

# Matched Analysis of Postoperative Pancreatic Fistula Using Fistula Risk Score According to Pancreaticenterostomy Methods

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## Research

**Keywords:** Pancreas, fistula, risk score, pancreaticojejunostom , pancreaticogastrostomy , pancreaticenterostomy

**Posted Date:** May 22nd, 2020

**DOI:** <https://doi.org/10.21203/rs.3.rs-29862/v1>

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# Abstract

**Background** 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. 159 patients were stratified into four groups according to the Clinical Risk Score-Pancreatic Fistula (CRS-PF). 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 15.1% and 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 two reconstructive methods. In High risk group (n=47), there was 4 (22.2%) POPF in PJ group and 9 (31.0%) in PG group, respectively (p=0.74). **Conclusions** In PD, there was no superior method of reconstruction with regards of POPF, even in high risk glands.

## Background

Postoperative pancreatic fistulas (POPF) 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 high risk gland for POPF. Recently a risk model for POPF was established by Callery and colleagues [1] with emphasis on POPF including grade B and C fistula according to international consensus definitions [2]. 10-point Fistula Risk Score for Pancreatic Fistula (CRS-PF) accurately predicts POPF after PD. This model, the CRS-PF, has been verified in its predictive performance by external validations [3,4]. 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 intra-operative factors [3].

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

## Patients And Methods

A retrospective review of 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 Yeouido St. Mary's Hospital institutional review board.

The database was analyzed to evaluate patients who underwent PD or PPPD between January 2008 and August 2019 in institution (by KY.P and EK.K). 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 the risk grade for fistula into 4 categories (Negligible, Low, Intermediate, High). POPF was graded and scored for each patient according to international consensus guidelines [2]. Operative details included operative time (time of incision to close of the wound), and EBL were obtained from the anesthesia record.

PJ anastomosis was performed by a two layers end to side duct to mucosa with or without stent. Trans-anastomotic stenting was variably used through the study periods. 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 placement of a single drain posterior to the choledochojejunostomy and PJ. Occasionally, a second drain can 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 two layers end to side invagination method with internal short stent. Transgastric incision was performed on anterior and posterior wall of stomach for pancreas stump invaginating into the antrum. Even though senior surgeon performed PD until 2010, and junior surgeon performed procedure consequently after then, the technique of PJ and PG are standardized in this study.

To compare the clinical variables of the two treatment groups, we conducted the chi square test or Fisher's exact test for categorical variables and the student T-test or Mann-Whitney t test for continuous variables, after assessing normality. Adjusted *p* value of 0.05 for confounders was considered statistically significant. All statistical analysis was performed with SPSS 18 (SPSS Corp, Chicago, IL).

## Results

### Overview

Overall 194 patients underwent PD in 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 underwent PD were part of the study. Seventy seven patients (48.4%) underwent PJ reconstruction during PD and 82 (51.6%) patients underwent PD with PG reconstruction.

### Demographics on both groups

Table 2 demonstrates patients' information including age, gender, and BMI for both groups. There were less patients undergone PD and external stent on pancreas in PG than PJ groups ( $p < 0.01$  on both). PG had equivalently soft pancreas comparing those undergoing PJ (37.7% vs 34.1%,  $p = 0.74$ ). While not reaching significance, patients who underwent PG had more EBL and longer operation time than those undergoing PJ ( $p = 0.09, 0.06$ ). Despite the differences seen for gland texture, underlying pathology, and pancreatic duct diameter, patients categorized into the four CRS-PF grades (Negligible, Low, Intermediate, High) were equivalently distributed for both groups ( $p = 0.17$ ).

## Clinical outcomes on both groups

Table 3 showed postoperative outcomes. Overall, Biochemical Leak occurred in 35 among 134 patients (22.0%) and POPF was observed in 24 of 159 patients (15.1%) including Grade B (n=14, 8.8%), and grade C (n=, 6.3%). The 14 Grade B fistula occurred equivalently on both group (9.1% vs 8.5%, p=0.78) required percutaneous drainage or angiographic control of POPF and eventually recovered without permanent sequelae. POPF (12.9% vs 17.1%, p=0.51) were equivalent in both PE. The rates of postpancreatectomy hemorrhage, delayed gastric emptying, abdominal abscess, reoperation, and complication were not different between two 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 POPF for those with intermediate and high CRS-PF score than for negligible and low CRS-PF scores (p=0.03). Additionally, POPF frequency was equivalent including high risk category on both methods of PE.

## Discussion

This is a paper dealing with the two different reconstruction options after a PD: a PJ vs a PG anastomosis. We used retrospectively data from institutional database and implement the prognostic fistula risk score described by Callery et al in order to differentiate between patients that are high risk vs low risk for anastomotic fistula. This is a first study comparing POPF according to PE using CRS-PF score. Even though many meta-analyses compared POPF rates between PJ and PG prior, those studies didn't use objective criteria for risk of POPF and the results were not conclusive. In this study, we tried to differentiate approach by stratifying patients according to the risk of developing a POPF.

Theoretically, PG could induce favorable outcome after PD with regards 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 removal of gastric and pancreatic secretions.

In meta-analysis, PG seemed to be superior to PJ with regards to lesser incidence of POPF and other complications such as biliary fistula and intra-abdominal fluid collection after PD [5-8]. Therefore, authors concluded surgeons should consider reconstructing the pancreatic remnant following PD with PG [6]. However, largest study [9] about POPF after PG and PJ could not demonstrate that one surgical procedure is 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 [9], author pointed out few studies clearly distinguished clinically significant pancreatic fistula which required a change in the patient's management.

Recently, investigators [10,11] recommended needs for randomized control trial recruiting specifically patients with "high risk pancreas" to be randomized to PG or PJ. In addition, author [11] focused on

limitation of previous studies and standardization of surgical techniques, definition of POPF, complication and perioperative management. Previous meta-analysis didn't showed objective criteria such as CRS-PF recording POPF yet.

Considering well known higher risk such as soft and non-dilated pancreatic duct, objective risk model for POPF was established by Callery and colleagues [1]. They proved the CRS-PF based on four 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 intra- 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 (1). The CRS-PF might organize the information on pancreatic fistula, although not always recorded according to standardized methodology before [3]. Herein we applied the CRS-PF for assessment of POPF according to the risk grades between PJ and PG.

Despite POPF can be observed in Low, Intermediate risk, clinically relevant form is mainly occurred in High risk glands (13/24, 54.1%). So, we have to focus on 'High Risk' gland and reveal which method of PE is feasible on high risks.

This study has several limitations requiring mention. First, the current work is not a randomized controlled study and, therefore, is subject to certain limitations secondary to the retrospective nature of the data collection. Secondly, this study includes two surgeons' procedure and the technique evolved over the study periods. In fact, senior surgeon favored PG with higher fistula rate and junior mainly performed PJ during later periods, with lower rate of POPF. However, we did not find any difference in the POPF rate at any CRS-PF within the study time period (data was not shown). Third, pancreas texture and duct size were a subjective assessment 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 estimating the blood loss after PD which can have wide surgeon specific or institution specific variation. The last, we used only a sample of 159 patients operated by two surgeons over the course of 12 years. As this study spans, some aspects of the perioperative care in pancreatic surgery have evolved making little difficult the comparison of patients operated in 2019 vs those operated in 2008. Nevertheless we made effort to keep perioperative protocol used constant throughout the study period.

In this series, small ducts (<2mm) were equivalently distributed on both PE. However, PG patients might be sometimes placed in the higher risk groups based on blood loss ( $p=0.09$ ). The "high risk" PG and PJ patients were around one third in each procedure but POPF in High risk was larger in PG (31.0%) than PJ (22.2%) without any significance. It might be up to various factors such as surgeon's skill, experience and preference of operative technique. Within the factors of the risk score, however, soft pancreas and non-dilated small main duct appear to be the greatest factor to predict POPF. When comparing surgeons, institutions or techniques, one should take in 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. POPF rate was similar on both procedures and overall rate was 15.1% in this study. Even in higher risk of glands, any procedure wasn't superior to another regarding POPF. Randomized controlled study of this subject is inevitable in future.

## Declarations

Acknowledgements Not applicable

Authors' contributions SM Lee was a major contributor in writing the manuscript. KY Paik reviewed the manuscript and gave the main idea of the study. KY Paik and JS Oh helped analyzed the patient data. SM Lee and JS Oh collected the patient data. KY Paik and EK Kim reviewed previous related article and gave the suggestion of the manuscript. All authors read and approved the final manuscript.

Funding This study was supported by research grants from Hanmi Healthcare, Inc.

Availability of data and materials The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Ethics approval and consent to participate Institute of Research Board of Yeouido St. Mary's Hospital.

Consent for publication Not applicable Competing interests

The authors declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

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## Tables

Table 1. Fistula Risk Score for Prediction of Clinically Relevant Pancreatic Fistula after Pancreaticoduodenectomy

Risk factor	Parameter	Points*
Gland texture	Firm	0
	Soft	2
Pathology	Pancreatic adenocarcinoma or pancreatitis	0
	Ampullary, duodenal, cystic, islet cell	1
Pancreatic duct diameter, mm	≥5	0
	4	1
	3	2
	2	3
	1	4
EBL, mL	≤400	0
	401-700	1
	701-1,000	2
	≥1,000	3

\*total 0 to 10;

Negligible-risk 0 points; Low-risk 1-2 points; Intermediate-risk 3-6 points; High-risk 7-10 points

EBL: estimated blood loss

Table 2. Comparison of demographics between PJ and PG.

PJ (N=77)	PG (N=82)	P-value	
Age (year,mean±SD)	65.6±9.9	62.6±10.9	0.153
Male (n,%)	45 (58.4)	48 (53.0)	0.449
BMI (Kg/m <sup>2</sup> ,mean±SD)	23.7±2.5	22.7±3.9	0.160
ASA (0/1/2/3)	0/24/38/15	3/33/35/11	0.14
PBD (n,%)	44(57.1)	38(46.3)	0.13
PD (n,%)	23(29.9)	5(6.1)	0.00
Stent(Internal/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 grades (n,%)			0.17
Negligible risk	0 (0)	2 (2.4)	
Low risk	9 (11.7)	7 (8.5)	
Intermediate risk	50 (64.9)	44 (53.7)	
High risk	18 (23.4)	29 (35.4)	
EBL (ml,mean±SD)	713.5±532.4	950.3±229.6	0.09
Op time (minutes,mean±SD)	422.8±106.5	470.3±108.7	0.06

PJ: pancreaticojejunostomy, PG: pancreaticogastrostomy, BMI: body mass index, ASA: American Society of Anesthesiology, PBD: preoperative biliary drainage, PD: pancreaticoduodenectomy, EBL: estimated blood loss

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	7 (9.1%)	7 (8.5%)	0.78
Grade C	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
Complication (n,%)	6(7.8)	4(4.9)	0.09
Reoperation (n,%)	4(5.2)	5(6.1)	0.54
Hospital day (days,mean±SD)	20.9±8.3	21.4±11.2	0.39

POPF: Postoperative pancreatic fistula, PPH: Postpancreatectomy hemorrhage, PD: pancreaticoduodenectomy, DGE: delayed gastric emptying

Table. 4 POPF according to Risk grades

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

NA: Not applicable