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ORIGINAL ARTICLE

A New Feasible Technique for Polytetrafluoroethylene Suture Buttress-Reinforced Pancreaticojejunostomy (PBRP): Mechanical Analysis and a Prospective, Randomized Controlled Trial

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Abstract

Objectives Postoperative pancreatic fistula (POPF) is a major concern after pancreatoduodenectomy (PD). We recently designed a new anastomotic method to reduce the rate of pancreatic fistula: polytetrafluoroethylene suture buttress-reinforced pancreaticojejunostomy (PBRP).

Methods An animal model and a computer simulation were used to measure the maximum stress and tensile strength of the pancreas with and without the suture buttresses. Then, a randomized controlled trial (RCT) was performed to compare the outcome of PD between patients who underwent PBRP vs traditional pancreaticojejunostomy (TP).

Results The maximum load in the animal model was significantly higher with the suture buttresses than without (5.47 ± 1.67 N vs 3.72 ± 1.36 N, $p < 0.01$), and in the computer simulation, the peak stress was lower with the suture buttresses than without (54.86 vs 486.8 MPa). There were no significant differences between the two groups in the overall frequency of POPF, but the rate of clinically relevant POPF was significantly lower in the PBRP group (2.8 vs 22.8%, $p = 0.028$). The pancreaticojejunostomy time was significantly longer in the PBRP group (19.57 ± 3.31 vs 17.17 ± 4.83 min, $p = 0.018$), and the PBRP group showed a shorter drainage tube retention duration (10 vs 12 days, $p = 0.006$) and postoperative hospital stay (13 d vs 15 d, $p = 0.031$).

Conclusions PBRP is a feasible and reliable procedure for preventing clinically relevant POPF. Additional multi-institution randomized trials should be conducted to confirm these results.

Keywords Postoperative pancreatic fistula · Pancreaticojejunostomy · Pancreatoduodenectomy · Biomechanics · Finite element modeling

Introduction

Pancreaticoduodenectomy (PD) has been established as a standard procedure for a variety of malignant and benign disorders involving the head of the pancreas or the periampullary region.[1,2] It is notable for its intricacy and high postoperative morbidity rate. Despite the increased safety of PD in recent decades, postoperative pancreatic fistula (POPF), which can result in abscess formation, peritonitis, sepsis, and hemorrhage, still greatly contributes to operation-related mortality, morbidity, hospital stay duration, and associated costs.[3–6] The incidence of POPF depends on several factors, including the

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pancreatic tissue quality, the diameter of the major pancreatic duct (MPD), the general condition and nutritional status of the patient, the skill of the surgeon, and the anastomotic method used in the pancreaticojejunostomy.[7,8] Among these, the anastomotic method is a key factor. Although attempts have been made to decrease the POPF rate by improving techniques for pancreatoenteric anastomosis and reconstruction,[9–11] no single method has been shown to be superior.

It is well known that the incidence of POPF is higher in patients with a soft pancreatic texture because the tissue is prone to developing parenchymal lacerations from the stress of sutures. Reducing the stress applied during suturing appears to be important for reducing the incidence of POPF.

Recently, we designed a new anastomotic method to reduce this stress: polytetrafluoroethylene suture buttress-reinforced pancreaticojejunostomy (PBRP), in which interrupted U-shaped 4–0 Prolene sutures are placed between the seromuscular layer of the jejunum and the pancreas with polytetrafluoroethylene suture buttresses. The aim of the present study was to introduce this novel anastomotic method and to estimate its curative effect. This study comprised a biomechanical study, a computer simulation, and a randomized controlled trial (RCT) of 70 patients.

Materials and Methods

Biomechanical Study

Twenty-one fresh porcine pancreases were obtained to simulate the process of suturing with U-shaped 4–0 Prolene sutures and suture buttresses (polymer pledget, 7 mm × 3 mm × 1.5 mm). The mechanical properties of the pancreatic tissue were measured with a dynamic testing instrument (800LE Mechanical Test System, Test Resources, Inc., MN) by the process shown in Fig. 1. The load was changed with the stretch offset (Fig. 2). The measurement data were processed using Bluehill software (Illinois Tool Works, Inc., USA).

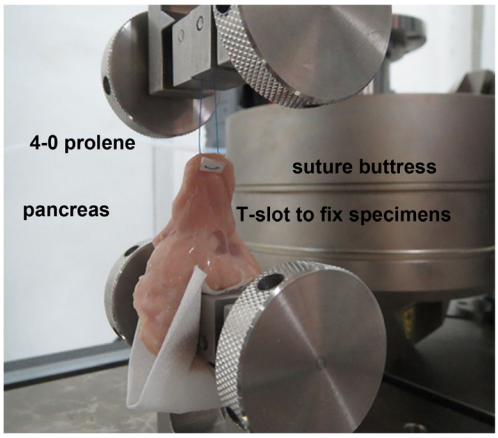

Fig. 1 Process of mechanical measurement. The suture was stretched tight gradually when the actuator was activated, and the induced specimen offset data were transferred to the analysis software

Computer Simulation

Finite element (FE) models of the pancreas were produced using ABAQUS software (ABAQUS 6.13, Simulia, Inc., USA). To effectively investigate the biomechanical behavior of the suture line, the line model of the truss element was simplified and applied to simulate two sutured parts of the postoperative pancreas (Fig. 3). The two parts of the pancreas and the suture line were assembled in ABAQUS. The FE model was meshed with 3972 hexahedral elements. The uniaxial tension of the suture line was loaded as the boundary using the connector element in ABAQUS. As linearly elastic, homogeneous, and isotropic materials, the pancreas and suture line were assigned elastic moduli and Poisson's ratios of 1.14 and 350 MPa and 0.4 and 0.3, respectively.

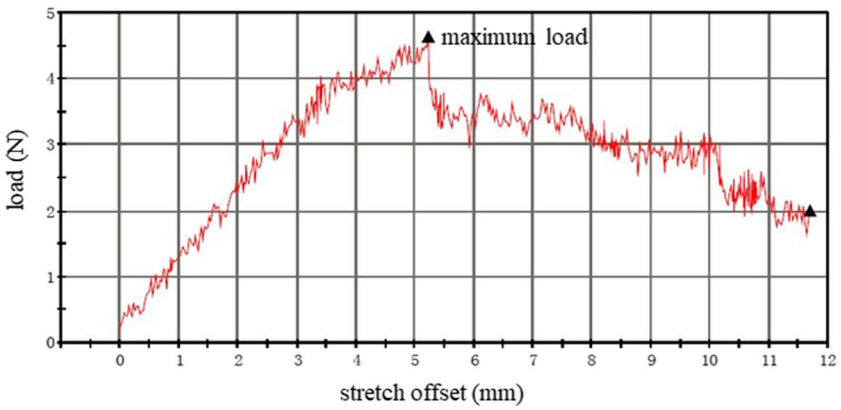

Fig. 2 Sample mechanical measurement data. The load gradually increased with the offset increasing at the beginning. Then, the load greatly declined at the point we called the maximum load

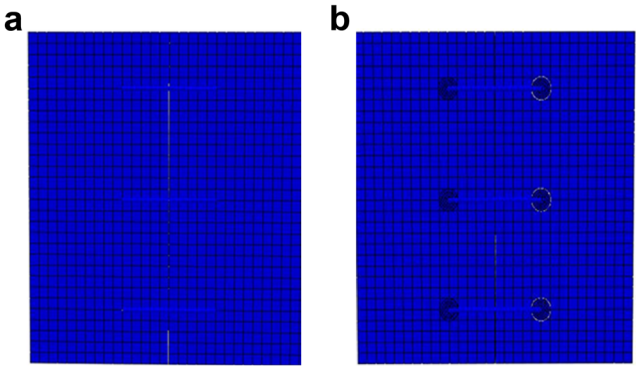

Fig. 3 FE models of the pancreas and suture line with and without suture buttresses. **a** Model without suture buttresses. **b** Model with suture buttresses

Clinical Trial

Study Design

To assess the efficacy of the method, patients from the Chinese Academy of Medical Sciences Cancer Hospital were recruited to undergo either PBRP or traditional pancreaticojejunostomy (TP). This study was conducted in accordance with the Declaration of Helsinki and approved by the Ethics Committee of the Chinese Academy of Medical Sciences Cancer Hospital (NCC2013S-010).

Patient Selection

Patients were recruited from the Chinese Academy of Medical Sciences Cancer Hospital between September 2013 and June 2017. All participants provided informed consent and were then screened to confirm their eligibility before randomization.

The inclusion criteria were as follows: (1) written informed consent, (2) male or female subjects aged 18 to 80 years, (3) no history of epigastric operation, and (4) resectability with radiographic assessment. The exclusion criteria were as follows: (1) severe comorbidities, including myocardial infarction, respiratory disorder requiring oxygen inhalation, hepatic cirrhosis, hemodialysis, or active malignant disease that could affect adverse events; (2) lymph node invasion of major blood vessels revealed by preoperative examination or intraoperative exploration; (3) metastatic cancer; (4) metastasis to the liver, lungs, or other organ according to enhanced abdominal CT and chest X-ray; (5) tumor invasion into adjacent organs revealed by preoperative examination or intraoperative exploration; (6) peritoneal dissemination; and (7) receiving neoadjuvant chemotherapy.

Randomization

Randomization was implemented using individual sealed envelopes prepared in advance by a statistician, allocating patients at a 1:1 ratio to either the PBRP or TP group. The envelopes were opened according to the operation order after completion of the pancreaticoduodenal resection and, if necessary, lymph node dissection.

Procedures and Treatment

Surgery All surgeries were performed by the same surgical team. Under general anesthesia, a median abdominal incision was made. The abdomen was explored to rule out distal metastasis before PD. No patient underwent additional organ resection. The MPD was identified after the pancreas was transected at the level of the left wall of the portal vein. If the MPD diameter was < 5 mm, a stent with a diameter approximating that of the MPD was permanently placed such that one end lay 4 to 5 cm within the MPD, directed toward the pancreatic body, and the other end lay 3 to 4 cm within the lumen of the jejunum.

Invagination anastomosis: approximately 2 cm of the cut edge of the pancreatic remnant was mobilized. An opening slightly smaller than the transection through the pancreas was created at the side of the jejunum by electrocautery. Then, the pancreatic stump was invaginated into the jejunum with two layers of sutures. For the inner layer, 4–0 Prolene was used to suture the full-thickness jejunum and the pancreatic remnant. Interrupted sutures were placed at approximately 1-cm intervals. The posterior wall was sutured before the anterior wall. For the outer layer, interrupted U-shaped 4–0 Prolene sutures with or without suture buttresses (polymer pledget, 7 mm × 3 mm × 1.5 mm) were placed between the seromuscular layer of the jejunum and the capsular parenchyma of the pancreatic remnant (Fig. 4).

Duct-to-mucosa anastomosis: An opening matching the size of the MPD was made by electrocautery in the jejunum, opposite the mesentery. The MPD was discontinuously anastomosed with the full-thickness jejunum using 5–0 Prolene at approximately 5-mm intervals. Sutures were placed in the anterior wall of the pancreatic duct in a fashion similar to those in the posterior wall. After all the sutures were placed, they were tied with knots to the outside. To reduce the anastomotic tension, a second layer of discontinuous U-shaped 4–0 Prolene sutures with or without suture buttresses (polymer pledget, 7 mm × 3 mm × 1.5 mm) was placed between the jejunal seromuscular layer and the capsular parenchyma of the pancreatic remnant.

The remaining procedures were routine. After all anastomoses were completed, two drains were placed near the sites of both the pancreaticojejunostomy and the cholangiojejunostomy and were brought out through the foramen of Winslow from the right side of the anterior abdominal wall.

Clinical Management Prophylactic antibiotics were routinely given 30 min preoperatively and were continued until postoperative day (POD) 3 unless infection was suspected. Neither

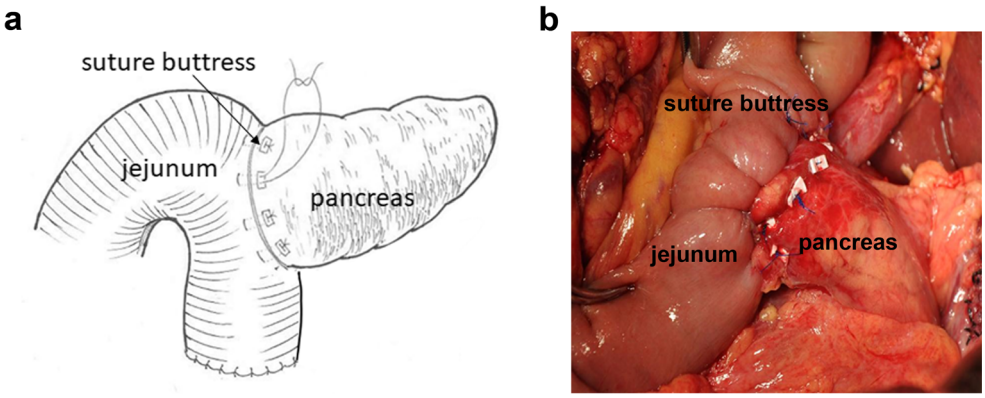

Fig. 4 Schematic diagram of PRBP

octreotide nor somatostatin was used prophylactically but could be given if a grade B or C PF was diagnosed. The abdominal drains were removed if POPF (according to PF as defined by the guidelines of the International Study Group on Pancreatic Fistula (ISGPF)) had not been diagnosed and the daily output was < 30 ml. Otherwise, the drains were retained until the daily output was < 30 ml. Amylase levels were measured in the output from the abdominal drains on PODs 3–7. When the levels were < 3 times the upper limit of normal, no additional measurements were made. Otherwise, amylase levels in the output continued to be monitored.

Table 1 The comparing of maximum load

	Group with suture buttress (*N*)	Group without suture buttress (*N*)	*P*
1	5.59244	4.89888	
2	5.08744	4.24552	
3	6.10238	3.64771	
4	3.25667	2.56073	
5	7.32619	7.17601	
6	5.37914	3.54615	
7	6.59636	3.93191	
8	5.03966	2.21261	
9	6.82804	5.51292	
10	4.2446	2.89977	
11	2.94256	1.75714	
12	6.41945	4.32903	
13	7.19529	2.84207	
14	4.16058	2.60213	
15	9.12255	5.14334	
16	4.65137	3.6191	
17	2.43595	1.87251	
18	3.32195	2.83933	
19	6.50948	5.08791	
20	6.51857	2.79361	
21	6.13962	4.63784	
$\bar{x} \pm s$	5.47 ± 1.67	3.72 ± 1.36	< 0.01

Primary and Secondary Outcomes POPF was defined according to the criteria of the ISGPF, i.e., an amylase level in drainage fluid collected on POD 3 that was more than three times the serum amylase level.[12] The primary endpoint was the incidence of clinically relevant POPF (ISGPF grade B or C).[12]

The secondary endpoints were overall postoperative morbidity, mortality, and postoperative hospital stay. Morbidity was defined as a complication of greater than grade II by the Clavien classification.[13] Biliary leakage was diagnosed if bile was observed in the abdominal drain and the total bilirubin exceeded the upper limits of normal. Delayed gastric emptying (DGE) and postpancreatectomy hemorrhage were defined according to a consensus definition by the ISGPS.[14] DGE was then classified as grade A, B, or C by the ISGPF clinical criteria based on the clinical course and postoperative management. Intra-abdominal infection was diagnosed on the basis of clinical signs, including purulent drainage with positive cultures and an elevated white blood cell count. Pulmonary infection was diagnosed based on X-ray changes and a positive sputum culture for bacteria. The discharge conditions were defined as follows: return to preoperative activities of daily living, no deep-site infections, normal laboratory data, no drains, and the possibility for oral nutrition above the basal metabolism. Mortality was defined as death within 90 days after surgery.

Clinical Data Collection Background demographic and clinical data were collected from the medical records. Surgical data (procedure duration, pancreaticojejunostomy duration, and blood loss) and pancreatic data (pancreas texture and MPD diameter) were collected during the operation. Postsurgical data were collected by one clinical nursing staff member blinded to the group assignment. All patients were reviewed on PODs 10, 30, and 90 for the presence of any complications or the need for readmission.

Statistical Analysis

All statistical analyses were performed using SPSS for Windows version 14.0 (SPSS, Chicago, IL, USA).

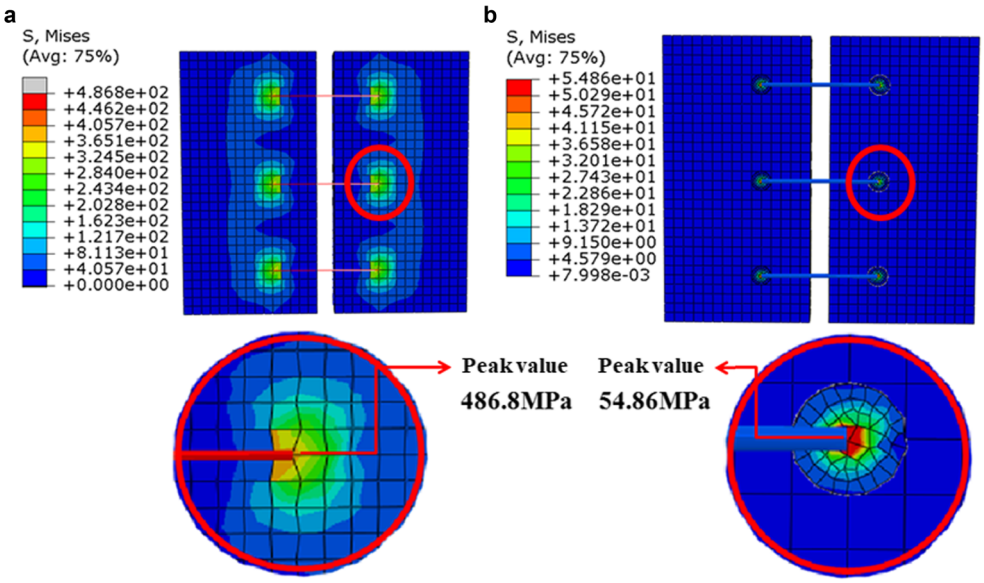

Fig. 5 Results of FE models. **a** Model without suture buttresses. **b** Model with suture buttresses. The color and shape represent the stress magnitude and range. The peak stress occurred in the area where the suture was connected with the pancreas. The peak stress (486.8 MPa) and the area of the stress are obviously greater in (**a**)

Continuous variables with a normal distribution are reported as mean ± SD and those with a non-normal distribution as median (range). Student's *t* test and Mann–Whitney *U* test respectively were used for analysis of these variables, and the chi-squared test or Fisher's exact test for categorical variables. $P < 0.05$ was considered statistically significant.

Results

Biomechanical Study

We obtained 21 sets of data. The maximum load was significantly higher in the PBRP group than in the control group (5.47 ± 1.67 N vs 3.72 ± 1.36 N) (Table 1).

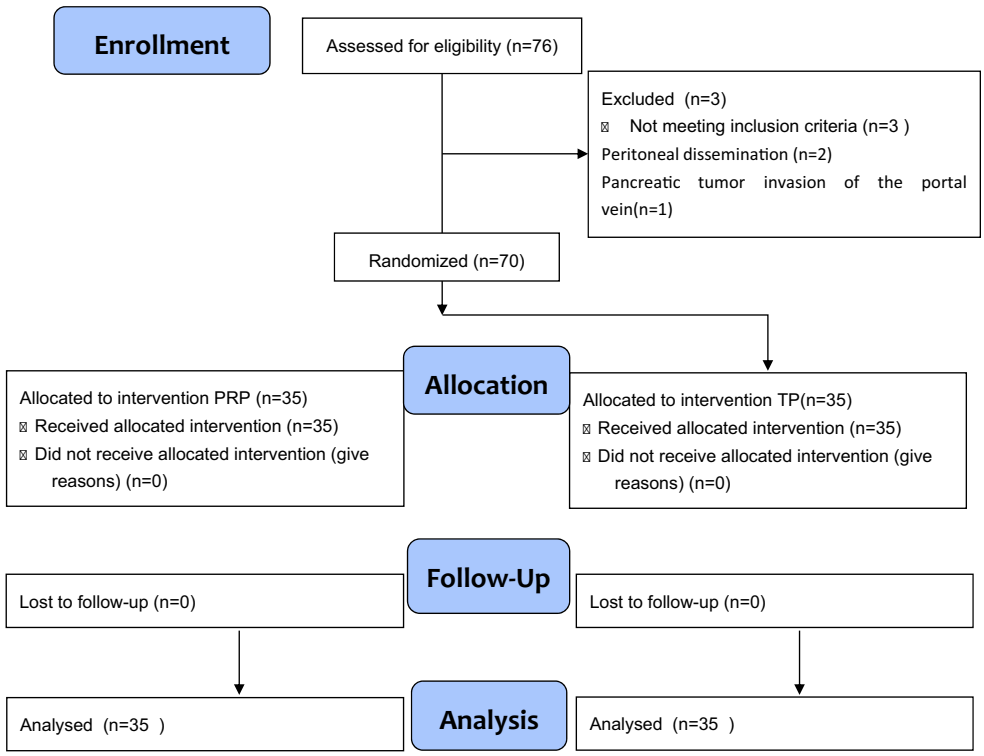

Fig. 6 CONSORT diagram for the study

Table 2 Demographic and pathological data of patients in the study

Variables	Group		*P* value
	PRBP ($n = 35$)	TP ($n = 35$)	
Gender			
Male	24 (68.6%)	20 (57.1%)	
Female	11 (31.4%)	15 (42.9%)	0.322
Age (years)	60.40 ± 10.097	58.17 ± 9.266	0.339
BMI (kg/m^2)	22.67 ± 3.26	24.25 ± 3.42	0.051
Diabetes	7(20%)	4(11.4%)	0.324
ASA			
I	1 (2.9%)	0	
II	31 (88.6%)	31 (88.6%)	
III	3 (8.5%)	4 (11.4%)	0.565
Jaundice	13 (37.1%)	17 (48.6%)	0.334
Albumin (g/L)	37.563 ± 5.462	39.434 ± 5.534	0.159
Pancreatic texture			
Soft	24 (68.6%)	20 (57.1%)	
Hard	11 (31.4%)	15 (42.8%)	0.458
MPD diameter			
< 3 mm	21 (60%)	16 (45.7%)	
≥ 3 mm	14 (40%)	19 (54.3%)	0.338
Pathology			
Pancreatic head cancer	11 (31.4%)	14 (40%)	
Distal cholangio cancer	9 (25.7%)	7 (20%)	
Ampullary cancer	6(17.1%)	4 (11.4%)	
Duodenal cancer	9 (25.7%)	10 (28.6%)	0.786
Anastomosis			
Invaginated pancreaticojejunostomy	13 (37.1%)	18 (51.4%)	
Duct-to-mucosa pancreaticojejunostomy	22 (62.8%)	17 (48.6%)	0.336

BMI body mass index, *ASA* American Society of Anesthesiologists, *MPD* main pancreatic duct

Computer Simulation

The peak stress occurred in the area where the sutures connected with the pancreas in both FE models, but the stress (486.8 MPa) and the area of the stress were both significantly greater in the model without the suture buttresses (Fig. 5).

Clinical Trial

Patient Enrollment

From September 2013 through June 2017, 76 patients were initially included in the study, but 3 were excluded because of tumor invasion or metastasis, and 3 patients did not provide written informed consent. Therefore, 70 patients were randomized, with 35 allocated to the PBRP group and 35 to the TP group. All 70 patients were included in the analysis, and there was no loss to follow-up during the study period (Fig. 6).

Baseline Characteristics

Table 2 shows that the two groups were comparable in terms of sex, age, BMI, ASA classification, and concomitant medical conditions. In addition, there were no significant differences between the groups in terms of MPD diameter, pancreas texture, pathological data, or anastomotic method.

Comparison of Surgical Safety and Postoperative Recovery

The two groups were similar in terms of the operative time, blood loss and rates of biliary fistula, DGE, and wound infection. Complications such as hemorrhage, intra-abdominal abscess, and cholangitis were not observed. The PBRP group had a significantly longer pancreaticojejunostomy time (19.57 ± 3.31 vs 17.17 ± 4.83 min, $p = 0.018$). No

Table 3 Comparison of surgery-related variables between two groups

Variables	Group		*P* value
	PRBP ($n = 35$)	TP ($n = 35$)	
Pancreaticojejunostomy time (min)	19.57 ± 3.31	17.17 ± 4.83	0.018
Operative time (min)	290.00 ± 60.02	285.60 ± 54.65	0.749
Blood loss (ml)	300 (50~800)	300 (50~600)	0.543
Biliary fistulae	1 (2.9%)	0	0.314
Delayed gastric emptying			
Grade A	1 (2.9%)	3 (8.6%)	
Grade B	0	1 (2.9%)	
Grade C	1 (2.9%)	0	0.382
Wound infection	3 (8.6%)	1 (2.9%)	0.303
Bleeding complications	0	0	–
Intestinal exhaust time (days)	4 (2~6)	5 (2~7)	0.169
Gastric tube detaining time (days)	6 (4~33)	6 (4~23)	0.430
Drainage tube detaining time (days)	10 (7~33)	12 (8~31)	0.006
Postoperative hospital stay (days)	13 (9~35)	15 (9~33)	0.031
Mortality	0	0	–

postoperative complications required surgical intervention, and all complications resolved after medical treatment. The time to first flatus and the gastric tube retention duration were similar in both groups; however, the drainage tube retention and postoperative hospital stay durations were significantly shorter in the PBRP group (Table 3).

For overall POPF, there was no significant difference between the groups (34.3 vs 42.8%, $p = 0.461$); however, the rate of clinical POPF was significantly lower in the PBRP group than in the TP group ($p = 0.028$) (Table 4). For patients with soft pancreas, we got the same result in the stratified analysis (Tables 5, 6). There was no statistical difference in the rate of POPF and clinical POPF between different anastomosis methods (Table 7). No mortality was observed in either group. After discharge, all patients recovered well within the 90-day follow-up period without emergency room visits or readmission.

Table 4 Rates of POPF

Variables	Group		*P* value
	PRBP ($n = 35$)	TP ($n = 35$)	
POPF	12 (34.3%)	15 (42.8%)	0.624
Grade A	11 (31.4%)	7 (20%)	
Grade B	1 (2.9%)	8 (22.8%)	
Grade C	0	0	
Clinically relevant POPF	1 (2.9%)	8 (22.8%)	0.028

POPF postoperative pancreatic fistula

Discussion

With recent advances in surgical techniques and perioperative management, the mortality rate of PD has decreased to less than 2%.[15,16] However, the incidence of POPF ranges from 3 to 45%.[17–19] Solid pancreaticojejunostomy anastomosis plays a crucial role in PD. However, the texture of the pancreas is generally soft, making it prone to developing parenchymal lacerations from shear forces applied during suturing and

Table 5 Stratified analysis of POPF according to pancreatic texture

Variables	Group		*P* value
	PRBP	TP	
Soft texture ($n = 44$)	9/24 (37.5%)	10/20 (50%)	0.598
Hard texture ($n = 26$)	3/11 (27.3%)	5/15 (33.3%)	NA

POPF postoperative pancreatic fistula, *NA* not available

Table 6 Stratified analysis of clinically relevant POPF according to pancreatic texture

Variables	Group		*P* value
	PRBP	TP	
Soft texture ($n = 44$)	1/24 (4.2%)	7/20 (35%)	0.025
Hard texture ($n = 26$)	0/11	1/15 (6.7%)	NA

POPF postoperative pancreatic fistula, *NA* not available

Table 7 Rates of POPF and clinically relevant POPF in different anastomoses

Variables	Invaginated pancreaticojejunostomy ($n = 31$)	Duct-to-mucosa pancreaticojejunostomy ($n = 39$)	P value
POPF	13/31 (41.9%)	14/39 (35.9%)	0.788
clinically relevant POPF	5/31 (16.1%)	4/39 (10.3%)	0.712

POPF postoperative pancreatic fistula

leading to POPF. Therefore, relieving these shear forces appears to be a key factor for preventing POPF.

Inspired by heart valve replacement surgery, we applied suture buttresses used in cardiac surgery to pancreaticojejunostomy for the first time. These suture buttresses can be used as protective "clothing" for the pancreas to reduce the shear forces from the sutures, especially in soft pancreatic parenchyma, and to increase the reliability of the anastomosis, thus preventing the occurrence of POPF.

First, we established two simple animal models using fresh porcine pancreases with or without suture buttresses. Then, we measured the force conditions using the 800LE Mechanical Test System, a state-of-the-art, electronic instrument designed for dynamic testing on a wide range of materials and components. The results showed that the suture buttresses significantly increased the ability of the porcine pancreas to resist damage. Then, we built two FE models of the pancreas and suture line with and without the suture buttresses and precisely calculated the stress conditions of the tissue. The results showed that both the stress and the area of the stress were significantly smaller in the model with the suture buttresses, laying a foundation for the clinical trial. Finally, we performed an RCT including 70 patients to compare the outcomes of PBRP and TP. In our study, all patients, regardless of pancreatic texture and comorbidities, were randomly assigned to one of the two groups to eliminate selection bias. The two groups were as close to identical as possible. The two groups had similar rates of overall postoperative morbidities, but the rate of clinical POPF was significantly lower in the PBRP group than in TP the group ($p = 0.028$), and the drainage tube retention and postoperative hospital stay durations were significantly shorter in the PBRP group. Type of anastomosis may affect the incidence of POPF. In our study, there was no statistical difference in the rate of POPF and clinical POPF between invaginated pancreaticojejunostomy and duct-to-mucosa pancreaticojejunostomy, which ensured that the association of PRBP with improved outcomes was specific to PRBP rather than the type of anastomosis performed. Infection is a major concern for surgeons when using these buttresses. While we have not observed any adverse effects of these buttresses, a longer follow-up time is needed for confirmation. Thus, PBRP was preliminarily shown to be a safe and effective method.

The success of this technique may be due to several aspects. From a materials science perspective, the suture buttress is made of polytetrafluoroethylene, which is safe for placement in the body, may promote tissue adherence and stimulate the growth of fibroblasts, and may promote adhesion between the pancreas and bowel pouch. In addition, the buttress is only 7 mm × 3 mm × 1.5 mm in size and can be tailored as needed to fit the pancreas. Regarding the anastomotic technique, we placed interrupted sutures for a better blood supply to the anastomotic stoma. Simultaneously, the suture buttresses reinforced the outer layer; therefore, this method is convenient to perform and does not increase the difficulty of the operation.

The main limitation of the study is related to its inherent biases as a single-institution study. Another limitation could be that few clinical cases were included. Finally, these results were obtained from a single surgeon and might not easily translate to other surgeons, thereby potentially lacking generalizability.

Conclusion

PRBP is a feasible and safe procedure for decreasing the incidence of clinical POPF despite its longer pancreaticojejunostomy time. However, larger-scale and multicenter clinical trials are needed to verify its clinical efficacy.

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Compliance with Ethical Standards

Conflict of Interest The authors declare that they have no conflict of interest.

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References

1. Jimenez RE, Fernandez-del Castillo C, Rattner DW, Chang Y, Warshaw AL. Outcome of pancreaticoduodenectomy with pylorus preservation or with antrectomy in the treatment of chronic pancreatitis. Annals of surgery. 2000;231(3):293–300.
2. El Nakeeb A, Salah T, Sultan A, El Hemaly M, Askr W, Ezzat H et al. Pancreatic anastomotic leakage after pancreaticoduodenectomy. Risk factors, clinical predictors, and management (single center experience). World J Surg. 2013;37(6):1405–18. doi:https://doi.org/10.1007/s00268-013-1998-5.
3. Vollmer CM, Jr., Sanchez N, Gondek S, McAuliffe J, Kent TS, Christein JD et al. A root-cause analysis of mortality following

major pancreatectomy. Journal of gastrointestinal surgery : official journal of the Society for Surgery of the Alimentary Tract. 2012;16(1):89–102; discussion −3. doi:https://doi.org/10.1007/s11605-011-1753-x.
4. Allen PJ, Gonen M, Brennan MF, Bucknor AA, Robinson LM, Pappas MM et al. Pasireotide for postoperative pancreatic fistula. The New England journal of medicine. 2014;370(21):2014–22. doi:https://doi.org/10.1056/NEJMoa1313688.
5. Malleo G, Pulvirenti A, Marchegiani G, Butturini G, Salvia R, Bassi C. Diagnosis and management of postoperative pancreatic fistula. Langenbeck's archives of surgery / Deutsche Gesellschaft fur Chirurgie. 2014;399(7):801–10. doi:https://doi.org/10.1007/s00423-014-1242-2.
6. Callery MP, Pratt WB, Kent TS, Chaikof EL, Vollmer CM, Jr. A prospectively validated clinical risk score accurately predicts pancreatic fistula after pancreatoduodenectomy. J Am Coll Surg. 2013;216(1):1–14. doi:https://doi.org/10.1016/j.jamcollsurg.2012.09.002.
7. Abete M, Ronchetti V, Casano A, Pescio G. [Pancreatic fistula after pancreaticoduodenectomy: risk factors and treatment]. Minerva chirurgica. 2005;60(2):99–110.
8. Poon RT, Lo SH, Fong D, Fan ST, Wong J. Prevention of pancreatic anastomotic leakage after pancreaticoduodenectomy. American journal of surgery. 2002;183(1):42–52.
9. Ansorge C, Strommer L, Andren-Sandberg A, Lundell L, Herrington MK, Segersvard R. Structured intraoperative assessment of pancreatic gland characteristics in predicting complications after pancreaticoduodenectomy. Br J Surg. 2012;99(8):1076–82. doi:https://doi.org/10.1002/bjs.8784.
10. Maggiori L, Sauvanet A, Nagarajan G, Dokmak S, Aussilhou B, Belghiti J. Binding versus conventional pancreaticojejunostomy after pancreaticoduodenectomy: a case-matched study. Journal of gastrointestinal surgery : official journal of the Society for Surgery of the Alimentary Tract. 2010;14(9):1395–400. doi:https://doi.org/10.1007/s11605-010-1212-0.
11. Ji W, Shao Z, Zheng K, Wang J, Song B, Ma H et al. Pancreaticojejunostomy with double-layer continuous suturing is associated with a lower risk of pancreatic fistula after pancreaticoduodenectomy: a comparative study. International journal of surgery (London, England). 2015;13:84–9. doi:https://doi.org/10.1016/j.ijsu.2014.11.034.
12. Bassi C, Dervenis C, Butturini G, Fingerhut A, Yeo C, Izbicki J et al. Postoperative pancreatic fistula: an international study group (ISGPF) definition. Surgery. 2005;138(1):8–13. doi:https://doi.org/10.1016/j.surg.2005.05.001.
13. Dindo D, Demartines N, Clavien PA. Classification of surgical complications: a new proposal with evaluation in a cohort of 6336 patients and results of a survey. Annals of surgery. 2004;240(2):205–13.
14. Wente MN, Bassi C, Dervenis C, Fingerhut A, Gouma DJ, Izbicki JR et al. Delayed gastric emptying (DGE) after pancreatic surgery: a suggested definition by the International Study Group of Pancreatic Surgery (ISGPS). Surgery. 2007;142(5):761–8. doi:https://doi.org/10.1016/j.surg.2007.05.005.
15. Kawai M, Tani M, Hirono S, Ina S, Miyazawa M, Yamaue H. How do we predict the clinically relevant pancreatic fistula after pancreaticoduodenectomy?—an analysis in 244 consecutive patients. World J Surg. 2009;33(12):2670–8. doi:https://doi.org/10.1007/s00268-009-0220-2.
16. Greenblatt DY, Kelly KJ, Rajamanickam V, Wan Y, Hanson T, Rettammel R et al. Preoperative factors predict perioperative morbidity and mortality after pancreaticoduodenectomy. Annals of surgical oncology. 2011;18(8):2126–35. doi:https://doi.org/10.1245/s10434-011-1594-6.
17. Bassi C, Buchler MW, Fingerhut A, Sarr M. Predictive factors for postoperative pancreatic fistula. Annals of surgery. 2015;261(4):e99. doi:https://doi.org/10.1097/sla.0000000000000577.
18. Zhang H, Zhu F, Shen M, Tian R, Shi CJ, Wang X et al. Systematic review and meta-analysis comparing three techniques for pancreatic remnant closure following distal pancreatectomy. Br J Surg. 2015;102(1):4–15. doi:https://doi.org/10.1002/bjs.9653.
19. Crippa S, Cirocchi R, Randolph J, Partelli S, Belfiori G, Piccioli A et al. Pancreaticojejunostomy is comparable to pancreaticogastrostomy after pancreaticoduodenectomy: an updated meta-analysis of randomized controlled trials. Langenbeck's archives of surgery / Deutsche Gesellschaft fur Chirurgie. 2016;401(4):427–37. doi:https://doi.org/10.1007/s00423-016-1418-z.