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Invaginated duct to mucosa pancreaticojejunostomy reduce postoperative pancreatic leakage

A matched case-controlled study

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Abstract

Postoperative pancreatic leakage is an obstacle in pancreaticoduodenectomy, which always follows pancreaticojejunostomy (PJ) failure. Dozens of PJ procedures have been reported, and none have shown superiority over others. Therefore, the present study is conducted to assess the potential advantages of invaginated duct-to-mucosa (D-M) PJ.

We retrospectively analyze the related data from patients who underwent pancreaticodedunostomy due to malignant tumors at the First Affiliated Hospital of Henan University of Science and Technology from January 2017 to August 2019. According to the different PJ procedures, the patients are divided into custom D-M group and invaginated D-M group. Matching by sex, age, pancreatic duct size, and pancreatic texture is performed. Pancreatic leakage and other complications are compared, and SPSS 16.0 is employed for analysis.

A total of 48 pairs of patients are included. Patients in both groups has almost the same baseline characteristics in terms of sex ($P = 1.000$), age ($P = .897$), American Society of Anesthesiologists status ($P = .575$), body mass index ($P = .873$), pancreatic duct size ($P = .932$), pancreatic texture ($P = 1.000$) and tumor origin ($P = .686$). No significant difference is observed in operative outcomes, such as operative duration ($P = .632$), PJ duration ($P = .748$), blood loss ($P = .617$) and number of required transfusions ($P = .523$). Pancreatic leakage is significantly decreased in the invaginated D-M group ($P = .005$). The differences in other complications, such as bleeding ($P = .617$), biliary leakage ($P = .646$), pneumonia ($P = .594$) and thrombosis ($P = .714$), do not reach statistical significance. The postoperative hospitalization duration is almost the same for both groups ($P = .764$).

Invaginated D-M PJ may reduce pancreatic leakage following pancreaticoduodenectomy.

Abbreviations: D-M = duct-to-mucosa, PD = pancreaticoduodenectomy, PJ = pancreaticojejunostomy.

Keywords: anastomosis, invaginated duct-to-mucosa anastomosis, pancreatic leakage, pancreaticodedunostomy, pancreaticojejunostomy

1. Introduction

Pancreaticoduodenectomy (PD) is one of the most problematic operations, with high morbidity and mortality rates.[1–4] Most cases of mortality are associated with pancreatic leakage, which is mainly secondary to pancreaticojejunostomy (PJ) failure. Although dozens of anastomotic procedures have been introduced, pancreatic leakage remains an obstacle in PD. While duct-to-mucosa (D-M) anastomosis and its modifications may be the most popular procedure, none of them have become the standard of care. Kakita anastomosis[5] and Blumgart anastomosis[6] are the most widely used procedures, with lower rates of pancreatic leakage. Hong single-stitch anastomosis[7] is also popular in China. However, none of these procedures have shown significant superiority over the others.[8] Regarding PJ, the invaginated procedure has remained popular since its introduction. Chen U-suture PJ[9] and Peng binding PJ[10] are still widely used. No consensus on the method of PJ has been reached yet.[11,12] All currently used procedures have some advantages, while, disadvantages exist either. We have developed a novel PJ procedure, invaginated D-M PJ, which theoretically enclose all the advantages.

2. Materials and methods

2.1. Patient characteristics

All patients who underwent PD for malignant tumors at the First Affiliated Hospital of Henan University of Science and Technology from January 2017 to August 2019 were included.

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All the data were included in this article.

All data generated or analyzed during this study are included in this published article [and its supplementary information files]. The datasets generated during and/or analyzed during the current study are publicly available.

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Table 1

Characteristics of included patients.

	Custom D-M (48)	Invaginated D-M (48)	*P*
Sex (M/F)	20/28	20/28	1.000
Age	61.7 ± 11.2	63.3 ± 10.5	.897
ASA			.537
I	5	7	
II	43	41	
BMI (kg/m^2)	24.8 ± 5.3	23.1 ± 3.8	.873
Pancreatic duct size (mm)	3.1 ± 1.0	3.4 ± 1.2	.932
Pancreatic texture			1.000
Firm	38	38	
Soft	10	10	
Tumor origin			.686
Biliary duct	18	15	
Pancreas	13	11	
Duodenum	6	10	
Ampulla	11	12	

ASA = American society of Anesthesiologists status, BMI = body mass index.

All operations are completed by the same team. This is a retrospectively designed clinical trial which is approved by the ethics committee of the First Affiliated Hospital of Henan University of Science and Technology.

According to the PJ procedure, we divide the patients into 2 groups: the custom D-M group and the invaginated D-M group. All patients included are 18 to 80 years old with an American Society of Anesthesiologists classification of 1 to 2 and a pathology-proven diagnosis. Enhanced CT and magnetic resonance cholangiopancreatography are routinely performed. All patients included have no vascular tumor invasion on enhanced CT and/or enhanced MR. In all patients, the pancreatic duct size is dilated more than 2 mm. For bias control, we match the patients according to age (±5 year), sex, pancreatic texture, and pancreatic duct size (±1 mm). These factors have been reported as important risk factors for pancreatic leakage.[9] All the characteristics of the patients in the 2 groups are listed in Table 1.

2.2. Operative procedure

All operations were performed under general anesthesia. PD was performed with local lymph node dissection. The jejunal limb was brought up through the retrocolic root. After end-to-side PJ, cholangiojejunostomy was performed with 4-0 knotless running sutures (Stratafix, Ethicon) approximately 8 cm distal to the PJ. Gastrojejunostomy was performed using a circular stapler (Panther) approximately 50 cm distal to the cholangiojejunostomy. An additional jejunojejunostomy was performed with 4-0 knotless sutures (Stratafix, Ethicon) approximately 10 cm distal to the gastrojejunostomy. The difference between the 2 groups was the PJ procedure. Patients in the custom D-M group underwent modified Blumgart anastomoses, as described by Shoji Kawakatsu.[8] The invaginated D-M procedure was performed as follows: 3-0 polypropylene sutures (Prolene, Ethicon) were employed to perform the anastomosis. The first stitch transfixed the pancreas from anterior to posterior approximately 1 cm from the superior border of the pancreatic neck, which was located 1.5 cm distal to the cut end of the pancreas. Seromuscular sutures in the jejunal limb at the antimesenteric margin. Then, the first knot was made anteriorly, as shown in Figure 1. The second stitch was approximately 1 cm away from the first knot, which was also 1.5 cm distal to the cut end of the pancreas. The second stitch transfixed the pancreatic neck from anterior to posterior (Fig. 2①); then, the needle was passed through the seromuscular layer of the jejunum 1 cm from the first stitch (Fig. 2①). The needle was passed through the pancreas from posterior to anterior approximately 1 cm distal to the cut end of the pancreas (Fig. 2②); then, it was passed through the seromuscular layer of the jejunum 1 cm from the first knot (Fig. 2③). The sutures were reinforced by duplicating the second suture (Fig. 2④). When the sutures reached the superior border of the pancreatic duct, suturing was suspended. Then, custom D-M anastomosis was performed using 4-0 polyglactin sutures (Vicryl Plus, Ethicon). After D-M anastomosis, PJ was continued as described above until reaching the inferior border of the pancreatic neck. The last stitch was just like the first one. When the needle was passed through the pancreatic neck approximately 1.5 cm distal to the cut end of the pancreas from anterior to posterior, it was passed through the seromuscular layer of the jejunal limb; then, the second knot was made (Fig. 3). Before tying the knot, moderate strengthening of every stitch was emphasized. Other points to emphasize include the following: the jejunal serosa was destroyed by electrocoagulation to accelerate healing of the cut end of the pancreas and jejunal limb, as described by Hong[7]; a pancreatic

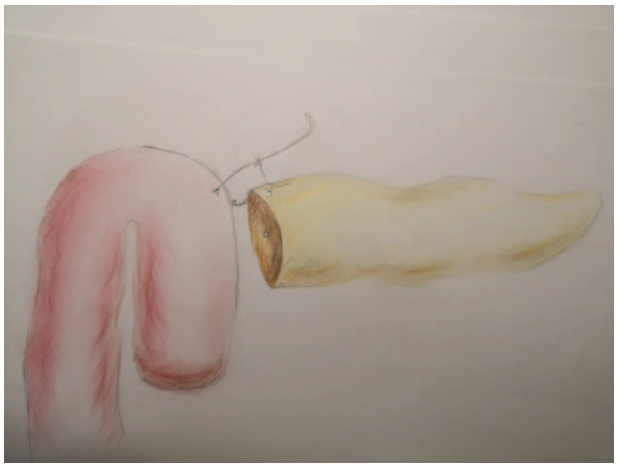

Figure 1. The first stitch of pancreaticojejunostomy.

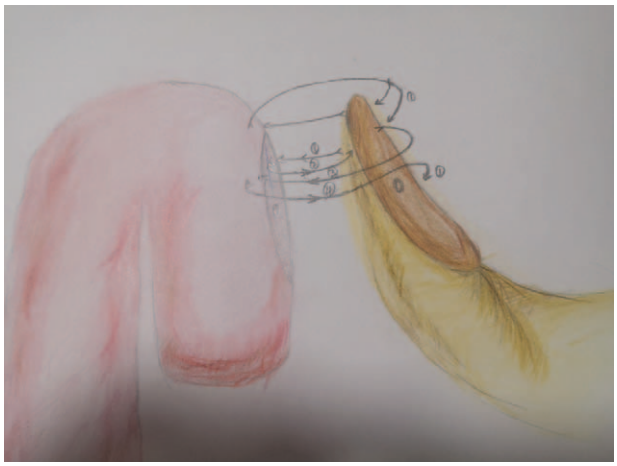

Figure 2. The second stitch of pancreaticojejunostomy.

Figure 3. Illustration of the completion of pancreaticojejunostomy.

duct stent should be placed when performing D-M anastomosis; and the pancreatic duct should be approximately 2 mm away from the cut end of the pancreas to facilitate invagination of the pancreatic duct into the mucosa of the jejunum. Additionally, drainage tubes should be placed around cholangiojejunostomy and PJ sites, with additional pelvic drainage when necessary. Peritoneal lavage with distilled water was performed before abdominal closure.

2.3. Perioperative management

Percutaneous transhepatic cholangial drainage was performed when cholangitis occurred. Anemia was routinely corrected to 90 g/L or above. Serum albumin was maintained at a normal level. Breathing exercises were performed for at least 2 days before the operation. The pressure of O_2 and CO_2 should be at a normal level, as determined by arterial blood gas analysis.

Postoperative management was performed according to the principle of enhanced recovery after surgery.[13] The gastric tube was removed after the operation when the patient had recovered from anesthesia. The abdominal drainage amylase test was routinely performed at 1, 3, and 7 days postoperatively, with an additional test when pancreatic leakage was suspected. At least 7 days postoperatively, abdominal drainage tubes were removed when the drainage volume was less than 20 ml/d. Abdominal CT scans were routinely performed to ensure the absence of ascites before drainage tube removal. Discharge criteria were set as recovery to a semifluid diet without symptomatic pancreatic leakage or biliary leakage at least 7 days postoperatively.

2.4. Definition

The primary endpoint is pancreatic leakage. Pancreatic leakage is detected following the International Study Group of Pancreatic Fistula guidelines.[14] The severity of pancreatic leakage is classified according to the International Study Group of Pancreatic Fistula criteria. The term bleeding refers to hematochezia, hematemesis or blood drainage from the abdominal cavity. The analysis of mortality is limited to 30 days postoperatively.

2.5. Statistical analysis

SPSS 16.0 is employed to analyze the data. The measurement data, including age, body mass index, pancreatic duct size, operative duration, PJ duration, blood loss, and postoperative hospitalization duration, are compared with *t* tests. Numerical data, such as sex, American Society of Anesthesiologists classification, pancreatic texture, tumor origin, number of required transfusions, pancreatic leakage, bleeding, biliary leakage, pneumonia, and thrombosis, are compared with chi square tests. $P < .05$ is considered to be significant.

3. Results

Finally, 48 pairs of patients are included in this study. Patients in both groups have similar baseline characteristics (Table 1). In terms of the operative outcomes, the total operative duration (224.6 ± 50.5 minute vs 209.8 ± 45.3 minute; $P = .632$) and PJ duration (15.3 ± 5.2 minute vs 13.8 ± 4.7 minute; $P = .748$) are similar between the 2 groups. No significant difference is observed in blood loss (250.6 ± 33.7 ml vs 280.1 ± 45.3 ml; $P = .617$) or the number of required transfusions (4/48 vs 7/48; $P = .523$) (Table 2).

The primary endpoint is pancreatic leakage. There is no case of grade C pancreatic leakage in either group. A significant difference is observed in the occurrence of grade A and grade B pancreatic leakage between the groups (15/48 vs 4/48; $P = .005$). Further comparison show that the difference mainly originate from a decreased risk of grade B pancreatic leakage in the invaginated D-M group (7/48 vs 1/48; $P = .027$). There are 3 cases of bleeding in the custom D-M group, including 1 case of intra-abdominal bleeding, and 1 case of bleeding in the invaginated D-M group. Other patients complained of hematochezia. The difference do not reach statistical significance ($P = .617$). All patients are cured by conservative treatment. No re-operations are performed. There are 3 cases of biliary leakage in the custom D-M group and 2 in the invaginated D-M group, but this difference is not significant ($P = .646$). Pneumonia is another common complication. There is no significant difference between the 2 groups (7/48 vs 10/48; $P = .594$). Thrombosis is not rare in older patients postoperatively; there are 5 cases in the custom D-M group and 3 in the invaginated D-M group that progress to lower limb venous thrombosis. The difference do not reach statistical significance ($P = .714$). There is no case of mortality in either group. No re-operation is performed. The postoperative hospitalization duration is similar between the 2 groups (12.4 ± 3.1 days vs 13.3 ± 3.8 days; $P = .764$) (Table 3).

4. Discussion

Pancreatic leakage following the pancreatic stump anastomotic failure is still the most fatal morbidity after PD. D-M PJ may be the most popular method worldwide. Although a series of

Table 2

Operative outcomes.

	Custom D-M (48)	Invaginated D-M (48)	*P*
Operation time (min)	224.6 ± 50.5	209.8 ± 45.3	.632
Pancreaticojejunostomy time (min)	15.3 ± 5.2	13.8 ± 4.7	.748
Blood loss (ml)	250.6 ± 33.7	280.1 ± 45.3	.617
Required transfusion	4	7	.523

Table 3

Postoperative outcomes.

	Custom D-M (48)	Invaginated D-M (48)	*P*
Pancreatic leakage			.005
Grade A	8	3	.109
Grade B	7	1	.027
Grade C	0	0	
Bleeding*	3	1	.617
Biliary leakage	3	2	.646
Pneumonia	7	10	.594
Thrombosis†	5	3	.714
Mortality	0	0	
Re-operation	0	0	
Postoperative hospitalization (d)	12.4 ± 3.1	13.3 ± 3.8	.764

* One in classical D-M group had intraabdominal bleeding who had transfusion; others had hematochezia. All of them recovered by conservative treatment.

† Represented as intermuscular venous thrombosis of lower extremity.

modifications have been introduced,[7–9] the rate of pancreatic leakage has not decreased. Each modification theoretically has some advantages over the others, but there are still disadvantages. Kakita D-M anastomosis[5] involves penetrating sutures to close the cut end of the pancreas and the serosa of the jejunal limb. These penetrating sutures tend to produce tangential shear following anastomotic failure, leading to pancreatic leakage. Blumgart anastomosis[8,15] involves transpancreatic U-sutures, which avoid tangential shear; additionally, the pancreatic stump can be covered by the jejunal serosa to prevent the knots from cutting through the pancreatic tissue. These U-sutures may cause ischemia of the pancreatic stump, which would hamper healing of the D-M anastomosis and increase the risk of pancreatic leakage from the cut end of the pancreas, followed by hemorrhage. Although the modified Blumgart method for anastomosis[8] adopts U-sutures to avoid shear force, the rate of pancreatic leakage is not significantly reduced. Perhaps the potential ischemia of the pancreatic stump offsets the potential benefit from less tangential shear force. Hong single-stitch D-M PJ[7] is similar to the procedure of Kakita anastomosis and also tends to produce tangential shear in the pancreatic stump. This method emphasizes destruction of the jejunal serosa by electrocoagulation, which may accelerate healing of the cut end of the pancreas and the jejunal limb. Chen anastomosis is in fact a form of invagination PJ. However, Chen U-sutures are somewhat different from Blumgart U-sutures. With Chen U-sutures, the shear force is parallel to the vessels, which greatly reduces the risk of ischemia in the pancreatic stump. Additionally, the pancreatic stump is invaginated into the jejunal serosa with Chen U-sutures, and the seromuscular layer of the jejunum can protect the pancreas from suture-induced rupture. Chen invagination anastomosis has a notable potential risk: if even 1 suture fails, a large anastomotic defect forms, which may lead to a high volume of pancreatic leakage. This event could be lethal. This is why we have adopted D-M PJ in recent years.

The invaginated D-M PJ anastomosis that we have described is indeed a modification of custom D-M PJ. D-M suturing was performed as usual. What should be emphasized is pancreatic duct stent implantation; this procedure may potentially reduce the risk of pancreatic leakage,[16,17] though controversy exists.[18] Four to six sutures may be suitable. Too many sutures may increase the risk of ischemia. Another thing that should be emphasized is the separation of the pancreatic duct. Separation of the pancreatic duct of 2 to 3 mm may facilitate invagination of the pancreatic duct into the mucosa of the jejunum, which may accelerate healing. The seromuscular suturing of the pancreatic stump and jejunum is similar to that in Chen U-suture procedure which ensure the pancreatic stump wholly invaginated into the jejunal seromuscular tissue. This procedure greatly decrease the tangential shear force of D-M anastomosis, thereby decrease the risk of pancreatic leakage. Destruction of the jejunal serosa by electrocoagulation accelerate healing of the pancreatic stump and jejunal serosa, which also decrease the risk of pancreatic leakage. In our procedure, what should be emphasized is the avoidance of suturing through the pancreatic duct to reduce pinhole pancreatic leakage. Another thing that should be emphasized is the moderate strengthening of every stitch before the last knot is tied when suturing the pancreatic stump and jejunal serosa. With running sutures, the potential time saving is obvious. Theoretically, the invaginated D-M PJ approach integrates all the advantages mentioned above without obvious disadvantages and reduces the risk of pancreatic leakage.

In our study, there is no case of grade C pancreatic leakage in each group. A decreased risk of grade B pancreatic leakage is observed with invaginated D-M PJ, which result in a significantly decreased risk of pancreatic leakage overall. Other complications are similar between the 2 groups. The theory underlying these results has been described above.

One limitation of this method is its adaptability, as it is not suitable for all patients. When the pancreatic duct is not dilated, invaginated D-M PJ is not suitable. As a retrospectively designed trial, bias may exist. Although patient matching is performed for some risk factors, matching is not for all factors. Additionally, the small sample may also lead to some bias.

5. Conclusions

Based on the limited practice, invaginated D-M PJ may reduce pancreatic leakage after PD. A prospective trial should be planned to further assess its superiority.

Author contributions

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Methodology: Guo-Liang Yao, Meng-Jiao An, Yong-Gang Fan.
Project administration: Yong-Gang Fan.
Supervision: Yong-Gang Fan.
Writing – original draft: Guo-Liang Yao, Meng-Jiao An.
Writing – review & editing: Yong-Gang Fan.

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