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Preoperative Body Mass Index-to-Prognostic Nutritional Index Ratio and Clinically Relevant Pancreatic Fistula After Pancreaticoduodenectomy

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Abstract

Background: Clinically relevant postoperative pancreatic fistula (CR-POPF) remains a major complication of pancreaticoduodenectomy. The body mass index-to-prognostic nutritional index (BMI/PNI) ratio combines readily available anthropometric and laboratory measurements. This study assessed its association with CR-POPF and explored a ratio for preoperative risk stratification.

Materials and methods: This prospective observational study consecutively enrolled 32 patients undergoing pancreaticoduodenectomy at a tertiary university hospital in Dhaka, Bangladesh, from December 2023 to November 2024. BMI and PNI were measured preoperatively. Outcomes were compared between patients with grade B or C fistula and those without CR-POPF. Continuous variables were summarized as medians and interquartile ranges and compared using the Mann-Whitney U test. Categorical comparisons used Fisher's exact test when expected cell counts were small.

Results: Ten patients developed CR-POPF (31.3%; exact 95% confidence interval, 16.1-50.0%). The median BMI/PNI ratio was 0.57 versus 0.43 in patients with and without CR-POPF, respectively. BMI was higher (24.4 versus 21.0 kg/m²; p=0.043), while PNI was lower (41.4 versus 49.5; p=0.002). The median BMI/PNI ratio yielded sensitivity of 80.0% (95% CI, 44.4-97.5%), specificity of 90.9% (95% CI, 70.8-98.9%), and accuracy of 87.5% (95% CI, 71.0-96.5%).

Conclusions: A higher preoperative BMI/PNI ratio was associated with CR-POPF in this small cohort. The exploratory ratio requires validation in an independent population before clinical adoption.

Categories: General Surgery, Oncology, Gastroenterology
Keywords: body mass index, pancreaticoduodenectomy, postoperative complications, postoperative pancreatic fistula, prognostic nutritional index

Introduction

Pancreaticoduodenectomy is performed for malignant and selected nonmalignant diseases of the pancreatic head and periampullary region [1]. Postoperative pancreatic fistula can complicate recovery and require prolonged drainage, additional procedures, or intensive treatment. Contemporary International Study Group on Pancreatic Surgery (ISGPS) criteria distinguish a biochemical leak from clinically relevant fistula [2]. This distinction matters when estimating complication rates and evaluating a predictive marker, because an elevated drain amylase concentration without a clinically consequential course does not constitute clinically relevant postoperative pancreatic fistula (CR-POPF) [2].

Fistula risk reflects both patient characteristics and features of the pancreatic remnant. The alternative Fistula Risk Score incorporates body mass index (BMI), pancreatic texture, and pancreatic duct diameter and has undergone international external validation [3]. Preoperative nutritional status is also relevant: a prospective study of 355 patients found higher overall complication and pancreatic fistula rates among patients who were malnourished or at risk of malnutrition [4]. A marker available before surgery could complement operative assessment and help identify patients requiring closer perioperative evaluation.

Prognostic nutritional index (PNI) combines serum albumin and the peripheral lymphocyte count. These measurements reflect overlapping nutritional, inflammatory, and immune processes, and PNI should

therefore not be interpreted as an isolated measure of dietary intake. Dividing BMI by PNI produces a higher ratio when BMI rises, PNI falls, or both occur. Sato et al. evaluated this ratio in 87 patients undergoing pancreaticoduodenectomy and reported an association with clinically relevant fistula [5]. Further evidence linking a lower preoperative PNI with progression from biochemical leak to CR-POPF supports investigation of the nutritional component of this marker [6].

The simplicity of the ratio is attractive in settings where height, weight, serum albumin, and blood counts are routinely available. However, its performance may depend on patient selection, disease distribution, surgical practice, and the definition of fistula. The present study therefore assessed the association of preoperative BMI, PNI, and BMI/PNI ratio with CR-POPF after pancreaticoduodenectomy and explored the discrimination and classification performance of BMI/PNI in a consecutive single-center cohort.

Materials And Methods

Study design and setting

This prospective observational study was conducted in the Department of Hepatobiliary, Pancreatic, and Liver Transplant Surgery at Bangabandhu Sheikh Mujib Medical University, Dhaka, Bangladesh, from December 2023 to November 2024. Bangabandhu Sheikh Mujib Medical University issued approval memorandum No. BSMMU/2023/13703 and registration No. 4675. The institution is now Bangladesh Medical University. Patients undergoing pancreaticoduodenectomy during the study period were recruited consecutively. Treatment was not assigned by the study protocol, and comparison groups were defined by postoperative fistula status.

Participants and sample size

Thirty-two patients were enrolled according to the eligibility criteria in Table *1*. This used a finite-population sample-size approach attributed to Krejcie and Morgan [7], based on an estimated annual population of 35 pancreaticoduodenectomies, an assumed population proportion of 0.50, a 5% margin of error, and a chi-square value of 3.841. These inputs produce an estimated sample size of approximately 32.15; However, this epidemiological sample size approach was not specifically designed for diagnostic accuracy studies. No dedicated sample size calculation based on the anticipated sensitivity, specificity, or area under the receiver operating characteristic curve (AUC) was performed. Accordingly, the enrolled sample should be considered an institutionally feasible exploratory cohort rather than a formally powered diagnostic accuracy sample. The study was not designed to establish precise diagnostic performance estimates or to support a multivariable prediction model.

Inclusion criteria	Exclusion criteria
Age 18–75 years	Age below 18 or above 75 years
Patients of either sex undergoing pancreaticoduodenectomy	Pancreaticoduodenectomy for pancreatic trauma
Written informed consent to participate	Unwillingness to participate

TABLE 1: Inclusion and exclusion criteria

The sample size was calculated by the following formula:

$$\begin{aligned}
n&=\frac{\chi^2 NP(1-P)}{e^2(N-1)+\chi^2P(1-P)}\\[6pt]
&=\frac{3.841\times35\times0.5(1-0.5)}{(0.05)^2(35-1)+3.841\times0.5(1-0.5)}\\[6pt]
&=\frac{33.60875}{1.04525}=32.15\\[6pt]
&\boxed{n\approx32}
\end{aligned}$$

n = sample size; N = population size =35; e = acceptable sampling error 5% = 0.05; x^2 = chi-square of degree of freedom 1 and confidence 95% = 3.841; P = Proportion of population = 0.5. Thus, n = 32.15. The calculated sample size is 32. The population proportion was assumed to be 0.50, as specified in the original Krejcie and Morgan (1970) formula [7], to yield the maximum required sample size in the absence of a reliable prior estimate. A margin of error of 5% was selected as the conventional acceptable level of precision at a 95% confidence level. The parameter d in the original Krejcie and Morgan formula and e in the formula presented in this manuscript represent the same statistical parameter, namely, the margin of error (degree of accuracy or precision). Figure *1* summarizes the study participant flow diagram.

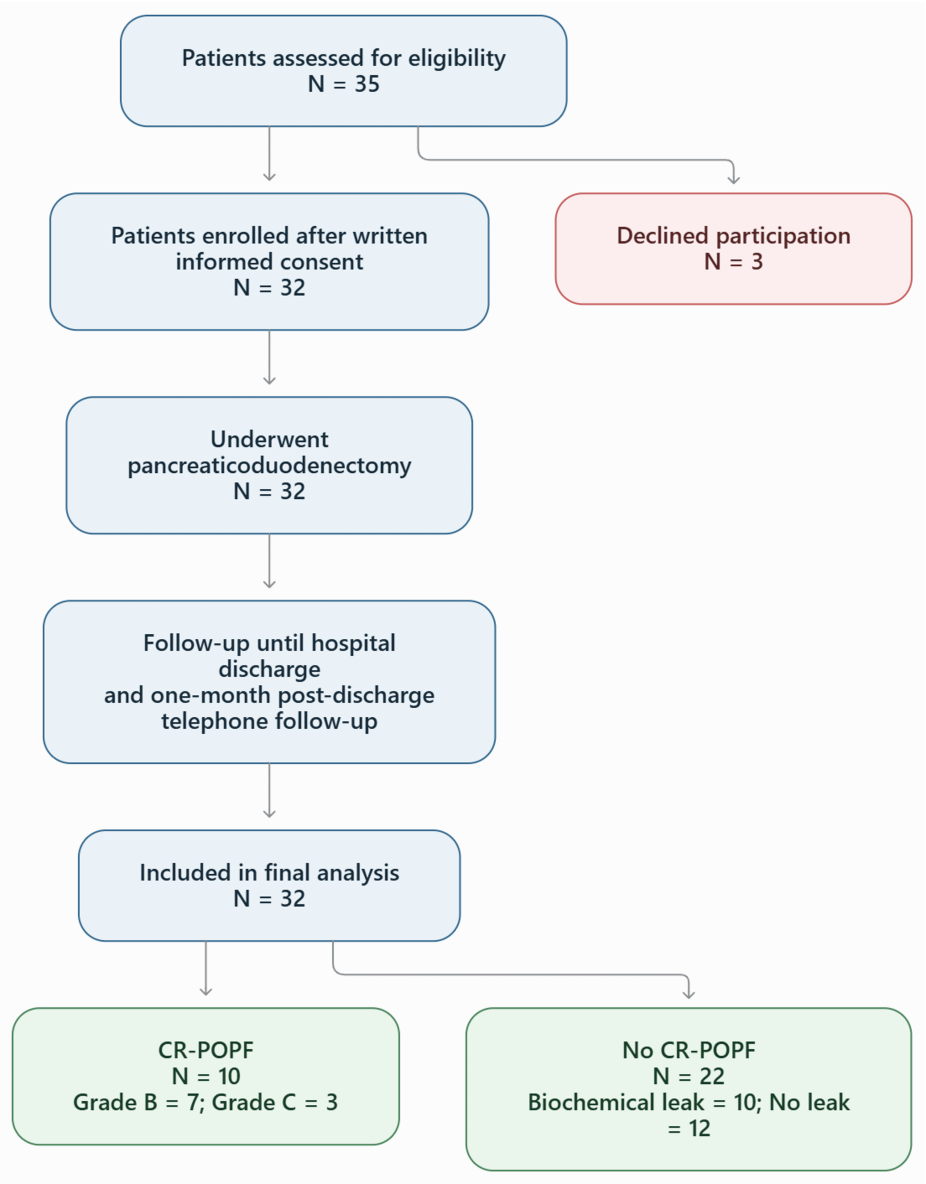


FIGURE 1: Study participant flow diagram according to STROBE-style prospective cohort flow

STROBE flow diagram showing participant screening, recruitment, follow-up, and final analysis. Of 35 potentially eligible patients, three declined participation, and 32 were enrolled. All enrolled participants underwent pancreaticoduodenectomy, completed the reported follow-up, and were included in the final analysis.

STROBE: Strengthening the Reporting of OBservational studies in Epidemiology; CR-POPF: clinically relevant postoperative pancreatic fistula

Preoperative assessment and index calculation

A structured data collection form recorded demographic characteristics, comorbidities, preoperative biliary drainage, diagnosis, anthropometric measurements, and laboratory results. Blood samples and anthropometric data were collected within one week before surgery. BMI was calculated as body weight in kilograms divided by height in meters squared. PNI was calculated as 10 × serum albumin (g/dL) + 0.005 × absolute lymphocyte count (cells/mm^3) [8]. All laboratory results were analyzed from the same blood sample. BMI/PNI was calculated by dividing BMI by PNI [5]. Albumin values recorded in g/L were converted to g/dL before this formula was applied.

Pancreatic texture, duct diameter, operative duration, and estimated blood loss were recorded intraoperatively. Final diagnoses were obtained from postoperative records and histopathology.

Surgical technique and postoperative care

Pancreaticoduodenectomy was performed using the department's standard operative technique. Pancreaticojejunostomy was performed using a duct-to-mucosa technique. Approximation sutures were passed through the pancreatic stump and the jejunal subserosal layer, followed by interrupted duct-to-mucosa sutures using 5-0 absorbable monofilament material. A 4-6 Fr pancreatic duct drainage tube was selected according to the main pancreatic duct size, secured at the anastomotic site, and externalized through the anterior abdominal wall. One or two intra-abdominal drains were placed near the pancreaticojejunostomy.

Oral intake was generally resumed on postoperative days 3-5 if there was no evidence of intra-abdominal complications. Peripancreatic drain fluid amylase was measured on postoperative day 3. Repeat measurements were performed when required. Peripancreatic drains were usually removed on or after postoperative day 7 when leakage was not evident. Pancreatic juice output through the external drainage system was recorded during postoperative days 1-3.

Outcome definitions and follow-up

The primary outcome was CR-POPF, defined as ISGPS grade B or C postoperative pancreatic fistula [2]. Under the 2016 ISGPS definition, postoperative pancreatic fistula is characterized by measurable drain-fluid output on or after postoperative day 3 with amylase activity greater than three times the institutional upper limit of normal serum amylase (25-115 U/L), when accompanied by a clinically relevant condition directly related to the fistula. An isolated elevation in drain-fluid amylase without clinical consequences is classified as a biochemical leak and is not CR-POPF. Grade B requires a change in clinical management, such as prolonged drainage or drain repositioning/intervention. Grade C requires fistula-attributable reoperation, organ failure, or death. The cohort was classified as 10 CR-POPF cases (seven grade B and three grade C) and 22 patients without CR-POPF (10 biochemical leaks and 12 with no pancreatic leak). The three grade C fistulas were related to organ failure followed by death. Other outcomes included delayed gastric emptying, biliary leak, infectious complications, reoperation, readmission, mortality, and postoperative hospital stay. Delayed gastric emptying was defined according to ISGPS criteria, based on delayed return to oral diet and the requirement for nasogastric decompression [9]. Biliary leak was defined as draining bilirubin at least three times the serum concentration on or after postoperative day 3 or the need for intervention for a biliary collection or bile peritonitis [10]. Infectious complications included wound, intra-abdominal, urinary, respiratory, biliary, and catheter-related infections. Mortality included death within 30 days or during a longer index hospitalization. After discharge the patients were followed up for one month over the telephone and advised to visit the outdoor or emergency department in any need. Hospital stay was measured from the first postoperative day until discharge or in-hospital death.

Statistical analysis

After compilation, data were entered and checked in Microsoft Excel 2019 (Microsoft Corporation, Redmond, WA, USA) and analyzed using IBM SPSS Statistics for Windows, Version 26 (Released 2018; IBM Corp., Armonk, New York, United States). Continuous variables were summarized as mean ± standard deviation or median with the 25th and 75th percentiles. Group comparisons for continuous variables used the Mann-Whitney U test. Differences between reported medians are descriptive contrasts, not Hodges-Lehmann estimates. The Mann-Whitney test evaluates distributional differences and is not generally a test of medians alone. When expected cell counts were below five, two-sided Fisher's exact tests were used for inference. Pearson χ^2 statistics and degrees of freedom are displayed alongside Cramér's V; for a 2 × 2 table, V is the square root of χ^2 divided by the sample size. Unadjusted odds ratios and approximate 95% log-Wald confidence intervals were also calculated. These intervals are imprecise with sparse cells. All comparisons were exploratory and used a two-sided significance threshold of 0.05 without adjustment for multiple testing. Supplementary calculations were performed using Python 3.11 (Python Software Foundation, Fredericksburg, VA) with SciPy 1.17.0.

The discriminatory performance of BMI, PNI, and BMI/PNI ratio for CR-POPF was evaluated using receiver operating characteristic (ROC) curve analysis. It was calculated using the non-parametric empirical method (coordinate-based method). The area under the curve (AUC) with 95% confidence intervals was calculated. The optimal BMI/PNI threshold was explored using the Youden index [11,12], calculated as sensitivity + specificity − 1. The analysis was considered exploratory because the threshold was evaluated in the same cohort in which its performance was assessed.

Results

Thirty-five potentially eligible patients were screened/approached during the study period. Three declined participation, and 32 provided written informed consent and were enrolled; all 32 were included in the analysis. The 32 participants had a mean age of 54.2 ± 7.9 years (range, 34-65 years), and 18 (56.3%) were male. Nineteen patients (59.4%) had reported comorbidity, and two (6.3%) underwent preoperative biliary drainage. Ampullary adenocarcinoma was the most frequent diagnosis. Baseline and perioperative summaries are presented in Table *2*.

Characteristic	Value
Age, years; mean ± SD (range)	54.2 ± 7.9 (34–65)
Male/female, n (%)	18 (56.3) / 14 (43.8)
Any comorbidity, n (%)	19 (59.4)
Preoperative biliary drainage, n (%)	2 (6.3)
Ampullary adenocarcinoma, n (%)	14 (43.8)
Pancreatic head carcinoma, n (%)	8 (25.0)
Distal bile duct carcinoma, n (%)	5 (15.6)
Duodenal carcinoma, n (%)	1 (3.1)
Chronic pancreatitis, n (%)	2 (6.3)
Solid pseudopapillary tumor/IPMN, n (%)	1 (3.1) / 1 (3.1)
Lymphocyte count, cells/mm³	2150 (1550–2700)
Albumin, g/dL	3.5 (3.2–4.1)
BMI, kg/m²	22.0 (20.1–25.3)
PNI	46.0 (41.9–52.9)
BMI/PNI	0.47 (0.40–0.56)
Soft/firm pancreas, n (%)	23 (71.9) / 9 (28.1)
Pancreatic duct diameter, n (%)	
≤3 mm	17 (53.1)
>3 mm	15 (46.9)
Operative duration, hours	5.0 (4.5–5.0)
Blood loss, mL	300 (250–300)

TABLE 2: Characteristics of the study cohort

N=32. Values are described as medians (25th–75th percentiles) unless otherwise indicated.

SD: standard deviation; BMI: body mass index; PNI: prognostic nutritional index; IPMN: intraductal papillary mucinous neoplasm

CR-POPF occurred in 10 patients (31.3%; exact 95% CI, 16.1-50.0%), comprising seven grade B and three grade C events. Ten additional patients had biochemical leaks, and 12 had no leaks. Delayed gastric emptying occurred in seven patients (21.9%) and infectious complications in 11 (34.4%). Three patients died (9.4%). Three patients died during hospital stays within two weeks due to grade C POPF (9.4%). The median hospital stay was 15.0 days (IQR, 12.0-22.7) (Table 3). Complications could overlap within the same patient.

Outcome	n/N (%)	95% CI for proportion
CR-POPF	10/32 (31.3)	16.1–50.0%
Grade B fistula	7/32 (21.9)	9.3–40.0%
Grade C fistula	3/32 (9.4)	2.0–25.0%
Biochemical leak	10/32 (31.3)	16.1–50.0%
No pancreatic leak	12/32 (37.5)	21.1–56.3%
Delayed gastric emptying	7/32 (21.9)	9.3–40.0%
Biliary leak	2/32 (6.3)	0.8–20.8%
Infectious complications	11/32 (34.4)	18.6–53.2%
Postoperative mortality	3/32 (9.4)	2.0–25.0%
Postoperative hospital stays, days*	15.0 (12.0–22.7)	–

TABLE 3: Postoperative outcomes

Statistical method: exact binomial (Clopper–Pearson) confidence intervals; no hypothesis test. Effect measure: incidence proportion, not a between-group effect.

*: median (Interquartile range); CR-POPF: clinically relevant postoperative pancreatic fistula; CI: confidence interval

Patients with CR-POPF had a higher median BMI (24.4 versus 21.0 kg/m^2) and a lower median PNI (41.4 versus 49.5). The median BMI/PNI ratio was 0.57 versus 0.43, a descriptive difference of 0.14. Lymphocyte count and albumin were also lower in the CR-POPF group. Continuous variable comparisons and descriptive contrasts are shown in Table *4*.

Variable	CR-POPF (n=10)	No CR-POPF (n=22)	Median difference	p	Test
Age, years	56.0 (51.5–61.2)	55.0 (47.2–60.0)	+1.0	0.458	Mann–Whitney U
Lymphocytes, cells/mm³	1600 (1314–2507)	2375 (1995–3087.5)	−775	0.022	Mann–Whitney U
Albumin, g/dL	3.4 (2.9–3.5)	3.7 (3.3–4.1)	−0.3	0.047	Mann–Whitney U
BMI, kg/m²	24.4 (21.3–26.2)	21.0 (19.7–22.8)	+3.4	0.043	Mann–Whitney U
PNI	41.4 (38.2–46.1)	49.5 (44.2–55.3)	−8.1	0.002	Mann–Whitney U
BMI/PNI	0.57 (0.52–0.65)	0.43 (0.37–0.48)	+0.14	<0.001	Mann–Whitney U
Operative duration, hours	5.0 (4.9–6.0)	5.0 (4.0–5.0)	0.0	0.084	Mann–Whitney U
POD3 external drain fluid amylase level, U/L	3502 (2437–4136.7)	282.5 (65–690)	+3219.5	<0.001	Mann–Whitney U
POD3 External drain tube output, mL	350 (287–412)	212.5 (175–255)	+137.5	<0.001	Mann–Whitney U
POD3 Pancreatic juice output, mL	300 (235–387)	200 (156–237.5)	+100	0.001	Mann–Whitney U

TABLE 4: Continuous variables by CR-POPF status

Values are medians (25th–75th percentiles). Effect measure: difference in reported medians (CR-POPF minus no CR-POPF), a descriptive contrast.

POD: postoperative day; SD: standard deviation; BMI: body mass index; PNI: prognostic nutritional index; U/L: unit/liter; CR-POPF: clinically relevant postoperative pancreatic fistula

Fisher's exact tests did not show statistically significant associations of sex, comorbidity, or pancreatic texture with CR-POPF (Table 5). Confidence intervals for the corresponding odds ratios were wide. These estimates should not be interpreted as demonstrating the absence of an association.

Comparison	CR-POPF	No CR-POPF	χ² / df	Cramér's V	OR (95% CI)	p	Test Name
Male versus female	8/10 (80.0%)	10/22 (45.5%)	3.334 / 1	0.323	4.80 (0.82–27.96)	0.124	Fisher's exact
Any comorbidity versus none	5/10 (50.0%)	14/22 (63.6%)	0.530 / 1	0.129	0.57 (0.13–2.60)	0.699	Fisher's exact
Soft versus firm pancreas	9/10 (90.0%)	14/22 (63.6%)	2.364 / 1	0.272	5.14 (0.55–48.37)	0.210	Fisher's exact

TABLE 5: Categorical associations with CR-POPF

Effect measures: Cramér's V and unadjusted odds ratio (OR) for the first category relative to the second. χ² is Pearson chi-square; df is degrees of freedom. Inference uses two-sided Fisher's exact tests because of small expected counts. OR CIs use a log-Wald approximation.

CR-POPF: clinically relevant postoperative pancreatic fistula

Among the 20 patients with either a biochemical leak or CR-POPF, the CR-POPF group had a lower PNI and a higher BMI/PNI ratio than the biochemical-leak group (Table 6). This comparison is exploratory and does not establish that all CR-POPF cases progressed through a documented biochemical-leak stage.

Variable	CR-POPF (n = 10)	Biochemical leak (n = 10)	Median difference	p	Statistical test
BMI, kg/m²	24.4 (21.3–26.2)	21.0 (18.7–22.0)	+3.4	0.089	Mann–Whitney U
PNI	41.4 (38.2–46.1)	50.7 (47.1–54.4)	−9.3	0.002	Mann–Whitney U
BMI/PNI ratio	0.57 (0.52–0.65)	0.42 (0.36–0.48)	+0.15	<0.001	Mann–Whitney U

TABLE 6: Exploratory nutritional comparisons of CR-POPF and biochemical leak

Effect measure: descriptive difference between medians (CR-POPF minus biochemical leak).

BMI: body mass index; PNI: prognostic nutritional index; CR-POPF: clinically relevant postoperative pancreatic fistula

A ROC analysis was used to assess the risk of POPF shown in Figure *2*. The Youden Index [5] was used to find out the best cutoff value in Table *7*. A cut-off of 0.533 was reported to maximize the Youden index among the thresholds. The denominators, sensitivity, and specificity, and the implied classification matrix are shown in Table *8*, with apparent performance estimates in Table *9*. These calculations assume that CR-POPF was the positive outcome and that a high BMI/PNI ratio defined a positive test. That is, near the BMI/PNI cutoff of 0.50, as previously explored by Sato et al. [5].

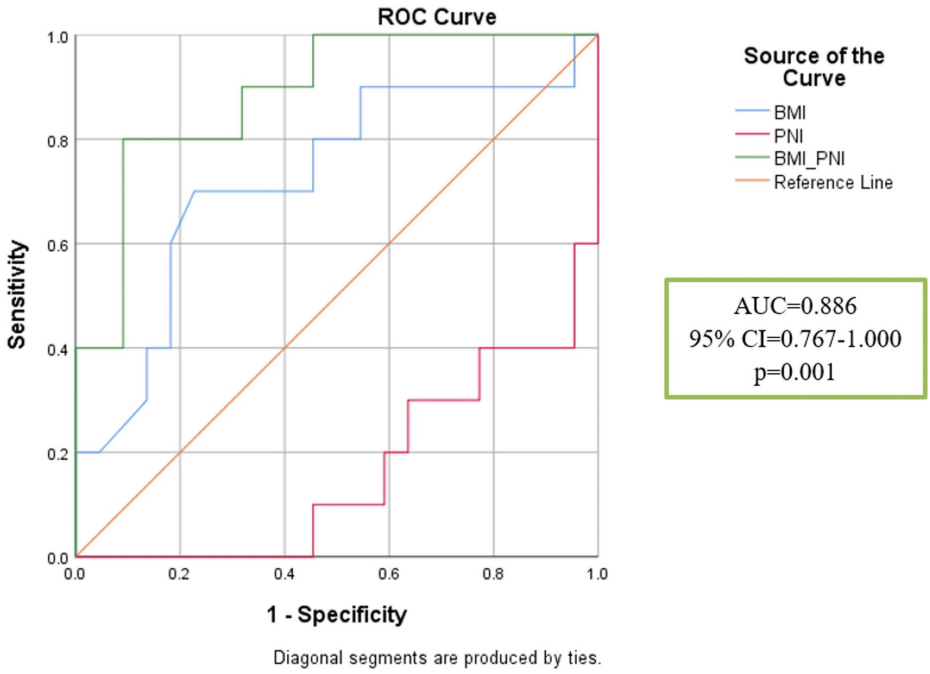


FIGURE 2: Receiver operating characteristic (ROC) curve analysis of preoperative body mass index (BMI), prognostic nutritional index (PNI), and BMI-to-PNI ratio for assessing postoperative pancreatic fistula (POPF)

The BMI-to-PNI ratio demonstrated the highest discriminatory ability (AUC = 0.886, 95% CI: 0.767–1.000, p = 0.001), followed by BMI (AUC = 0.725). PNI showed an inverse direction of discrimination (AUC = 0.164). The diagonal reference line represents chance-level discrimination.

BMI: body mass index; PNI: prognostic nutritional index

BMI/PNI	Sensitivity (%)	Specificity (%)	Youden index
0.522	80.0	86.4	66.4
0.533	80.0	90.9	70.9
0.541	70.0	90.9	60.9

TABLE 7: Youden Index-based selection of the optimal BMI/PNI cutoff for predicting CR-POPF

BMI: body mass index; PNI: prognostic nutritional index; CR-POPF: clinically relevant postoperative pancreatic fistula

Classification	CR-POPF	No CR-POPF	Total
High ratio/test positive	8	2	10
Low ratio/test negative	2	20	22
Total	10	22	32

TABLE 8: Classification matrix for the optimal BMI/PNI cutoff of 0.533

BMI: body mass index; PNI: prognostic nutritional index; CR-POPF: clinically relevant postoperative pancreatic fistula

Measure	Numerator/denominator	Estimate	95% CI
Sensitivity	8/10	80.0%	44.4–97.5%
Specificity	20/22	90.9%	70.8–98.9%
Positive predictive value	8/10	80.0%	44.4–97.5%
Negative predictive value	20/22	90.9%	70.8–98.9%
Accuracy	28/32	87.5%	71.0–96.5%

TABLE 9: Apparent classification performance of the BMI/PNI threshold (0.533)

Statistical method: exact binomial (Clopper–Pearson) CIs; no null-hypothesis test for these performance measures. Effect/performance measures are the displayed proportions. Positive and negative predictive values depend on the CR-POPF prevalence in this cohort.

BMI: body mass index; PNI: prognostic nutritional index; CR-POPF: clinically relevant postoperative pancreatic fistula

The ROC curve of the BMI/PNI ratio to assess the risk of POPF suggested the best cut-off point was 0.533, with a sensitivity of 80.0% and a specificity of 90.9%. ROC curve analysis demonstrated that the preoperative BMI-to-PNI ratio had the highest discriminatory ability for assessing risk of POPF, with an AUC of 0.886 (95% CI: 0.767-1.000, p = 0.001). Preoperative BMI also showed acceptable discriminatory performance (AUC = 0.725). In contrast, PNI demonstrated an inverse predictive direction, with an AUC of 0.164, indicating that lower PNI values were associated with an increased risk of POPF. The ROC curve for the BMI-to-PNI ratio remained well above the diagonal reference line, suggesting good discriminatory performance.

Discussion

This prospective cohort provides preliminary evidence of an association between a higher preoperative BMI/PNI ratio and CR-POPF after pancreaticoduodenectomy. The clinically relevant endpoint occurred in 10 of 32 patients. A higher BMI and lower PNI characterized the CR-POPF group, producing a higher ratio than in the comparison group. The observed median contrast is clinically interpretable as a difference in the marker's distribution, but its uncertainty cannot be quantified from the medians and quartiles alone. The exploratory threshold showed encouraging apparent classification performance.

The direction of the findings is consistent with Sato et al., who reported a higher BMI/PNI ratio in patients with clinically relevant fistula and explored a cut-off of 0.5 [5]. The threshold of 0.533 reported in this cohort is numerically close, but this does not establish transportability. Both the underlying distribution of the marker and clinical outcome frequency influence performance. A threshold must be tested prospectively without re-optimization in a separate cohort to determine whether its apparent accuracy is reproducible. The present sample supplies an initial local observation rather than a validated prediction rule.

A plausible interpretation is that the ratio combines different aspects of operative vulnerability. BMI partly reflects body size and adiposity, whereas PNI incorporates albumin and circulating lymphocytes. However, this cohort did not directly measure pancreatic fat, visceral adiposity, inflammatory burden, or tissue-healing mechanisms, so these explanations remain hypotheses. The association between BMI and postoperative pancreatic fistula has also been reported in studies evaluating prediction models after pancreaticoduodenectomy. Zhu et al. identified BMI and serum albumin, together with pancreatic duct diameter, pathological diagnosis, triglyceride level, and intraoperative blood loss, as independent variables in their prediction model [13]. Patients may have a normal or high BMI with multiple macronutrient deficiencies. PNI may be affected by inflammation, disease processes, and infection. So, solely BMI or PNI can't determine the fistula risk or associations; thus, the BMI/PNI ratio does. These findings support further investigation of preoperative nutritional and anthropometric parameters as potential markers of postoperative fistula risk. The association between nutritional status and postoperative outcomes reported by Kim et al. supports careful preoperative assessment but does not establish that changing BMI/PNI itself would prevent fistula [4].

The biochemical-leak subgroup comparison also suggests that the PNI component may relate to clinical severity. Aydin et al. found that lower preoperative PNI was associated with progression from biochemical leak to clinically relevant fistula in a retrospective series [6]. The current analysis compares outcome groups and lacks patient-level timing of progression. The finding is best treated as exploratory support for a future study with standardized serial assessment.

The distinction between biochemical leak and CR-POPF materially changes the interpretation of this cohort. The study combines 20 patients under an older broad fistula label, but half of those patients had a biochemical leak. Under contemporary criteria, the clinically relevant rate is 31.3%, not 62.5% [2]. Reporting biochemical leaks separately improves comparability with studies using the revised ISGPS definition and prevents an inflated impression of clinically consequential fistula.

The categorical analyses illustrate the uncertainty produced by the small sample. Although male sex and soft pancreatic texture had odds ratios above one, their confidence intervals were very wide. Failure to reach statistical significance is not evidence that established risk factors are irrelevant. In the internationally validated alternative Fistula Risk Score, BMI, texture, and duct diameter contributed to risk estimation [3]. The present cohort cannot establish incremental value beyond those variables because no verified adjusted analysis or direct comparison with a validated score was done.

Higher postoperative drain amylase and pancreatic juice output were reported in patients with CR-POPF. These variables may inform postoperative surveillance, but they occur after the preoperative decision point. Drain amylase also contributes to the fistula definition, which limits interpretation of its group association as an independent predictive finding. Sakamoto et al. evaluated postoperative changes in PNI together with serum amylase in a separate prediction setting [14]. That approach should be distinguished from evaluating a marker intended for use before surgery; combining measurements across time without specifying when predictions are made can obscure clinical usefulness.

Strengths and limitations

Strengths include prospective recruitment, consecutive sampling, a defined surgical setting, and use of measurements available in routine care. Important limitations are the single-center design, 32-patient sample, only 10 CR-POPF events, and restriction to adults aged 18-75 years. Residual confounding by gland characteristics, disease, comorbidity, or perioperative care remains possible. Multiple exploratory comparisons increase the chance of incidental findings.

Recent evidence also emphasizes the limitations of currently available prediction models. A 2025 scoping review found that only a minority of evaluated risk-stratification tools had undergone external validation, highlighting the need for further validation before their routine clinical implementation [15]. The optimal BMI/PNI cut-off of 0.533 in this study was derived using the Youden index and evaluated in the same small cohort. No internal validation using bootstrap resampling or cross-validation was performed, and no independent external validation was available. This data-driven threshold selection may have introduced optimism and overestimation of the apparent diagnostic performance. Therefore, the reported sensitivity, specificity, predictive values, and accuracy should be interpreted cautiously and should not be considered validated estimates of performance in other populations.

Conclusions

A higher preoperative BMI/PNI ratio was associated with CR-POPF after pancreaticoduodenectomy in this small prospective cohort. The ratio is a candidate for further study. This observational study does not demonstrate that nutritional intervention prevents fistula or that BMI/PNI outperforms existing risk scores.

Additional Information

Author Contributions

All authors have reviewed the final version to be published and agreed to be accountable for all aspects of the work.

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