Shen’s Whole-Layer Tightly Appressed Anastomosis Technique for Duct-to-Mucosa Pancreaticojejunostomy in Pancreaticoduodenectomy

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Background: Postoperative pancreatic fistulas (POPFs) due to anastomotic leaks are always closely related to significant morbidity and mortality following pancreaticoduodenectomy (PD). A series of modified anastomotic methods have been proposed. The object of our study was to provide a novel anastomotic method for operations involving the Child technique, termed the "whole-layer tightly appressed anastomosis technique".

Material/Methods: An improved pancreatic whole-layer suture technique was used when we performed the duct-to-mucosa pancreaticojejunoanastomosis; this method ensured the tight joining of the pancreatic stump and jejunum and decreased the pinholes in the pancreatic stump. This new method was used in 41 patients, and was compared with the traditional duct-to-mucosa anastomosis technique that was used in 50 patients as controls.

Results: The POPF rate was much lower in the new method group than in the control group (6, 14.63% and 20, 40.00%, respectively, P=0.010). There were 5 grade A POPF patients and 1 grade B POPF patient in the study group. In the control group there were 12 grade A POPF patients, 7 grade B POPF patients, and 1 grade C POPF patient. The study group exhibited a lower morbidity rate (7, 17.07% vs. 16, 32.00%, P=0.022) and a reduced hospital stay (17.16 d vs. 22.92 d, P=0.001).

Conclusions: The whole-layer tightly appressed anastomosis technique presented in our study is a safer anastomotic method than the traditional duct-to-mucosa pancreaticojejunostomy technique. This new technique effectively reduced the incidence of POPF after PD and decreased the postoperative morbidity.

MeSH Keywords:
Pancreatic Fistula • Pancreaticoduodenectomy • Pancreaticojejunostomy

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Background

Kausch performed the first pancreaticoduodenectomy (PD) in 1909 [1]. Whipple evolved this operation and made it a standard procedure in the 1940s [2]. To date, this operation has remained the only potential approach for the radical cure of pancreatic head or peripancreatic benign or malignant lesions. PD considerably promotes the survival time of patients with pancreatic head or peripancreatic malignancies. However, this technique is still complex and difficult for surgeons due to its high rate of complications, especially those resulting from postoperative pancreatic fistulas (POPFs) due to the pancreaticoenteric anastomosis. POPFs can lead to intra-abdominal infections, sepsis, and intra-abdominal hemorrhages, and it accounts for most of the postoperative deaths [3,4]. Over the past 70 years, many surgeons have provided various types of modified techniques for pancreaticojejunoanastomosis to prevent POPF [5]. Although POSFs have considerably decreased with the evolution of operative techniques, the occurrence of pancreatic fistulas remains approximately 4%–30% based on multiple center reports [6,7]. The morbidity rate after PD has remained high, in the range of 38–58.5%, over the past 2 decades [8]. At present, the duct-to-mucosa (DMA) pancreaticojejunoanastomosis and end-to-end techniques are the 2 primary methods of anastomosis. There is still no consensus regarding the best method to reduce the incidence of POPF following PD. POPFs appear to be inevitable.

In 2014, our group established the whole-layer tightly appressed anastomosis method, which was a new technique for duct-to-mucosa pancreaticojejunoanastomosis following PD. We achieved fairly good results. At present, this technique has been used in 41 patients who have undergone PD. The safety, feasibility, and increased satisfaction associated with this technique for preventing POPF have been demonstrated by our perioperative outcomes. In this retrospective article, we elucidate this new technique and compare it with the traditional standard duct-to-mucosa method to demonstrate its clinical efficiency.

Material and Methods

Patients

A total of 91 patients were included in this retrospective study. From March 2014 to June 2015, we performed the whole-layer tightly appressed technique in 41 patients (study group) after PD and utilized the standard duct-to-mucosa method in 50 patients (control group). The patients were selected randomly and informed consents were obtained from all 91 patients. Perioperative data were retrieved for all patients. Pathology information was collected from the pathology reports. The same team completed all operations. The patients in the control group exhibited no significant differences in age, sex, or BMI from the study group (Table 1). All patients had total serum total bilirubin levels below 300 μmol/L, unless they accepted endoscopic retrograde cholangiopancreatography (ERCP) or biliary drainage. Among the 91 patients, 79 patients were diagnosed with a malignant disease, including carcinoma of the pancreatic head in 55 patients, adenocarcinoma of ampulla in 4 patients, adenocarcinoma of the duodenum in 8 patients, pancreatic neuroendocrine tumors in 11 patients, and pancreatic undifferentiated carcinoma in 1 patient. Twelve patients were diagnosed with benign lesion, including intraductal papillary mucinous neoplasm (IPMN) in 5 patients, solid-pseudopapillary tumor of pancreas (SPT) in 1 patient, adenoma of the ampulla in 3 patients, adenoma of the duodenum in 1 patient, pancreatic serous cystadenoma in 1 patient, and chronic pancreatitis in 1 patient. Of the 91 patients, 15 patients (16.48%) were classified as having diabetes mellitus (DM).

Before the operations, all patients underwent ultrasonography, computed tomography (CT) or magnetic resonance imaging (MRI), and other essential tests to locate the tumor and rule out surgical contraindications.

Definition of POPF

In our center, amylase activity in the drain tube is routinely measured every other day beginning on day 3 after the operation.
and continuing until the drain tube was removed. According to the International Study Group on Pancreatic Fistula (ISGPF) criteria[9], POPF was defined as “a drain output of any measurable volume of fluid on or after postoperative day 3 with an amylase content greater than 3 times the serum amylase activity”. Grade A POPFs are also termed “transient fistulas” not needing treatment or extra hospital stays. Grade B POPFs require nothing by mouth (NPO), enteral or parenteral nutrition, and long-term drain maintenance; CT scans may show abdominal collection(s), and grade B POPFs are always combined with sepsis that requires antibiotic treatment. Grade C POPFs are the most dangerous and always result in intra-abdominal collections, sepsis, and multiple organ failure, and require supervision in the intensive care unit (ICU) and reoperation.

**Surgical techniques**

Standard PD(s) were performed in all patients. The pancreas was transected with margins at least 2 cm from the tumor. After the specimen was removed, we performed anastomotic reconstruction in the following sequence: end-to-side duct-to-mucosal PJ (interrupted anastomosis), end-to-side choledochojejunostomy, and end-to-side gastrojejunostomy. Biliopancreatic reconstruction was performed using a loop of the jejunum that was brought up through the retrocolic route in all patients.

**Whole-layer tightly appressed technique**

**Pancreatic stump preparation**

The pancreas was dissected with an electric knife. The posterior wall of the stump was mobilized for nearly 2–3 cm to facilitate suture placement, and we performed careful hemostasis. The pancreatic duct was identified by inspection or with the gentle use of a probe. We measured the diameters of the pancreatic ducts and chose suitable stents for draining the pancreatic juice. All procedures were assisted by the use of magnifying loupes. Finally, we put staying sutures on the inferior and superior borders of the pancreatic stump.

**Posterior row of the outer layer of the anastomosis**

The single loop was approximated to the pancreatic stump to do the pancreaticojejunostomy. The outer-layer suturing was performed with double-needle 3-0 Prolene line (Prolene TM; Ethicon; Johnson & Johnson; New Jersey, USA) continuous suturing of the pancreatic parenchyma and the seromuscular layer of the jejunum. The intestinal margins and pancreatic margins were 1 cm, and the needle spacing was approximately 0.5 cm. Next, we tied the Prolene with relatively low tension.

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**Figure 1.** (A) First, we pushed the needle through the O-ring at full thickness in the jejunum. Next, we pushed the needle through the epithelium of the main pancreatic duct and then pulled the needle out from the pancreatic serosa to include the whole layer of the pancreatic parenchyma. (B) The treatments of the upper and lower sides of the pancreatic parenchyma. We first pushed the needle out from the middle of the pancreatic parenchyma and then inserted the needle in situ and pulled it out from the pancreatic serosa.
Opposing to the pancreatic duct, an enterotomy (2–3 mm in diameter or appropriately enlarged based on the diameter of the main duct) was made at the jejunum (O-ring) via electrocautery (Figure 2A). First, we put the needle through the epithelium of the main pancreatic duct and then pulled the needle out from the pancreatic serosa, including the entire layer of the pancreatic parenchyma (Figure 1A, Figure 2B). Second, we placed the needle through the O-type ring at its full thickness in the intestinal wall. Then we tightened the needle and finished 1 suture. Five interrupted 5-0 sutures (Prolene) were placed; 1 suture in the middle and 2 on each side. Notably, because the upper and lower sides of pancreatic parenchyma were relatively thick, we first pulled the needle out from the middle of the pancreatic parenchyma and then inserted the needle in situ and pulled it out from the pancreatic serosa (Figure 1B). These needles can subsequently be tightened. Then, a matching stent tube (ventricular drainage tube, based

**Posterior row of the inner layer (the whole-layer tightly appressed anastomosis technique)**

we placed the needle through the O-ring was approximately 2–3 mm. (B) The suturing of the posterior row of inner layer of the anastomosis. The needle went through the whole layer of the pancreatic parenchyma. We utilized the interrupted suturing method. (C) The insertion of the stent tube. (D) The suturing of the anterior row of inner layer of the anastomosis. (E) Completing the suturing of inner layer.

Figure 2. Intraoperative photographs of the formation of the pancreaticojejunostomy anastomoses. (A) The enterotomies were made with electrocautery. The diameter of the O-ring was approximately 2–3 mm. (B) The suturing of the posterior row of inner layer of the anastomosis. The needle went through the whole layer of the pancreatic parenchyma. We utilized the interrupted suturing method. (C) The insertion of the stent tube. (D) The suturing of the anterior row of inner layer of the anastomosis. (E) Completing the suturing of inner layer.
Results

A total of 91 consecutive patients from March 2014 to Jun 2015 underwent PD performed by the same surgical team. All operations were completed successfully and included 41 operations using whole-layer suturing technique and 50 standard duct-to-mucosa pancreaticojunostomies. There were no significant differences in age, sex, BMI, incidence of diabetes mellitus (DM) (Table 1), preoperative serum total bilirubin, or peripancreatic factors, such as operating time, blood loss, blood transfusion rate intraoperative, pancreatic texture, tumor size, or the presence of malignancy on histology (Table 2).

POPF rate and morbidity

Incidence of POPF

The overall POPF rate was 28.57% (26/91). The incidence of POPF in patients who underwent operations with the whole-layer suturing technique (study group) was 14.63% (6/41) and that in the patients who underwent standard DMA (control group) anastomosis was 40.00% (20/50, p = 0.010; Table 2). Grade A POPF was observed in 4 patients (5/41 12.20%) in the study group and in 10 patients (12/50, 24.00%) in the control group. Grade B POPFs were observed in 1 patient in the study group (2.43%) and 7 patients (14.00%) in the control group. The presence of Grade C pancreatic fistula was noted in 1 patient (2.00%) in the control group. There was a significant difference in the POPF rate between the study group and the control group (P = 0.010). Moreover, the study group had less Grade B and C pancreatic fistulas than in the control group (2.43% vs. 16.00%, respectively, P = 0.038).

Additionally, variables including age, sex, BMI, level of serum bilirubin, incidence of DM, operating time, blood-loss, histological tumor type, and pancreatic texture, were not associated with the occurrence of POPFs (Table 3). Some reports have come to the conclusion that patients whose main pancreatic ducts are ≤3 cm are at a greater risk of POPF [10], but no significant differences were observed in our study (Table 3). Interestingly, we found that the intraoperative blood transfusion affected the occurrence of POPF (Table 3). Patients who accept intraoperative blood transfusion might have an increased risk of POPF (Table 4). In addition, our study included both benign and malignant cases, so we did not add the peritumoral invasion and peritumoral metastatic lymph nodes to the risk factors to prevent bias [11].

Postoperative morbidity and mortality

The study group had a much lower morbidity rate than in the control group (7/41, 17.07% vs. 16/50, 32.00%, respectively, P = 0.022). Furthermore, there were significant differences in the

on the diameter of the main pancreatic tube, 1–2 cm longer than the length of pancreatic duct of distal stump) was inserted in the pancreatic duct and jejunal lumen after the posterior side of the inner layer was completed (Figure 2C).

Anterior rows of inner and outer layers of the anastomosis

The inner layer and outer layers were completed with the same method described previously. The inner layer was completed with four or five 5-0 interrupted Prolene sutures (Figure 2D, 2E). The outer layer was completed with the additional continuous 3-0 polypropylene sutures.

Traditional DMA Anastomosis

In the control group, the posterior outer row of 3-0 Prolene sutures was placed as we described previously. We held the sutures with tension, and the pancreatic duct was then identified. A small, full-thickness jejunotomy was then created via electrocautery opposite the pancreatic duct. The posterior inner layer was then created using 6-0 Prolene sutures. In the conventional method, we placed the needle through the pancreatic duct, including the pancreatic parenchyma (inner 1/3 of the radius). A matching stent tube was inserted in the pancreatic duct and jejunal lumen. The anterior layers of the PJ were performed in the reverse order and in the same manner.

Other anastomoses

End-to-side hepaticojejunostomy and side-to-side gastrojejunostomy were performed sequentially. The gastrojejunostomy was performed behind the transverse colon. After completing all 3 anastomoses, 2 double-lumen drains were placed in the vicinity of the pancreatic anastomosis and the biliary-enteric anastomosis.

Postoperative patient care

The amylase in the drain output was routinely measured beginning on postoperative day 3 and continuing every 2 days until the tube was removed. CT scans were typically performed on days 5–7 after the operation to evaluate whether any intra-abdominal collections were present and to select the follow-up therapeutic regimen.

Statistical analyses

The continuous variables are expressed as the means (±SDs) and were compared with Student’s t test. The chi-square test was used to compare the categorical data. P values less than 0.05 were considered to be significant. We analyzed the data using SPSS 19.0 (IBM Co., Armonk, NY, USA).
time of oral intake (5.11 d vs. 7.20 d, P=0.005), time of drainage tube removal (11.55 d vs. 17.83 d, P=0.008), and postoperative hospital stay (17.16 d vs. 22.92 d, P=0.001). Five out of 6 patients in the study group and 15 of 16 patients in the control group had complications of Clavien-Dindo grade 1 or 2. There was one grade 3 complication in the study group. One patient experienced a transient intra-abdominal hemorrhage on the 7th day after the operation and recovered with NPO, a continued somatostatin injection pump, parenteral nutrition, and other symptomatic treatments. Another grade 3 complication occurred in the control group. A patient accepted reoperation due to an intra-abdominal hemorrhage and uncontrolled hemorrhagic shock (Table 5). However, in the absence of complications, the postoperative stays, times of oral intake, and times of drainage tube removal were similar in the study and control groups (Table 2).

### Discussion

Despite advances in surgical technique and perioperative treatment, POPF remains the most common and problematic complication following PD, and POPF is also the main reason for postoperative mortality. The postoperative complication rate remains high, varying from 20% to 60% [12]. With the marked improvement in postoperative outcomes of PD in recent years, postoperative morbidity has considerably decreased [13]. Some large centers can even control their postoperative morbidities by approximately 5%. POPF can worsen the clinical outcomes of patients who have undergone PD. The Mannheim Clinic series demonstrated that 20% of POPFs were directly responsible for the postoperative deaths [4]. Therefore, surgeons have been working to reduce POPFs in recent decades. To reduce

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**Table 2.** Intraoperative data and postoperative outcomes.

| Event                          | Study group | Control group | P value |
|--------------------------------|-------------|---------------|---------|
| Operating time (min)           | 234.50±44.12 | 252.32±49.94 | 0.062*  |
| Blood loss (ml)                | 351.46±407.42 | 454.00±352.95 | 0.202*  |
| Time of anastomosis (min)      | 15.73±1.75  | 15.48±1.79   | 0.057*  |
| Blood transfusion              | 10          | 21           | 0.078** |
| Tumor size (cm)                | 3.12±1.48   | 3.65±1.73    | 0.210*  |
| Malignant/Benign               | 33/8        | 46/4         | 0.128** |
| POPF                           | 6           | 20           | 0.010** |
| Grade A                        | 5           | 12           |         |
| Grade B                        | 1           | 7            |         |
| Grade C                        | 0           | 1            |         |
| Grade B+C                      | 1           | 8            | 0.038** |
| Diameter of pancreatic duct ≤3 cm | 26        | 36           | 0.382** |
| Soft pancreas                  | 15          | 23           | 0.467** |
| Complication                   | 7           | 16           | 0.022** |
| Grade 1–2                      | 6           | 15           |         |
| Grade 3–5                      | 1           | 1            |         |
| Reoperation                    | 0           | 1            | 1.000** |
| Time of intake                 | 6.29±2.14   | 9.50±4.94    | 0.116*  |
| Time of drain-tube-off (d)     | 15.76±7.04  | 22.92±8.20   | 0.001*  |
| No. of complications           | 7           | 16           |         |
| Time of intake                 | 6.29±2.14   | 9.50±4.94    | 0.116*  |
| Time of drain-tube removal     | 24.86±12.20 | 20.94±9.57   | 0.415*  |
| Postoperative stay             | 23.43±9.40  | 28.63±8.97   | 0.221*  |

POPF = post-operative pancreatic fistula. * Unpaired t test; ** chi-square test; # data for patients with postoperative complications.
In the present study, we introduced a new technique for duct-to-mucosa pancreatocjejunostomy anastomosis and compared this technique with the standard pancreatocjejunostomy. The operating time, blood loss, transfusion rate, and time of anastomosis of the new technique were not increased relative to those in the control group. These findings indicate that our surgical technique is one of the most important factors.

In the present study, we introduced a new technique for duct-to-mucosa pancreatocjejunostomy anastomosis and compared this technique with the standard pancreatocjejunostomy. The operating time, blood loss, transfusion rate, and time of anastomosis of the new technique were not increased relative to those in the control group. These findings indicate that our surgical technique is one of the most important factors.

### Table 3. Risks for POPF.

| Event                              | POPF (n=26) | Non-POP (n=65) | P value |
|------------------------------------|-------------|----------------|---------|
| Age (y)                            | 58.35±11.25 | 57.89±13.47    | 0.880*  |
| Sex (male/female)                  | 19/7        | 43/22          | 0.522*  |
| BMI (kg/m²)                        | 23.64±3.17  | 22.91±5.27     | 0.513*  |
| Preoperative serum total bilirubin (μmol/L) | 72.01±81.67 | 104.98±109.17 | 0.191*  |
| Incidence of DM (cm)               | 6/20        | 9/56           | 0.284** |
| Pancreatic texture (soft/hard)     | 9/17        | 29/36          | 0.382** |
| Pathology (malignant/benign)       | 25/1        | 54/11          | 0.168*  |
| Pancreatic duct diameter ≤3 cm     | 20/42       |                |         |
| Blood loss (ml)                    | 437.92±399.54 | 396.92±411.37 | 0.835*  |
| Intraoperative transfusion (%)     | 13/13       | 18/47          | 0.043** |
| Operating time (min)               | 285.00±59.92 | 275.38±77.91  | 0.573*  |

BMI – body mass index; DM – diabetes mellitus. * Unpaired t test; ** chi-square test.

POPFs, a variety of techniques have been used and modified in the management of the pancreatic remnants following PD. However, none of these techniques have exhibited clearly superior outcomes [14]. It is well known that the risk factors for POPF consist primarily of 3 aspects: 1) patient factors, including age, preoperative jaundice level, nutrition status, and others; 2) technical factors, including operation time, blood loss, anastomosis technique, and drain management; and 3) pancreatic factors, including pancreatic texture, pancreatic duct size, blood supply of the cut end, and others [15]. The surgical technique is one of the most important factors.

Various factors can contribute to POPF. Other centers have reported that pancreatic duct diameter is a major contributing factor, particularly when a duct-to-mucosa anastomosis is performed on a small duct [16]. However, in our study, the average pancreatic duct diameters were similar between the patients who experienced POPFs and those who did not. Moreover, the numbers of patients with a pancreatic duct smaller than 3 cm were not significantly different between the patients who experienced POPFs and the patients who did not (Table 3). This may explain why we commonly placed internal transanastomotic stents for drainage, even in patients with small pancreatic ducts, although some reports and meta-analyses have not found statistically significant differences in incidence of POPFs due to internal stent insertion [17–19]. Additionally, a soft pancreas is always thought to be a risk factor for POPF [20]. Our data indicated no significant difference in pancreatic remnant texture between the patients with and without POPFs.

The greatest limitation of PD is the PJ reconstruction. As we previously described, the duct-to-mucosa pancreatocjejunostomy, end-to-end invagination pancreatocjejunostomy, and pancreatocgastrostomy techniques are the most commonly used procedures for reconstruction, and surgeons choose a suitable method based on the intraoperative situation. However, some reports have come to the conclusion that the DMA technique is superior to the invagination technique in terms of long-term anastomotic patency and function, based on a canine model [21]. El Nakeeb et al. reported that there was no difference in POPF incidence between the 2 methods but that the invagination technique might decrease POPF severity and the incidence...
Table 4. Logistic regression of risk factors of PF after pancreaticoduodenectomy.

| Value                          | B    | SE   | Wals | P value | OR   | 95%CI   |
|-------------------------------|------|------|------|---------|------|---------|
| Total PFs transfusion         | 0.960| 0.480| 3.993| 0.046   | 2.611| 1.019–6.693 |

B – regression coefficient; PF – pancreatic fistula; Wals – χ² value.

Table 5. Postoperative complications in 91 patients.

| Postoperative complications | Study group | Control group |
|------------------------------|-------------|---------------|
| Ascites                      | 2           | 3             |
| Gastrointestinal hemorrhage  | 1           | 1             |
| Delayed gastric emptying     | 1           | 2             |
| Biliary fistula              | 0           | 3             |
| Pulmonary infection          | 0           | 1             |
| Wound infection              | 1           | 2             |
| Urinary tract infection      | 0           | 1             |
| Abdominal infection          | 2           | 4             |

Conclusions

The whole-layer suturing technique for duct-to-mucosa pancreaticojejunostomy in pancreaticoduodenectomy effectively reduces the rate of POPF (especially grade B and C pancreatic fistulas) after PD. This method is safer, more reliable, and more favorable than the traditional duct-to-mucosa technique and provides better surgical outcomes.
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