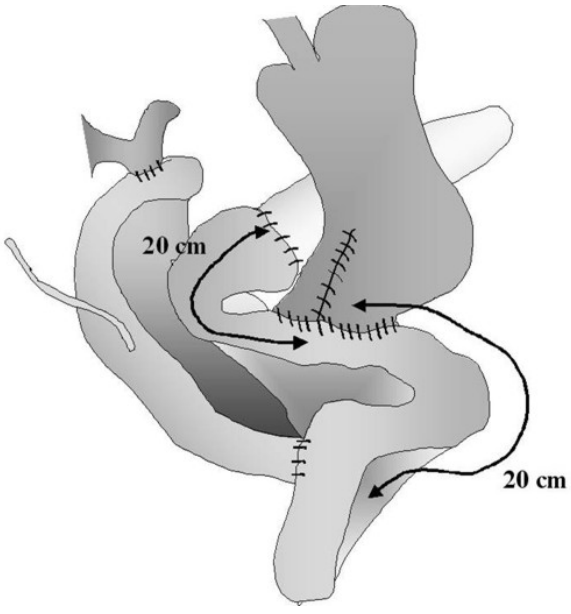

Figure 2. Schema of separated loop reconstruction method. The jejunum is reflected upward through an incision in the transverse mesocolon, and anastomosed end-to-side with the choledochus. At 20 cm distal to this biliary anastomosis, the jejunum is interrupted and the end of the pancreas is inserted into the bowel by means of an invagination technique. At 20 cm distal to this pancreatico-jejunostomy, the jejunum is anastomosed to the stomach in an end-to-side fashion. Approximately 20 cm distal to the gastrostomy, a Y-type reconstruction of the jejunum is made with the distal end of the biliary route.

NOVEL MODIFIED RECONSTRUCTION METHOD

Background

As suggested by the pathogenesis of the congenital choledochal cyst, reflux of pancreatic juice into the biliary tree could have an adverse effect on the bile duct wall. In particular, lysolecithin, which is converted from bile lecithin by pancreatic juice components, including phospholipase A, causes severe cellular injury. Phospholipase A itself is activated by lysolecithin, and these enzymes strongly interact. In Child's type reconstruction, one of the most common reconstruction methods, the hepatojejunostomy site is several centimeters distal to the pancreatico-jejunostomy site. Once leakage develops at the hepatojejunostomy site, the presence of pancreatic juice will exacerbate the leakage problem. A similar problem occurs with the Whipple method, in which the hepato- and pancreatico-jejunostomy anastomoses are reversed. Thus, the association of pancreatico-jejunostomy with life-threatening postoperative complications can be explained by the enzyme activation theory. Therefore, the safest type of anastomosis is one in which the mixture of pancreatic and biliary enzymes is contained, such as in a jejunojejunostomy. A novel modified type of reconstruction, the separated loop method, which

Table 1. Postoperative complication after pancreaticoduodenectomy. Modified results of the previous report [38] with recent cases.

	Reconstruction method		
	Imanaga	**Pancreaticogastrostomy**	**Separated loop method**
Required term of nasogastric tube (days; mean±SD)	5.2±4.8	9.2±8.4	1.1±1.4
Pancreatic fistula	19.2%	6.5%	5.1%
Mortality	3.7%	0	0

prevents pancreatic leakage and critical secondary complications, has been well tolerated (Figure 2).

Operative Procedure

The jejunum is transected at about 20 cm from Treitz's ligament, reflected upward through an incision in the transverse mesocolon, and anastomosed end-to-side with the choledochus by one layer of interrupted 4-0 polydioxanone surgical suture. At 20 cm distal to this biliary anastomosis, the jejunum is interrupted, and the end of the pancreas is inserted into the bowel by means of an invagination technique. The pancreatico-jejunostomy is made in two layers with interrupted sutures of 3-0 silk and 4-0 polydioxanone to hold the end of the pancreas in place in the invaginated bowel. At 20 cm distal to this pancreaticojejunostomy, the jejunum is anastomosed to the stomach in an end-to-side fashion. Approximately 20 cm distal to the gastrostomy, a Y-type reconstruction of the jejunum is made with the distal end of the biliary route. Biliary or pancreas duct drainage tubes are not necessary, and just one drainage tube is placed that is pulled out within 4 days after surgery. The full details were described previously [37].

Outcome

The separated loop method, as a Billroth II reconstruction, was evaluated at a single institution by comparison to pancreaticogastrostomy or the Imanaga method, as Billroth I reconstructions, according to postoperative patient condition determined from blood test values and complications incurred [37, 38]. Of 127 patients undergoing pancreaticoduodenectomy, 31 were selected for pancreaticogastrostomy, 26 for the Imanaga method, and 58 for the separated loop method. PG was achieved with an invagination anastomosis, which was constructed with two layers of interrupted sutures from an anterior gastrostomy and a pancreatic duct tube exiting through the stomach and abdominal wall.

There were no significant differences between pancreaticogastrostomy and the Imanaga and separated loop methods in terms of mean total blood loss, operation time, or changes in patient body weight. However, delayed gastric emptying was the most frequent cause of morbidity and was observed exclusively among patients undergoing pancreatico-gastrostomy (12.9%). Of the patients undergoing the Imanaga method, 19.2% showed a high amylase level in their drainage fluid, with 3.7% mortality due to abdominal bleeding after postoperative day 52. In 6.5% and 5.1% of the patients undergoing pancreatico-gastrostomy or the separated loop method, respectively, a high amylase level was detected, but no problematic clinical events were observed (Table 1). No patient required re-operation. Compared with the Imanaga method and pancreaticogastrostomy, values of postoperative blood tests were more favorable for the separated loop method. The postoperative condition of our patients who underwent separated loop reconstruction was good, suggesting that this method reduces the incidence of serious complications immediately after surgery.

More Recent Alteration for Pancreas Anastomosis

In the separated loop method, suturing of the anterior outer layer can lead to pancreas injury, especially with soft pancreas tissue; therefore, in recent cases, the anterior layer is made in single for incomplete invagination. Before beginning anterior layer suturing, two transpancreatic U-sutures are placed with 4-0 polydioxanone surgical suture (Figure 3). The U-suture needle is inserted from the anterior outside of the jejunum about 1 cm distal to the cut edge and is then withdrawn from the inside of the jejunum lumen. Ligation of the U-suture leads the pancreas stump into the jejunum with no strain on the edge of the pancreas [39]. We experienced no pancreatic fistula in 16 other patients with incomplete invagination of the pancreas stump. A greater number of cases must be accumulated to confirm the present findings and will be demonstrated in near future.

CONCLUSION

Certain reports have shown no clear evidence for or against one particular method of pancreaticoenteric

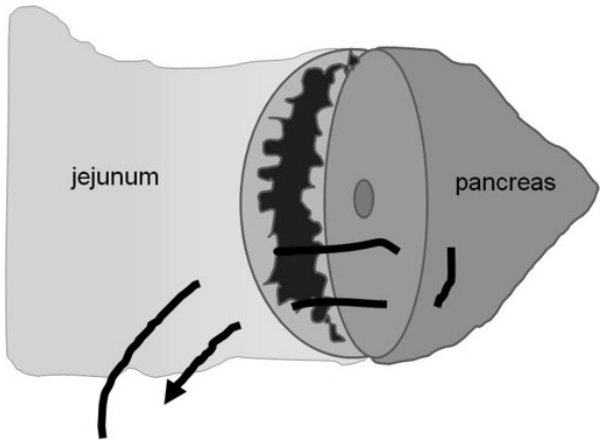

Figure 3. Pancreaticojejunostomy. The transpancreatic U-suture was needled from the anterior outside of jejunum to the cut edge.

anastomosis [40, 41]. The choice of pancreatic anastomotic method might be based on individual experience and adherence to basic principles such as good exposure and visualization; fine, non-strangulating suture placement to produce a patent, watertight anastomosis; and preservation of the blood supply [42]. As long as pancreaticoduodenectomy is performed, the argument for safety should be continued, and even for non-expert surgeons or in cases of soft pancreas texture, the favorite method of the surgeon that causes no anxiety will be chosen. There is still no agreement as to which reconstruction method is best, but early-term observation after pancreatico-duodenectomy indicates that the separated loop method might be superior to the other methods.

Conflict of interest The authors have no potential conflict of interest

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