Retrospective Comparative Analysis of POPF Using Fistula Risk Score According to Pancreaticoenterostomy Method

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Background: The aim of this study is to examine whether pancreaticogastrostomy (PG) or pancreaticojejunostomy (PJ) is the better reconstructive method to reduce postoperative pancreatic fistula (POPF) after pancreaticoduodenectomy (PD) according to the fistula risk.

Methods: An institutional database was reviewed for patients undergoing PD between January 2008 and August 2019. A total of 159 patients were stratified into 4 groups according to the Clinical Risk Score-Pancreatic Fistula. POPF according to 4 risk groups was compared between PJ and PG.

Results: Of the 159 patients, 82 underwent PG (51.6%) and 77 underwent PJ (48.4%) reconstruction. POPF rate was 17.1% (n = 14) in the PG group and 12.9% (n = 10) in the PJ group (P = 0.51). POPF rates were not different in intermediate, low, and negligible risks between 2 reconstructive methods. In the high-risk group (n = 47), there were 4 POPFs (22.2%) in PJ group and 9 (31.0%) in the PG group, respectively (P = 0.74).

Conclusion: In PD, there was no superior method of reconstruction with regard to POPF, even in high-risk glands.

Key words: Postoperative pancreatic fistula (POPF) – Risk score – Pancreaticoenterostomy

Clinically relevant postoperative pancreatic fistulas (CR-POPFs) are still a significant source of morbidity after pancreaticoduodenectomy (PD). However, the best reconstruction method to reduce occurrence of fistula is not conclusive, especially in glands at high risk for POPF. Recently a risk model for POPF was established by Callery et al\(^1\) with emphasis on CR-POPF including grade B and C fistula according to international consensus definitions.\(^2\) The 10-point Fistula Risk Score for Pancreatic Fistula (CRS-PF) accurately predicts CR-POPF after PD. This model, the CRS-PF, has been verified in its
predictive performance by external validations. The CRS-PF is a clinically useful tool for POPF risk stratification after PD and allows the surgeon to address patients at increased risk using intraoperative factors.

In this study, CRS-PF was applied to patients undergoing PD according to pancreaticoenterostomy (PE), including pancreaticojejunostomy (PJ) and pancreaticogastrostomy (PG), and the impact of factors affecting the score for both procedures was analyzed. The purpose of this investigation is to examine whether PG or PJ is the better reconstructive method to reduce CR-POPF after PD according to fistula risks.

**Materials and Methods**

A retrospective review of the institutional pancreatic resection database was performed on prospectively and retrospectively collected data, including clinical, operative, and pathologic information on all patients undergoing pancreatic head resection. Data collection and analysis were approved by the Institutional Review Board.

The database was analyzed to evaluate patients who underwent PD or PPPD between January 2004 and December 2016 in our institution. Patients undergoing total pancreatectomy were excluded. Additionally, patients were excluded if all 4 risk factors for CRS-PF were not available within the record. The intraoperative risk factor for pancreatic fistula was fully recorded, including diagnosis or pathology, pancreatic duct size, pancreas texture, and estimated blood loss (EBL; Table 1). Each patient was stratified by the risk grade for fistula into 1 of 4 categories (negligible, low, intermediate, high). POPF was graded and scored for each patient according to international consensus guidelines, and only patients with CR-POPF were included (grades B and C).

Operative details included operative time (time of incision to close of the wound), and EBL was obtained from the anesthesia record. PJ anastomosis was performed by a 2-layer end-to-side duct-to-mucosa with or without stent. Transanastomotic stenting was variably used through the study periods. External stent was not used after 2016 during PJ because of inconvenience. Final pathologic findings were recorded from the medical chart.

Although the use of a surgical drain varied throughout the course of the series, the most common practice was the placement of a single drain posterior to the choledochojejunostomy and PJ. Occasionally, a second drain could be placed anterior to the PJ for high-risk anastomoses, most often for a soft or fatty infiltrated pancreatic remnant.

PG anastomosis was performed by a 2-layer end-to-side invagination method with internal short stent. Transgastric incision was performed on the anterior and posterior walls of the stomach for pancreas stump invaginating into the antrum.

To compare the clinical variables of the 2 treatment groups, we conducted the chi-squared test or Fisher exact test for categoric variables and the student t-test or Mann-Whitney t test for continuous variables, after assessing normality. An adjusted P value of 0.05 for confounders was considered statistically significant. All statistical analysis was performed with SPSS software (version 24.0, IBM SPSS Statistics, Armonk, New York).

**Results**

**Overview**

Overall, 194 patients underwent PD in the study time periods, and 20 patients undergoing total pancreatectomy were excluded. Additionally, 15 patients were excluded if all 4 risk factors for CRS-PF were not available within the record. Therefore, in the study time periods, 159 patients who underwent PD were part of the study. A total of 77 patients (48.4%) underwent PJ reconstruction dur-

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**Table 1** Fistula risk score for prediction of clinically relevant pancreatic fistula after PD

| Risk factor        | Parameter                          | Points |
|--------------------|------------------------------------|--------|
| Gland texture      | Firm                               | 0      |
|                    | Soft                               | 2      |
| Pathology          | Pancreatic adenocarcinoma or       | 0      |
|                    | pancreatitis                       |        |
|                    | Ampullary, duodenal, cystic, islet cell | 1      |
| Pancreatic duct    | ≥45                                | 0      |
| diameter, mm       | 4                                  | 1      |
|                    | 3                                  | 2      |
|                    | 2                                  | 3      |
|                    | 1                                  | 4      |
| EBL, mL            | ≤400                               | 0      |
|                    | 401–700                            | 1      |
|                    | 701–1000                           | 2      |
|                    | ≥1000                              | 3      |

*Negligible risk, 0 points; low risk, 1–2 points; intermediate risk, 3–6 points; high risk, 7–10 points.

*Total 0 to 10.
ing PD, and 82 patients (51.6%) underwent PD with PG reconstruction.

Demographics of both groups

Table 2 demonstrates patients’ information, including age, sex, and body mass index for both groups. There were fewer patients undergoing PD and fewer external stents in the PG group than in the PJ group \((P, 0.01\) for both). There were similar proportions of soft pancreas in the group receiving PG and in the PJ group \((37.7\% \text{ versus } 34.1\%, P = 0.74\)). Although this did not reach significance, patients who underwent PG had more EBL and longer operation time than those who underwent PJ \((P = 0.09, 0.06\)). Despite the differences seen for gland texture, underlying pathology, and pancreatic duct diameter, patients categorized into the 4 CRS-PF grades (negligible, low, intermediate, and high) were evenly distributed for both groups \((P = 0.17\)).

Clinical outcomes in both groups

Table 3 showed postoperative outcomes. Overall, POPF was observed in 24 of 159 patients (15.1%), including grade B \((n = 14; 8.8\%)\) and grade C \((n = 10; 6.3\%)\). The 14 grade B fistula occurred equivalently in both groups \((9.1\% \text{ versus } 8.5\%; P = 0.78\)), required percutaneous drainage or angiographic control of POPF, and eventually recovered without permanent sequelae. POPFs \((12.9\% \text{ versus } 17.1\%, P = 0.51)\) were equivalent in both PEs. Classic Whipple operation was performed more often in the PJ group than in the PG group \((29.9\% \text{ versus } 6.1\%, P < 0.001)\). The rates of postpancreatectomy hemorrhage, delayed gastric emptying, abdominal abscess, reoperation, and medical complications, such as myocardial infarction, pneumonia, stroke, acute kidney injury, etc, were not different between the 2 groups. There were 8 patients with 30-day mortality during study periods, and there was no difference between the 2 groups.

POPF according to risk category and PE

Table 4 demonstrates the POPF rates according to risk grades on both methods of PE. As expected, there were significantly more overall POPFs for those with intermediate and high CRS-PF scores than for those with negligible and low CRS-PF scores \((P = 0.03)\). Additionally, POPF frequency was equivalent including the high-risk category on both methods of PE.

Table 2 Comparison of demographics between PJ and PG

|                | PJ (n = 77) | PG (n = 82) | \(P\) value |
|----------------|------------|------------|-------------|
| Age, mean ± SD, yr | 65.6 ± 9.9 | 62.6 ± 10.9 | 0.153       |
| Male, n (%)      | 45 (58.4)  | 48 (53.0)  | 0.449       |
| Body mass index, mean ± SD, kg/m² | 23.7 ± 2.5 | 22.7 ± 3.9 | 0.160       |
| ASA, 0/1/2/3, n (%) | 0/24/38/15 (0/31.2/49.4/19.5) | 3/33/35/11 (36.6/40.2/42.7/13.4) | 0.14        |
| PBD, n (%)       | 44 (57.1)  | 38 (46.3)  | 0.13        |
| PD, n (%)        | 23 (29.9)  | 5 (6.1)    | 0.00        |
| Stent,内部/external, n (%) | 51/26 (66.2/33.8) | 82/0 (100.0/0.0) | 0.00        |
| Soft gland, n (%) | 29 (37.7)  | 28 (34.1)  | 0.74        |
| Risk grade, n (%) | 0 (0)      | 2 (2.4)    | 0.17        |
| Negligible       | 0 (0)      | 2 (2.4)    | 0.17        |
| Low             | 9 (11.7)   | 7 (8.5)    | 0.17        |
| Intermediate     | 50 (64.9)  | 44 (53.7)  | 0.17        |
| High            | 18 (23.4)  | 29 (35.4)  | 0.17        |
| EBL, mean ± SD, mL | 713.5 ± 532.4 | 950.3 ± 229.6 | 0.09        |
| Operative time, mean ± SD, min | 422.8 ± 106.5 | 470.3 ± 108.7 | 0.06        |

ASA, American Society of Anesthesiologists; PBD, preoperative bile drainage.

Table 3 Comparison of clinical outcomes between PJ and PG

|                | PJ (n = 77) | PG (n = 82) | \(P\) value |
|----------------|------------|------------|-------------|
| POPF, n (%)    | 10 (12.9)  | 14 (17.1)  | 0.51        |
| Grade B, n (%) | 7 (9.1)    | 7 (8.5)    | 0.78        |
| Grade C, n (%) | 3 (3.9)    | 7 (8.5)    | 0.65        |
| PPH, n (%)     | 7 (9.1)    | 11 (13.4)  | 0.46        |
| Abscess, n (%) | 12 (15.6)  | 7 (8.5)    | 0.22        |
| PD, n (%)      | 23 (29.9)  | 5 (6.1)    | 0.00        |
| DGE, n (%)     | 6 (7.8)    | 6 (7.3)    | 0.15        |
| Medical complication, n (%) | 6 (7.8) | 4 (4.9) | 0.09 |
| Reoperation, n (%) | 4 (5.2) | 5 (6.1) | 0.54 |
| Hospital stay, mean ± SD, days | 20.9 ± 8.3 | 21.4 ± 11.2 | 0.39 |
| 30-day mortality | 3 (3.9) | 5 (6.1) | 0.41 |

DGE, delayed gastric emptying; PPH, postpancreatectomy hemorrhage.
Discussion

This may be the first study comparing CR-POPF according to PE using CRS-PF score. Even though many prior meta-analyses compared POPF rates between PJ and PG, those studies did not use objective criteria for risk of POPF, and the results were not conclusive.

Theoretically, PG could induce a favorable outcome after PD with regard to POPF. Exocrine pancreatic secretions are easily activated in the presence of intestinal enterokinase and bile, but not in the acidic gastric environment, and postoperative gastric decompression can result in the removal of gastric and pancreatic secretions.

In meta-analysis, PG seemed to be superior to PJ with regard to lesser incidence of POPF and other complications, such as biliary fistula and intra-abdominal fluid collection after PD. Therefore, authors concluded surgeons should consider reconstructing the pancreatic remnant following PD with PG.

However, the largest study about POPF after PG and PJ could not demonstrate one surgical procedure to be better than the other. PJ may have little or no difference from PG in overall POPF rate (PJ, 24.3%; PG, 21.4%). In this study, authors pointed out that few studies clearly distinguished clinically significant pancreatic fistula that required a change in the patient’s management.

Recently, investigators recommended the need for randomized control trials specifically recruiting patients with “high-risk pancreas” to be randomized to PG or PJ. In addition, authors focused on the limitations of previous studies and the standardization of surgical techniques, definition of POPF, complication, and perioperative management. Previous meta-analysis have not yet shown objective criteria, such as CRS-PF recording POPF.

Considering well-known higher risks, such as soft and nondilated pancreatic duct, an objective risk model for POPF was established by Callery et al. They proved the CRS-PF based on 4 easily identifiable intraoperative parameters, such as pancreatic duct diameter, pancreas texture, pathology, and EBL.

The CRS-PF is a clinically useful tool for POPF risk stratification after PD and allows for targeted intraoperative and postoperative measures to address patients at increased risk. Multi-institutional experience also confirmed the CRS-PF as a valid tool for predicting the development of CR-POPF after PD. The CRS-PF might organize the information on pancreatic fistula, although this was not always recorded according to standardized methodology before. Herein we applied the CRS-PF for assessment of CR-POPF according to the risk grades between PJ and PG.

Despite the fact that CR-POPF can be observed in low-risk and moderate-risk groups, the clinically relevant form mainly occurs in high-risk glands. So, we have to focus on “high-risk” glands and reveal which method of PE is feasible for high-risk ones.

This study has several limitations requiring a mention. First, the current work is not a randomized controlled study, and therefore it is subject to certain limitations secondary to the retrospective nature of the data collection. Secondly, this study includes 2 surgeons’ procedures, and the technique evolved during the study periods. In fact, the senior surgeon favored PG with higher fistula rate, and the junior surgeon mainly performed PJ during later periods, with lower rates of CR-POPF. The junior surgeon has been setting Blumgart anastomosis since 2012, after which point 5 patients experienced CR-POPF. However, we did not find any difference in the POPF rate at any CRS-PF within the study time period. Third, pancreas texture and duct size were subjective assessments and could have variance between surgeons, and they would ideally be measured in an objective and scientific fashion. However, these measurements may be easier to standardize than measurements of EBL after PD, which can have wide surgeon-specific or institution-specific variation.

In this series, PG is associated with the lesser of PDAC/chronic pancreatitis, but soft pancreas and

Table 4 POPF according to risk grade

| Risk Grade       | Overall (N = 159) | PJ (n = 77) | PG (n = 82) | P value |
|------------------|-------------------|------------|------------|---------|
| Negligible risk, % (n) | 0.0 (0/2)          | —          | 0 (0/2)    | NA      |
| Low risk, % (n)   | 6.2 (1/16)         | 0 (0/9)    | 14.3 (1/7) | 0.49    |
| Intermediate risk, % (n) | 10.6 (10/94)     | 12.0 (6/50) | 9.1 (4/44) | 0.75    |
| High risk, % (n)  | 27.7 (13/47)       | 22.2 (4/18) | 31.0 (9/29) | 0.74    |

NA, not available.
small ducts were equivalently distributed in both. However, PG patients are sometimes placed in the higher risk groups based on blood loss ($P = 0.083$). The “high-risk” PG and PJ pts represented around one third in each procedure, but CR-POPF in high risk was larger in PG (31%) than PJ (18%) patients, without any significance.

It might be up to various factors, such as the surgeon’s skill, experience, and preference of operative technique. Within the factors of the risk score, however, soft pancreas and nondilated small main duct appear to be the greatest factors to predict POPF. When comparing surgeons, institutions, or techniques, one should take into consideration that blood loss is a controllable factor and by including it in the CRS-PF, a surgeon or technique that has an increased blood loss during surgery would benefit from having patients with a higher blood loss attributed to a higher risk.

In conclusion, as previously shown, CRS-PF is a very good predictor for pancreatic fistula. The CR-POPF rate was similar in both procedures, and the overall rate was 16.4% in this study. Even in glands of higher risk, no procedure was superior to another regarding CR-POPF. A future randomized controlled study on this subject is inevitable.

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