

Application of a novel embeddedness-like pancreaticojejunostomy anastomosis technique used in pancreaticoduodenectomy

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Abstract. Optimized pancreaticojejunostomy anastomosis was used to investigate the effects on the incidence rate of postoperative complications in pancreaticoduodenectomy. The data of 250 patients who underwent pancreaticoduodenectomy between August 2011 and December 2015 were analyzed; all surgery was performed by a single team. The first 100 surgeries were performed using traditional pancreaticojejunostomy anastomosis, whereas the next 150 patients underwent novel pancreaticojejunostomy anastomosis (the experimental group). General information, disease status and the occurrence rate of postoperative complications [postoperative pancreatic fistula (POPF), biliary leakage, delayed gastric emptying, bleeding and mortality] within 30 days of surgery were observed. In the first group, 56 patients had POPF (56%), the proportion of grades A, B and C was 44% (n=44), 9% (n=9) and 3% (n=3), respectively; in the experimental group, 30 patients had POPF (20%), the proportion of grades A, B and C was 14.67% (n=22), 5.33% (n=8) and 0%, respectively. Furthermore, in the experimental group, none of the patients exhibited postoperative bleeding or succumbed during surgery. The application of the novel embeddedness-like pancreaticojejunostomy anastomosis technique in pancreaticoduodenectomy was safe and effective, and may reduce the incidence of POPF in future.

Introduction

Pancreaticoduodenectomy (PD) is the standard procedure used to treat patients with resectable tumors in the pancreatic head and periampullary regions (1). The postoperative mortality rate of this procedure has decreased to 1-4% owing

to the progression of surgical techniques; however, postoperative complication rates remain as high as 30-60% (2), of which the most alarming complication is the postoperative pancreatic fistula (POPF) (3). Previously, POPF has been considered to be the central connection of multiple postoperative complications, and is closely associated with increased rates of sepsis and mortality (4). A clinical grading system for POPF was introduced by the International Study Group for Pancreatic Fistula (ISGPF) to be associated with the severity of postoperative complications (5). It is divided into three grades, as follows: Grade A, grade B and grade C. Lowering the incidence rates of POPF effectively, in particular grade B and/or grade C POPF (5,6), is critical to decrease the degree of postoperative intervention treatment, reduce hospital stays and mortality rates (5). Of all the surgical steps in PD, pancreatic-enteric reconstruction is recognized as one of the most critical for postoperative recovery (7), thus the ideal pancreatic-enteric reconstruction must be convenient yet reliable. In the present study, a novel anastomosis technique designated embeddedness-like pancreaticojejunostomy technique (a technique which inlaid the pancreas into the intestinal stump) was employed to investigate the clinical utility of this novel technique and its effect on the incidence rate of postoperative complications.

Patients and methods

General information. Between August 2011 and December 2015, 250 consecutive patients from the Zhongshan Hospital of Fudan University (Shanghai, China) with benign or malignant tumors in the pancreatic head or periampullary region were registered and enrolled in the present study. Patients with distant metastasis at the initial diagnosis, past medical history of other kinds of tumors or increased value of bilirubin were excluded in this study. All patients underwent PD or pylorus-preserving PD (PPPD) by a single surgery team. Between August 2011 and August 2013, 100 patients (the first group), underwent PD or PPPD via the traditional interrupted end-to-end pancreaticojejunostomy anastomosis; between August 2013 and December 2015, the remaining 150 patients underwent PD or PPPD, using the novel pancreaticojejunostomy anastomosis technique, termed the novel embeddedness-like pancreaticojejunostomy anastomosis technique. The present study was approved by the ethics committee of Fudan University and

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performed in accordance with the ethical guidelines of The Declaration of Helsinki (8). Written informed consent was obtained from each participant.

Surgical procedures and pancreatic-enteric reconstruction. Radical PD was performed for the patients with malignant tumors, whereas PD was performed for the patients with benign tumors. Of the 250 patients, the first 100 patients underwent the one-layer interrupted end-to-end pancreaticojejunostomy anastomosis technique, which included the following procedures: End-to-end Child's pancreaticojejunostomy by interrupting sutures in one layer; end-to-side choledochojejunostomy by interrupting sutures in one layer and end-to-side gastrojejunostomy by running sutures in one layer (9). The latter 150 patients to undergo pancreatic-enteric anastomosis underwent Child's PD, a type of PD that is different from the traditional Whipple procedure, and involves the anastomosis of the pancreas and jejunum (10), with the aforementioned novel technique, which consisted of certain specific operating procedures. Approximately 4 stitches were applied for the interrupted closure of the residual pancreas. During the operation period, the diameter of the pancreatic duct was measured and a plastic stent with a diameter between 2-5 mm was selected accordingly (Fig. 1). Subsequently, one end of the stent was inserted into the pancreatic duct and anchored by absorbable sutures, and the other end was inserted into the jejunum 10 cm from the choledochojejunal anastomosis (Fig. 2A). The edge of the residual pancreas and the tissue 2 cm away from the cut margin of the jejunum were then stitched together with two sutures and consolidated with another two sutures for embedding (Fig. 2B). Interrupted anastomosis was performed between the monolayer of the pancreatic envelope and all layers of the jejunum (Fig. 2C). Notably, the intrapancreatic duct tubes were not inserted into the jejunum in the first group.

Placement of drainage tubes. During surgery, a suction drain was placed beneath the pancreaticojejunal anastomosis (to test the level of amylase), exiting the right side of the abdomen. A drain was also placed over the pancreaticojejunal anastomosis and behind the gastrojejunal anastomosis, exiting the left side of the abdomen. A further suction drain was placed behind the hepaticojejunal anastomosis, exiting the right side of the abdomen. All suction drains were connected with multi-hole latex tubing (11).

Postoperative management. Patients were regularly managed and were transferred to normal wards if the condition was stable following surgery. In the postoperative period, the nasogastric tube, which drained the digestive juice, was removed if gastrointestinal function was recovered; oral diet gradually continued if no complications, including delayed gastric emptying (DGE) (12) or POPF, occurred. The volume of drainage was measured daily and amylase levels were tested on postoperative days 3 and 6 (the value was tested from the juice of drainage tube). On day 7 following surgery, if the outputs were less than 20 ml per day, fluid amylase levels were normal and no evident hydrops were detected on the abdominal computed tomography (CT) images, the drainage tubes were removed.

Definition of postoperative complications. According to the proposal of the ISGPF (5), POPF was defined as the output of any measurable volume of drainage fluid from an surgically placed drain on or after postoperative day 3, with an amylase content >3 times the upper normal serum value (specifically >690 U/l; normally <230 U/l). Grade A POPF: No clinical signs or symptoms were observed, except for the elevated fluid amylase level. Grade B POPF: Classical clinical manifestations were common and signs of organ dysfunction may be present; usage of antibiotics, nutritional support and sufficient drainage were required. Grade C POPF: The patient's condition was generally worse, with severe sepsis and organ failure that may lead to mortality, in which surgical interventions were required.

Biliary leakage was defined as the presence of bile-like fluids from drainage tubes near the hepaticojejunal anastomosis, with a drainage output ≥ 50 ml per day for >3 days. DGE was confirmed when the nasogastric tube was maintained for ≥ 10 days with an output ≥ 800 ml per day, or patients vomited following the removal of the nasogastric tube and required reinsertion (excluding intestinal obstruction, anastomotic stenosis or other mechanical factors). Bleeding was identified as the presence of hemorrhagic fluids from intra-abdominal drains or the nasogastric tube with a progressive decline of hemoglobin (measured via regular bloodtest) for which a transfusion of three units of blood in 24-48 h or emergency surgical hemostasis was required. Wound infection was defined as erythema and induration of a wound with purulent discharge and with a positive bacterial culture. Pulmonary infection was constituted by the presence of pneumonia or atelectatic alterations on radiographs associated with a positive sputum bacterial culture.

Study endpoints. The primary study endpoints of the present study were the incidence or C grade POPF. The endpoint was defined as; once the fistula occurred, it was managed accordingly. The recorded POPF grade in the present study were measured as the grade observed once the POPF was stabilized. Secondary endpoints were the rates of other postoperative complications, in-hospital mortality and the duration of postoperative hospital stay.

Data collection and statistical analysis. Demographic and clinical data, details of the surgical process, pathological diagnosis, postoperative course and complications were documented. The pancreatic ducts were divided into dilated and non-dilated ducts, according to preoperative CT or magnetic resonance imaging results. The texture of remnant pancreatic tissue was segmented into soft or fibrotic on the basis of intraoperative judgment. All data was imported into the computer and a database was established. The statistical analysis was performed using SPSS 16.0 statistical software (SPSS, Inc., Chicago, IL, USA). Continuous data were expressed as the mean \pm standard deviation. Comparisons of continuous variables were performed using Student's t-test, and comparisons of categorical variables were performed using χ^2 test or Fisher's exact test where appropriate. All statistical tests were two sided, and $P < 0.05$ was considered to indicate a statistically significant difference.

Results

The clinical data of the 250 patients that underwent PD are listed in Table I. According to the definition of pancreatic fistula proposed by the ISGPF, in the experimental group, 30 patients (20%) developed pancreatic fistula in this group, including 22 grade A fistulas (14.67%), 8 grade B fistulas (5.33%), but no grade C pancreatic fistula developed in this group, as presented in Table II. All fistulas healed spontaneously or following conservative treatment. A total of 3 patients developed a biliary fistula in this group, which healed following enhanced drainage; 5 patients developed DGE, of which all patients were cured following conservative treatment. No patients exhibited postoperative bleeding in this group. Compared with the experimental group of patients, the traditional group 56 patients experienced POPF (56%), with the number of patients with grade A, B and C fistulas 44, 9 and 3, respectively ($P < 0.001$; Table II). Of the 3 patients suffering from grade C POPF, 2 were concomitant with postoperative bleeding. In addition, compared with the novel anastomosis, 4 patients developed biliary fistula ($P = 0.681$) in this group and 6 patients developed DGE ($P = 0.712$).

Discussion

The perioperative mortality rate of PD has declined to $< 5\%$ in the past decade owing to advances in technology; however, the postoperative complication rate, in particular the rate of pancreatic fistula, has not declined effectively (13). The reported incidences of pancreatic fistula range between 5 and 50%, depending on the definition of pancreatic fistula (14). Therefore, the pancreatic fistula remains one of the major problems that pancreatic surgeons encounter; it is a problem that may affect the smooth completion of pancreatic surgery and improved recovery following surgery. A randomized contrast study conducted by de Castro *et al* (15) demonstrated that the major complications of PD, including intra-abdomen hemorrhage, abdominal abscess, sepsis and even mortality, were associated with POPF. Pancreatic-enteric reconstruction has been regarded as a complex anastomosis, and is even known as the first anastomosis employed by pancreatic surgeons. Therefore, to reduce POPF effectively, particularly grade C POPF, by reducing secondary complications is of surgical interest.

Certain variations between the two groups examined in the present study include: i) The internal stenting of pancreaticojejunostomy, ii) the suture patterns of the anastomosis and iii) the embeddedness form of the novel pancreaticojejunostomy. All three steps were necessary to the novel procedure. A systematic evaluation performed in a previous study (16) concluded that the internal stenting of pancreaticojejunostomy had no significant effect on preventing the formation of postoperative pancreatic fistula; therefore, an intra-pancreatic stent was not employed in the PD steps. However, when the PD procedure was conducted in the experimental group (between August 2013 and December 2015), the implanting of an internal stent was performed during anastomosis due to the essential nature as a part of the novel technique. Collectively, the data produced in the present study has shown that there was a decrease in the incidence rates of postoperative complications using the basis of the three aforementioned steps.



Figure 1. Schematic diagram of the intra-pancreatic drainage tube.

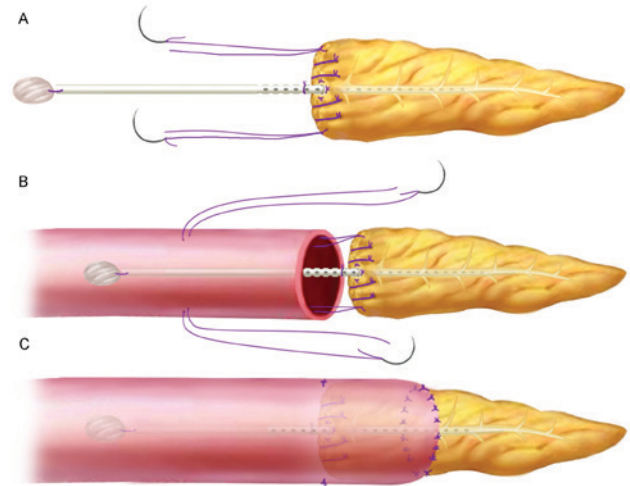


Figure 2. Surgical steps of the novel embeddedness-like pancreaticojejunostomy anastomosis. (A) One end of the stent was inserted into the pancreatic duct and the other end was inserted into the jejunum 10 cm from the choledochojunal anastomosis. (B) Edge of the residual pancreas and the tissue 2 cm away from the cut margin of the jejunum were stitched together with two sutures and consolidated with another two sutures for embedding. (C) Interrupted anastomosis was performed between the monolayer of the pancreatic envelope and all layers of the jejunum.

In recent years, the technique and efficiency of the pancreaticojejunostomy has markedly improved. The methods of pancreatic-enteric reconstruction are listed as follows: End-to-side pancreaticojejunostomy, duct-to-mucosa pancreaticojejunostomy, end-to-end invagination pancreaticojejunostomy, bundled pancreaticojejunostomy and side-to-side pancreaticojejunostomy (3). End-to-end invagination pancreaticojejunostomy involves the invagination of the whole residual pancreas into the jejunum, which is simple to perform, but its reliability is unclear. End-to-side pancreaticojejunostomy has the advantages of strong suitability for varying sizes of residual pancreas by ensuring the diameter of pancreas to match the jejunum; however, the limited marginal space into the jejunum required each suture to be stitched firmly (17). Duct-to-mucosa pancreaticojejunostomy includes the direct anastomosis between the pancreas and jejunum in the mucosal layer, which is advantageous as there is no size restriction for the residual pancreas; however, the technique is difficult to perform. Providing that pancreatic ducts are normal, microsurgical methods are required to complete anastomosis. Bundled pancreaticojejunostomy is characterized by the insertion of the pancreatic stump into the jejunum, with the pancreas and jejunum being bundled into a surrounding position. The mucosa of the jejunum are removed providing the residual pancreas and enteric cavity are mismatched; side-to-side pancreaticojejunostomy is commonly applied for the patients suffering from chronic pancreatitis concomitant with a dilated main-pancreatic duct (≥ 10 mm), pancreatolithiasis and persistent pain. It has been reported that there are numerous pancreaticojejunostomy methods. A systematic review performed by Lai *et al* (18)

Table I. Clinicopathological characteristics of 250 pancreaticoduodenectomy patients.

Category	Traditional anastomosis	Novel anastomosis
Age, years ^a	63.27±12.67	60.44±14.38
Sex, male/female	52/48	70/80
Jaundice (n)	56 (56)	86 (57.3)
PD, n (%)	20 (20)	20 (13.3)
PPPD, n (%)	80 (80)	130 (86.7)
Pathological types		
Malignant neoplasms of pancreatic head, n (%)	45 (45)	72 (48)
IPMN, n (%)	14 (14%)	22 (14.7%)
Inflammatory lesions of pancreatic head, n (%)	1 (1%)	2 (1.3%)
Distal common bile duct carcinoma, n (%)	8(8%)	5 (3.3%)
Duodenal papillary carcinoma, n (%)	12 (12%)	15 (10%)
Benign tumor, n (%)	20 (20%)	29 (19.3%)
Other tumor, n (%)	0 (0)	5 (3.3%)
End-to-end anastomosis by disrupted sutures in one layer, n (%)	100 (100%)	150 (100%)
Texture of pancreatic stump		
Soft, n (%)	45 (45%)	69 (46%)
Fibrotic, n (%)	55 (55%)	81 (54%)
Dilated pancreatic duct, n (%)	59 (59%)	82 (54.7%)
Usage of somatostatin, n (%)	25 (25%)	42 (28%)
Operation time, min ^a	172±70.14	193.12±54.38
Amount of intraoperative bleeding, ml ^a	145±123.34	133.12±160.78
Average hospital stay, days	16.5	14.5

^aData presented as mean ± standard deviation. PD, pancreaticoduodenectomy; PPPD, pylorus preserving PD; IPMN, intraductal papillary mucinous neoplasm.

Table II. Complications following pancreaticoduodenectomy.

Complication category	Traditional anastomosis, n (%)	Novel anastomosis, n (%)	P-value
Pancreatic fistula grade			<0.001
Grade 0	44 (44)	120 (80.00)	
Grade A	44 (44)	22 (14.67)	
Grade B	9 (9)	8 (5.33)	
Grade C	3 (3)	0	
Biliary fistula	4 (4)	3 (2.00)	0.681
Delayed gastric emptying	6 (6)	5 (3.33)	0.712
Bleeding	2 (2)	0	NS

NS, not significant.

revealed that certain surgical factors, including surgical (PD versus PPPD) and anastomosis types (pancreaticojejunostomy versus pancreaticogastrostomy), internal duct stents have not been reported to be associated with statistically significant incidence rates of POPF. Finding a method to prevent POPF in pancreatic intestinal anastomosis is one of the primary problems faced by current pancreatic surgeons. However, appropriate matching methods and effective anastomosis

techniques serve as vital means for decreasing the occurrence of pancreatic fistula. A systematic review demonstrated that no pancreatic reconstruction technique was applicable to all types of pancreatic remnants (13). In order to release the pancreas, careful hemostasis must be performed to ensure a sufficient blood supply, correctly matching intestinal sizes and residual pancreatic tissue, and practical and reliable stitching are all effective measures to prevent pancreatic fistula.

Notably, certain issues must be addressed during the clinical practical application of the novel procedure: i) There was a higher possibility of mismatch of aperture sizes between the pancreatic residual end and jejunum end in all 150 patients that underwent end-to-end pancreaticojejunostomy. Exhibiting a great degree of elasticity, the jejunum may be suitable for the residual pancreas to set into it; however, if the size gap between the pancreas and jejunum are too great, side-to-end anastomosis should also be considered. During surgery, the diameter of the pancreatic duct was measured and a plastic stent with the correct diameter, ranging between 2 and 5 mm was selected accordingly. One end of the stent was inserted into the pancreatic duct and anchored by absorbable sutures; the other end was inserted into the jejunum, 10 cm from the choledochojejunal anastomosis. ii) Difficulties in detecting the main pancreatic duct may be due to the thinness of the main pancreatic duct, anatomical variation, and the incorrect ligation of the pancreatic duct due to electrocoagulation and hemostasis, respectively. On account of these surgical challenges, pancreatic surgeons should be familiar with the anatomical location of the pancreatic duct, avoid excessive heat when cutting off the pancreas and press on the pancreatic tail to determine the location of main duct by observing the spill of pancreatic juice. Of the 150 cases of PD in the present study, all pancreatic ducts were identified and intubated successfully; the hemostasis of the remnant pancreas may be conducted by electrocoagulation. Furthermore, the interrupted suturing that was performed not only effectively prevented bleeding of the remnant pancreas, but may also have minimized the occurrence of pancreatic leakage.

For the novel technique, as the pancreatic ducts were intubated in advance, suturing the wound surface could be performed with ease. Anastomotic blood supply is a precondition for the healing of pancreatic anastomosis; providing the distance between the remnant pancreas and the jejunum edge is 1 cm, the remnant pancreas can be intubated into the jejunum. However, the mucosa of the end of the jejunum should be reserved to ensure an adequate blood supply, which can be ensured via the interrupted suturing of end-to-end pancreaticojejunostomy anastomosis.

In conclusion, the present study demonstrated that the application of the novel embeddedness-like anastomosis in PD did not decrease the overall incidence of POPF; however, the incidence of high-grade POPF was decreased, therefore reducing the rate of severe postoperative morbidity.

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