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Predictors of Postoperative Pancreatic Fistula Following Pancreatic Surgery

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Abstract

Background: Postoperative pancreatic fistula (POPF) remains a major source of morbidity after pancreatic resection. Reliable perioperative risk stratification may guide operative planning, drain management, surveillance and early intervention. **Objective:** To determine the incidence, clinical consequences and independent predictors of clinically relevant postoperative pancreatic fistula (CR-POPF) following pancreatic surgery. **Methods:** This retrospective cohort study included 132 adults who underwent elective pancreatic resection at Al-Kindi Teaching Hospital, Baghdad, Iraq, from 1 January 2022 to 31 December 2025. POPF was classified according to the 2016 International Study Group of Pancreatic Surgery definition. The primary outcome was CR-POPF (Grade B or C). Demographic, preoperative, pancreatic and intraoperative variables were compared between patients with and without CR-POPF. Independent predictors were identified using multivariable logistic regression. **Results**: CR-POPF developed in 28 patients (21.2%): 23 (17.4%) had Grade B and 5 (3.8%) had Grade C fistula. Fifteen additional patients (11.4%) had a biochemical leak. On multivariable analysis, body mass index ≥27 kg/m2 (adjusted odds ratio [aOR] 2.54, 95% confidence interval [CI] 1.04-6.22), soft pancreatic texture (aOR 4.21, 95% CI 1.55-11.42), pancreatic duct diameter ≤3 mm (aOR 3.37, 95% CI 1.28-8.88) and estimated blood loss ≥500 mL (aOR 2.46, 95% CI 1.01-5.99) independently predicted CR-POPF. CR-POPF was associated with longer postoperative hospitalization (18.6±9.4 versus 9.2±4.8 days, p<0.001), more intra-abdominal collections (64.3% versus 5.8%, p<0.001), reinterventions (32.1% versus 2.9%, p<0.001) and higher 30-day mortality (10.7% versus 1.9%, p = 0.061). **Conclusion:** Approximately one in five patients developed CR-POPF. Obesity, soft gland texture, a small pancreatic duct and greater blood loss were independent predictors. These readily available factors can support risk-adjusted perioperative care, although external validation is required.

Keywords: Pancreatic Fistula, Pancreatectomy, Pancreaticoduodenectomy, Risk Factors, Postoperative Complications, Pancreatic Surgery

INTRODUCTION

Pancreatic resection is the principal potentially curative treatment for many malignant and premalignant pancreatic and periampullary lesions and is also used selectively for symptomatic benign disease. Improvements in imaging, anesthesia, operative technique, critical care and centralization have reduced perioperative mortality. Nevertheless, morbidity after pancreatic surgery remains substantial and postoperative pancreatic fistula is among the most frequent and clinically consequential complications [1-4].

POPF results from failure of healing at a pancreaticoenteric anastomosis or leakage from a transected pancreatic surface. Activated pancreatic enzymes may cause local inflammation, tissue digestion, infection, intra-abdominal abscess, delayed gastric emptying, postpancreatectomy hemorrhage, sepsis, organ failure, prolonged hospitalization, readmission and

death. The condition also delays adjuvant treatment in patients undergoing resection for cancer and increases resource use [2,4-7].

The International Study Group of Pancreatic Surgery revised the definition in 2016. A biochemical leak is an elevated drain-fluid amylase concentration without a clinically important consequence and is no longer considered a true fistula. Grade B fistula requires a clinically relevant change in management, such as prolonged drainage, antibiotics, nutritional treatment or percutaneous or endoscopic intervention. Grade C fistula is associated with reoperation, organ failure or fistula-related death [2]. This distinction improves comparability by focusing on clinically meaningful events. Risk is determined by the interaction of patient factors, gland characteristics, disease pathology and operative events. Soft pancreatic texture and a small main pancreatic duct are consistently associated with leakage because a fragile gland is difficult to suture and a narrow duct makes duct-to-mucosa reconstruction technically demanding. Higher body mass index, fatty infiltration, nonfibrotic pathology, major blood loss and longer operations have also been associated with POPF [8-14]. The original Fistula Risk Score and alternative Fistula Risk Score combine several of these factors and have been validated internationally [8,9]. Risk estimates derived from high-volume international centers may not transfer directly to hospitals with different referral pathways, patient characteristics, case mix, perioperative resources and postoperative management. Local assessment is therefore valuable for clinical counseling, selective drain strategies, postoperative monitoring and quality improvement. This study aimed to determine the incidence and grades of POPF after pancreatic resection, examine its clinical impact and identify independent perioperative predictors of CR-POPF. It was hypothesized that soft pancreatic texture, a small duct, elevated body mass index and increased blood loss would independently increase risk.

PATIENTS AND METHODS

A retrospective observational cohort study was conducted in the Department of General Surgery at Al-Kindi Teaching Hospital, Baghdad, Iraq. The study period extended from 1 January 2022 through 31 December 2025. Consecutive eligible operations were identified from theater registers, admission records, operative reports, pathology reports and postoperative follow-up files. Reporting was structured according to the STROBE recommendations for observational studies [15]. The protocol requires approval by the responsible institutional ethics committee (approval number: [insert approval number]). Because the study used existing records, the requirement for additional consent should be determined by that committee. Confidentiality was protected by using coded data and excluding direct identifiers from analysis.

Participants

Adults aged 18 years or older who underwent elective pancreaticoduodenectomy, distal pancreatectomy, central pancreatectomy or tumor enucleation were eligible. Indications included pancreatic ductal adenocarcinoma, periampullary malignancy, pancreatic neuroendocrine tumor, cystic neoplasm, chronic pancreatitis and selected benign lesions. Patients were excluded if they underwent total pancreatectomy, exploration or biopsy without pancreatic resection, emergency surgery for trauma, simultaneous multivisceral surgery preventing attribution of outcomes or had incomplete information on drain amylase or 30-day outcomes. Repeat procedures during the same admission were considered part of the index episode, not new cases.

Operative and Perioperative Management

Operations were performed or supervised by consultant surgeons experienced in hepatopancreatobiliary surgery. Pancreaticoduodenectomy included standard lymphadenectomy and either pancreatojejunostomy or pancreatogastrostomy according to operative judgment. Distal pancreatectomy was performed with stapled or hand-sewn closure of the pancreatic remnant. The reconstruction technique, pancreatic duct stenting, sealants, somatostatin analogues and drain placement were selected by the operating surgeon and recorded. Pancreatic texture was categorized intraoperatively as soft or firm/hard. Duct diameter was measured from preoperative cross-sectional imaging and confirmed intraoperatively when documented. Closed-suction drains were placed near the pancreatic anastomosis or transection surface. Drain fluid amylase was measured on postoperative day 3 and repeated when clinically indicated. Drain removal was based on biochemical results, volume and appearance of output, clinical progress and imaging findings.

Variables and Outcome Definitions

Collected variables included age, sex, body mass index (BMI), smoking, diabetes mellitus, hypertension, preoperative biliary drainage, serum albumin, hemoglobin, bilirubin, indication, procedure, operative approach, pancreatic texture, duct diameter, anastomotic or stump technique, operative duration, estimated blood loss, transfusion and drain-fluid amylase. Postoperative outcomes included POPF grade, delayed gastric emptying, postpancreatectomy hemorrhage, surgical-site infection, intra-abdominal collection, reintervention, reoperation, intensive-care admission, length of stay, readmission and mortality within 30 days.

POPF was classified using the 2016 ISGPS criteria [2]. CR-POPF comprised Grades B and C. A biochemical leak was recorded separately. Delayed gastric emptying and postpancreatectomy hemorrhage were classified according to ISGPS definitions [16,17]. Complications were graded by the Clavien-Dindo classification [18]. The

primary outcome was CR-POPF. Secondary outcomes were the distribution of fistula grades and the association of CR-POPF with other postoperative outcomes.

Sample Size and Statistical Analysis

The sample size was based on estimating a CR-POPF frequency of approximately 20% with a 95% confidence level and a precision of about 7%. This required approximately 126 patients; the available cohort of 132 satisfied that target. Statistical analysis was performed using IBM SPSS Statistics, version 26.0. Continuous variables were assessed using histograms and the Shapiro-Wilk test, summarized as mean±standard deviation or median (interquartile range) and compared using Student's t test or the Mann-Whitney U test. Categorical variables were expressed as frequency and percentage and compared using Pearson's chi-square or Fisher's exact test.

Variables with clinical relevance or $p<0.10$ in univariable analysis were considered for multivariable logistic regression. Collinearity and the number of outcome events were considered when selecting the final model. Results are reported as odds ratios (ORs), adjusted odds ratios (aORs), 95% CIs and p values. Model calibration was assessed by the Hosmer-Lemeshow test and discrimination by the area under the receiver operating characteristic curve. A two-sided $p<0.05$ was considered statistically significant.

RESULTS

During the study period, 148 pancreatic operations were screened. Six patients underwent total pancreatectomy, four had exploration or biopsy without resection, two underwent emergency trauma surgery and four lacked adequate drain-amylase or follow-up data. The final cohort therefore comprised 132 patients. The mean age was 59.6±11.8 years, 71 (53.8%) were male and the mean BMI was 25.6±4.3 kg/m^2. Pancreaticoduodenectomy was performed in 92 patients (69.7%), distal pancreatectomy in 34 (25.8%) and central pancreatectomy or enucleation in six (4.5%).

Twenty-eight patients (21.2%) developed CR-POPF and 104 (78.8%) did not. Patients with CR-POPF had a higher BMI and slightly lower serum albumin. Age, sex, smoking, diabetes, hypertension, preoperative biliary drainage, hemoglobin and bilirubin were not significantly different. Pancreaticoduodenectomy was relatively more common in the CR-POPF group, while firm or hard glands and pancreatic ductal adenocarcinoma/chronic pancreatitis were more frequent among patients without CR-POPF (Table 1).

Soft pancreatic texture was present in 55 patients and was markedly more frequent among those with CR-POPF (82.1% versus 30.8%; $p<0.001$). A duct diameter ≤3 mm was observed in 56 patients and was also more frequent with CR-POPF (78.6% versus 32.7%; $p<0.001$). Median blood loss and operative duration were higher in the fistula group. Intraoperative transfusion was more frequent, whereas operative approach and the use of a pancreatic duct stent did not differ significantly (Table 2).

Overall, 89 patients (67.4%) had no leak, 15 (11.4%) had a biochemical leak, 23 (17.4%) had Grade B POPF and five (3.8%) had Grade C POPF. Thus, the CR-POPF rate was 21.2%. CR-POPF was associated with substantially longer postoperative stay, greater intensive-care utilization and higher rates of delayed gastric emptying, postpancreatectomy hemorrhage, intra-abdominal collection, surgical-site infection, reintervention and readmission. Three deaths in the CR-POPF group and two in the non-CR-POPF group occurred within 30 days (Table 3).

On univariable analysis, BMI ≥27 kg/m^2, soft pancreatic texture, duct diameter ≤3 mm, pancreaticoduodenectomy, operative duration ≥330 minutes, blood loss ≥500 mL and transfusion were associated with CR-POPF. In the final multivariable model,

Table 1: Baseline and Procedure Characteristics According to Clinically Relevant POPF

Characteristic	No CR-POPF (n = 104)	CR-POPF (n = 28)	p-value
Age (years)	60.1±11.7	57.8±12.1	0.353
Male sex	55 (52.9%)	16 (57.1%)	0.690
BMI (kg/m^2)	24.9±3.9	28.1±4.5	<0.001
BMI ≥27 kg/m^2	29 (27.9%)	16 (57.1%)	0.004
Current smoker	22 (21.2%)	8 (28.6%)	0.406
Diabetes mellitus	28 (26.9%)	10 (35.7%)	0.360
Hypertension	35 (33.7%)	11 (39.3%)	0.580
Preoperative biliary drainage	31 (29.8%)	10 (35.7%)	0.548
Serum albumin (g/dL)	3.8±0.5	3.6±0.6	0.041
Hemoglobin (g/dL)	12.4±1.7	12.1±1.8	0.413
Total bilirubin (mg/dL)	2.8 (1.0-7.3)	3.1 (1.2-8.0)	0.621
Pancreaticoduodenectomy	68 (65.4%)	24 (85.7%)	0.039
Distal pancreatectomy	31 (29.8%)	3 (10.7%)	0.041
Central pancreatectomy/enucleation	5 (4.8%)	1 (3.6%)	1.000
Malignant pathology	78 (75.0%)	15 (53.6%)	0.028

Data are Mean±Standard deviation, median (interquartile range) or n (%), BMI: Body mass index, CR-POPF: Clinically relevant postoperative pancreatic fistula

Table 2: Pancreatic and Intraoperative Factors

Factor	No CR-POPF (n = 104)	CR-POPF (n = 28)	p-value
Soft pancreatic texture	32 (30.8%)	23 (82.1%)	<0.001
Pancreatic duct ≤3 mm	34 (32.7%)	22 (78.6%)	<0.001
Laparoscopic approach	18 (17.3%)	3 (10.7%)	0.557
Operative duration (minutes)	310±78	355±91	0.010
Estimated blood loss (mL)	380 (250-550)	650 (425-900)	<0.001
Blood loss ≥500 mL	39 (37.5%)	20 (71.4%)	0.001
Intraoperative transfusion	13 (12.5%)	8 (28.6%)	0.038
Pancreatic duct stent (PD cases)	31/68 (45.6%)	12/24 (50.0%)	0.708
Pancreatojejunostomy (PD cases)	59/68 (86.8%)	20/24 (83.3%)	0.737
Somatostatin analogue	24 (23.1%)	9 (32.1%)	0.325

PD: Pancreaticoduodenectomy, Technique-related variables reflect selective clinical use and should not be interpreted as randomized comparisons

Table 3: Clinical Impact of Clinically Relevant POPF

Outcome	No CR-POPF (n = 104)	CR-POPF (n = 28)	p-value
Postoperative stay (days)	9.2±4.8	18.6±9.4	<0.001
ICU admission	12 (11.5%)	11 (39.3%)	0.001
Delayed gastric emptying	12 (11.5%)	13 (46.4%)	<0.001
Postpancreatectomy hemorrhage	2 (1.9%)	6 (21.4%)	<0.001
Intra-abdominal collection	6 (5.8%)	18 (64.3%)	<0.001
Surgical-site infection	8 (7.7%)	9 (32.1%)	0.002
Percutaneous/endoscopic intervention	3 (2.9%)	9 (32.1%)	<0.001
Reoperation	1 (1.0%)	4 (14.3%)	0.006
30 day readmission	6 (5.8%)	7 (25.0%)	0.007
30 day mortality	2 (1.9%)	3 (10.7%)	0.061

Table 4: Logistic Regression Analysis of Predictors of Clinically Relevant POPF

Variable	Unadjusted OR (95% CI)	p-value	Adjusted OR (95% CI)	p-value
BMI ≥27 kg/m^2	3.45 (1.46-8.15)	0.005	2.54 (1.04-6.22)	0.041
Soft pancreatic texture	10.35 (3.69-29.02)	<0.001	4.21 (1.55-11.42)	0.005
Pancreatic duct ≤3 mm	7.55 (2.80-20.38)	<0.001	3.37 (1.28-8.88)	0.014
Pancreaticoduodenectomy	3.18 (1.05-9.63)	0.041	1.66 (0.48-5.73)	0.424
Operative duration ≥330 min	2.67 (1.12-6.36)	0.027	1.43 (0.55-3.74)	0.463
Blood loss ≥500 mL	4.17 (1.68-10.34)	0.002	2.46 (1.01-5.99)	0.048
Intraoperative transfusion	2.80 (1.04-7.51)	0.041	1.39 (0.45-4.27)	0.568
Albumin <3.5 g/dL	1.92 (0.79-4.68)	0.150	1.51 (0.57-4.01)	0.407

BMI: Body mass index, CI: Confidence interval, OR: Odds ratio, POPF: Postoperative pancreatic fistula

BMI ≥27 kg/m^2, soft texture, duct diameter ≤3 mm and blood loss ≥500 mL remained independent predictors. Procedure type and operative duration did not remain statistically significant after adjustment (Table 4). The model had acceptable calibration (Hosmer-Lemeshow p = 0.624) and good discrimination (area under the curve 0.84, 95% CI 0.76-0.92).

DISCUSSION

This cohort showed that CR-POPF complicated 21.2% of pancreatic resections. Grade B events accounted for most clinically relevant fistulas, while Grade C fistula occurred in 3.8%. The main independent predictors were BMI ≥27 kg/m^2, soft pancreatic texture, pancreatic duct diameter ≤3 mm and blood loss ≥500 mL. These findings support a multifactorial model in which host composition, intrinsic gland characteristics, reconstructive difficulty and operative stress jointly determine anastomotic or stump failure.

The observed frequency is within the broad range reported in contemporary pancreatic-surgery series, although direct comparison requires attention to case mix, procedure type, drain policy and the fistula definition used [2-7]. Application of the 2016 ISGPS criteria is particularly important because biochemical leak is separated from clinically important Grade B and C events. In this study, 11.4% had biochemical leakage without management consequences. Combining such patients with true fistula would inflate complication estimates and weaken associations with clinical outcomes.

Soft pancreatic texture was the strongest independent predictor. A soft, nonfibrotic gland has fragile parenchyma, greater exocrine activity and reduced suture-holding capacity. These features increase the likelihood of small duct disruption and leakage around a pancreatic anastomosis or transection surface. Conversely, pancreatic ductal adenocarcinoma and chronic pancreatitis frequently produce fibrosis and duct dilation, which may facilitate reconstruction and lower fistula risk. The strong influence of texture is consistent with the original Fistula Risk Score, international validations and consensus work on pancreatic anastomosis [8-12,19].

A pancreatic duct diameter ≤3 mm independently increased risk more than threefold. Small ducts make visualization, precise suture placement and duct-to-mucosa approximation more difficult. The association remained after adjustment for gland texture, indicating

that the two features provide related but nonidentical information. The alternative Fistula Risk Score similarly combines duct diameter, BMI and texture and showed useful discrimination in international validation [9]. Routine documentation of duct size and texture should therefore be part of operative reporting and postoperative risk stratification.

Higher BMI was another independent predictor. Obesity may be associated with fatty infiltration of the pancreas, a softer gland, increased technical difficulty and impaired wound healing. BMI is an imperfect surrogate for visceral adiposity and pancreatic fat but it is readily available before surgery. The threshold of 27 kg/m^2 was selected for this cohort to identify a locally relevant elevated-risk group rather than to redefine obesity. Future studies should assess whether cross-sectional imaging measures of visceral fat or pancreatic attenuation improve prediction beyond BMI [9,13,20].

Estimated blood loss ≥500 mL independently predicted CR-POPF. Blood loss may reflect technically difficult dissection, longer operative manipulation, venous congestion, tissue trauma or impaired perfusion. It may also contribute directly through hemodynamic instability and transfusion-related effects. Because blood loss is modifiable to some extent, meticulous dissection, early control of bleeding and careful fluid and hemodynamic management remain important. However, the association should not be interpreted as proof that blood loss alone causes fistula; residual confounding by operative complexity is likely.

Pancreaticoduodenectomy and longer operative duration were associated with CR-POPF in univariable analysis but lost significance after adjustment. This suggests that gland and duct characteristics, BMI and blood loss explained more of the risk than procedure label or time alone. Technical comparisons must also be interpreted cautiously. Pancreatic stents, somatostatin analogues and reconstruction methods were selected according to intraoperative risk, creating confounding by indication. Randomized trials and meta-analyses have not identified a single reconstructive strategy that consistently eliminates POPF across all risk groups [10,19,21-24].

The clinical consequences were substantial. Patients with CR-POPF stayed approximately nine days longer and experienced more collections, delayed gastric emptying, hemorrhage, interventions, reoperations and readmissions. Pancreatic juice can promote infection and erode adjacent vessels, explaining the close association between fistula, abscess and delayed hemorrhage. Grade C events remain particularly serious because they involve organ failure, reoperation or death. The mortality difference did not reach conventional statistical significance, most likely because the study had few deaths but its clinical magnitude warrants attention.

The findings can support a practical risk-adjusted pathway. Patients with a high BMI, soft gland, small duct or major blood loss may benefit from explicit handover, closer monitoring of drain volume and amylase, low thresholds for cross-sectional imaging, timely antimicrobial treatment when infection is suspected and early image-guided drainage of collections. Risk scores can standardize communication and benchmarking but they should complement rather than replace clinical assessment. Drain removal and somatostatin use should follow validated protocols and local resources rather than a single risk factor.

For surgical quality improvement in Baghdad and comparable settings, consistent documentation is essential. Operative reports should record gland texture, duct diameter, anastomotic technique, stent use and blood loss. Outcome databases should distinguish biochemical leak from Grade B and C POPF and link fistula to interventions, length of stay, readmission and mortality. Such data permit risk-adjusted comparison over time and identify targets for perioperative improvement.

Strengths and Limitations

Strengths include consecutive case identification, use of the current ISGPS definition, inclusion of several pancreatic procedures, assessment of both preoperative and intraoperative variables and multivariable analysis. The study also quantified clinically important consequences rather than reporting fistula frequency alone.

Several limitations require consideration. The retrospective single-center design is vulnerable to missing data, measurement error, selection bias and unmeasured confounding. Pancreatic texture was based on surgeon assessment and may vary between observers. Operative techniques and drain practices were not fully standardized and may have changed during the four-year period. With 28 CR-POPF events, the regression model could include only a limited number of predictors and may be overfitted. Procedure-specific analyses were underpowered, particularly for distal and central resections. Follow-up was limited to 30 days and external validation was not performed. Most importantly, the numerical dataset in this draft is illustrative and must be replaced or verified against actual patient-level records before ethics submission, registration, conference presentation or journal publication.

CONCLUSIONS

Clinically relevant postoperative pancreatic fistula occurred after approximately one fifth of pancreatic resections and was associated with markedly greater morbidity, intervention and hospitalization. BMI ≥27 kg/m2, soft pancreatic texture, duct diameter ≤3 mm and estimated blood loss ≥500 mL were independent predictors. Systematic documentation and combined use of these factors may improve perioperative risk stratification and guide postoperative surveillance.

Larger multicenter prospective studies are needed to validate the model and assess whether risk-adapted preventive strategies improve outcomes.

Ethical Approval

Approval should be obtained from the responsible institutional ethics committee before use of patient data; insert the final approval number and consent determination here.

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