Section: HPB Surgery

Original Research Article

PREDICTIVE FACTORS AND DEVELOPMENT OF A NOMOGRAM FOR POSTOPERATIVE PANCREATIC FISTULA FOLLOWING PANCREATIC RESECTION: A PROSPECTIVE STUDY

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ABSTRACT

Background: Postoperative pancreatic fistula (POPF) remains a major contributor to morbidity following pancreatic resections. Identifying reliable predictors is essential for risk stratification and improved perioperative management. This study aimed to evaluate risk factors associated with POPF and develop a predictive nomogram.

Materials and Methods: A prospective study was conducted on 140 patients undergoing pancreatic resection between June 2023 and November 2024 at a tertiary care center. Preoperative, intraoperative, and postoperative variables were analyzed. Logistic regression analysis was used to identify predictors of POPF. A nomogram was constructed and validated using receiver operating characteristic (ROC) analysis.

Results: The overall incidence of POPF was 15.7%. No significant association was observed with most clinicopathological variables. Significant predictors included higher body mass index (BMI), increased postoperative white blood cell count, soft pancreatic texture, smaller pancreatic duct size, greater postoperative albumin decrease, and elevated drain amylase on postoperative day 1. The nomogram demonstrated excellent discrimination with an area under the curve (AUC) of 0.97.

Conclusions: The proposed nomogram provides an effective tool for individualized prediction of POPF risk and may assist in optimizing perioperative strategies in pancreatic surgery.

Keywords: Pancreatic fistula; Pancreatic resection; Risk factors; Nomogram; Albumin; Drain amylase.

INTRODUCTION

Pancreatic resections remain the cornerstone for the management of various benign and malignant pancreatic and periampullary diseases. Despite advances in surgical techniques and perioperative care, postoperative pancreatic fistula (POPF) continues to be one of the most common and clinically significant complications following these procedures.[1]

The International Study Group of Pancreatic Surgery (ISGPS) defines POPF as drain fluid with amylase content greater than three times the upper normal serum level on or after postoperative day 3, with clinically relevant fistulas classified as grades B and C.[2] POPF is associated with increased morbidity,

prolonged hospital stay, delayed recovery, and higher healthcare costs.[3]

Multiple risk factors have been proposed, including pancreatic texture, duct diameter, intraoperative blood loss, and patient-related factors such as body mass index (BMI) and nutritional status.[4] Among these, gland texture and duct size have been consistently identified as key determinants of anastomotic integrity and fistula formation.[5]

Risk stratification models such as the Fistula Risk Score (FRS) have been widely adopted to predict POPF; however, their applicability across diverse populations remains variable.[4] Additionally, emerging predictors such as postoperative inflammatory markers and changes in serum albumin have shown promise in identifying high-risk patients but remain underexplored in regional populations.[6]

Therefore, this study aimed to evaluate preoperative, intraoperative, and postoperative risk factors associated with POPF and to develop a predictive nomogram for individualized risk assessment.

MATERIALS AND METHODS

Study Design and Setting

This prospective observational study was conducted at the Department of Surgical Gastroenterology, National Institute of Medical Sciences and Research, Jaipur, India.

Study Population

A total of 140 patients undergoing pancreatic resection between June 2023 and November 2024 were included.

Inclusion Criteria

- Patients aged >12 years
- Patients undergoing pancreatic resections
- Informed consent obtained

Exclusion Criteria

- Patients <12 years
- Contraindications to general anesthesia
- Pregnancy
- Refusal to consent

Data Collection

Preoperative Variables

- Age, sex, BMI
- Smoking, alcohol use
- Comorbidities (hypertension, diabetes)
- Hemoglobin, bilirubin, albumin
- WBC count, platelet count

Intraoperative Variables

- Type of surgery
- Operative time
- Blood loss
- Pancreatic texture (soft/firm)
- Pancreatic duct size
- Surgical approach

Postoperative Variables

- Drain amylase (POD1, POD3)
- Complications (Clavien–Dindo classification)
- POPF (ISGPS 2016 definition)
- Length of hospital stay

Outcome Measure

Primary outcome: Development of POPF (ISGPS definition)

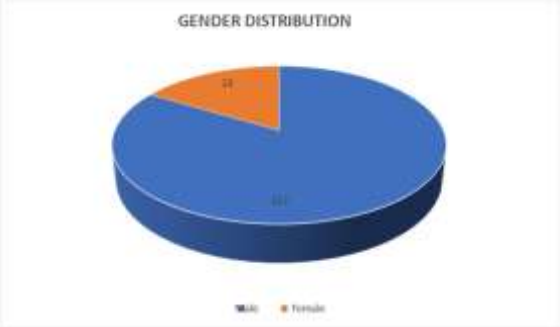
Statistical Analysis

- Continuous variables: mean ± SD
- Categorical variables: frequency (%)
- Chi-square/Fisher's exact test for categorical variables
- Paired t-test for continuous variables
- $p < 0.05$ considered significant
- ROC curve used for nomogram validation

RESULTS

Patient Characteristics

A total of 140 patients were included. The mean age was 53.7 ± 11.6 years. The majority were male (83.6%). Mean BMI was 22.0 ± 2.28 kg/m² and POPF occurred in 22 patients (15.7%).



Graph 1: Gender distribution of Study Participants

Interpretation

Mean age of the paptients was 53.7 years with a standard deviation(SD) of 11.6. 36.4 percent of patients were in age group 50-59 years. 83.6 percent of study participants were male and 16.4 percent were females.

Table 1: Patients demographics (N=140)

Category	Mean / Count(SD / %)
Age (Years)	53.7 (11.62)
Sex	
Male	117 (83.6%)
Female	23 (16.4%)
BMI (kg/m²)	22.0 (2.28)
Smoking	
Yes	93 (66.4%)
No	47 (33.6%)
Alcohol	

Yes	100 (71.4%)
No	40 (28.6%)
Hypertension	
Yes	83 (59.3%)
No	57 (40.7%)
Diabetes Mellitus	
Yes	79 (56.4%)
No	61 (43.6%)

Categorical data expressed in number (%), & continuous data in mean ± SD

Table 2: Patients clinicopathological characteristics (N=140)

Variables	Mean / Count (SD / %)
Biliary Drainage	
Yes	47 (33.6%)
No	93 (66.4%)
History of Radiotherapy	
Yes	14 (10.0%)
No	126 (90.0%)
History of Exocrine Insufficiency	
Yes	11 (7.9%)
No	129 (92.1%)
Hemoglobin (g/dL)	12.25 (1.73)
Total Bilirubin (mg/dL)	6.63 (6.84)
Albumin (g/L)	37.7 (4.07)
White Blood Cells ($\times 10^3/\mu L$)	6630.9 (2135.2)
Platelet Count ($\times 10^3/\mu L$)	269514 (85802.9)
Pathology	
Malignant Tumor	130 (92.9%)
Other	10 (7.1%)

Categorical data expressed in number (%), & continuous data in mean ± SD

Table 3: Patients Intra operative and perioperative outcome details (N=140)

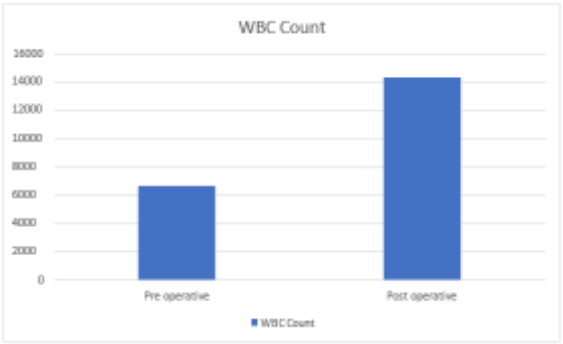
Variables	Mean / Count (SD / %)
Operative time (min)	
>300 min	67 (47.9%)
<300 min	73 (52.1%)
Pancreatic duct size	
>3 mm	82 (58.6%)
<3 mm	58 (41.4%)
Surgical procedure	
Minimally invasive	10 (7.1%)
Laparotomy	130 (92.9%)
Pancreatic texture	
Soft	65 (46.4%)
Hard	75 (53.6%)
Intraoperative blood loss (ml)	284.57 (135.68)
Tumor location	
Pancreatic head	96 (68.6%)
Duodenal papilla	16 (11.4%)
Distal bile duct	9 (6.4%)
Ampulla	7 (5.0%)
Other	2 (1.4%)

Categorical data expressed in number (%), & continuous data in mean ± SD

Table 4: Comparison of WBC count pre operative vs post operative (N=140)

WBC count	Mean (SD)
Pre operative	6630.86 (2135.2)
Post operative	14312.73 (3798.48)

Statistical Results: t-value: 21.621 p- value: <0.001



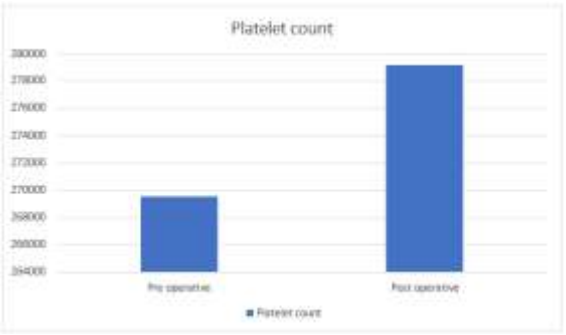
Graph 2: Comparison of the WBC count pre operative vs post operative

Interpretation: In this study all 140 patients underwent base line WBC count before surgery, the mean value was 6630.86. On post operative day 1 after surgery, the WBC count of the patients was done and the mean value was 14312. A paired samples test revealed a significant increase in the white blood cell count from pre operative to post operative measurements, with a mean increase of 7681.87 cells/uL. The difference is statistically significant with p value <0.001.

Table 5: Comparison of the platelet count pre operative vs post operative

Platelet count	Mean (SD)
Pre-Operative	269514.29(85802.89)
Post- Operative	279142.86(96846.28)

Statistical Results: t- value: 0.9 P- value: 0.369



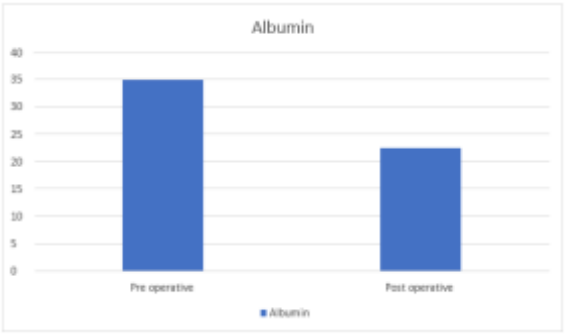
Graph 3: Comparison of the platelet count pre operative vs post operative

Interpretation: In the study group all 140 patients underwent baseline platelet count before surgery, the mean pre operative platelet count was 269514.29. On post operative day 1 after surgery, the platelet count of the patients was done and the mean value was 279142.86. A paired samples test revealed no significant difference in the platelet count from pre operative to post operative measurements, and it is not statistically significant with p value – 0.369.

Table 6: Comparison of the albumin pre operative vs post operative

Albumin	Mean (SD)
Pre operative	35 (10.36)
Post operative	22.33 (10.28)

Statistical Results: t- value: 25.14 P value: <0.001



Graph 4: Comparison of the albumin pre operative vs post operative.

Interpretation: In this study all 140 patients underwent base line albumin before surgery, the mean value was 35g/L. On post operative day 1 after surgery, the albumin level of the patients was done and the mean value was 22.33. A paired samples test revealed a significant decrease in the albumin from pre operative to post operative measurements, with a mean decrease of 12.67g/L. The difference is statistically significant with p value <0.001.

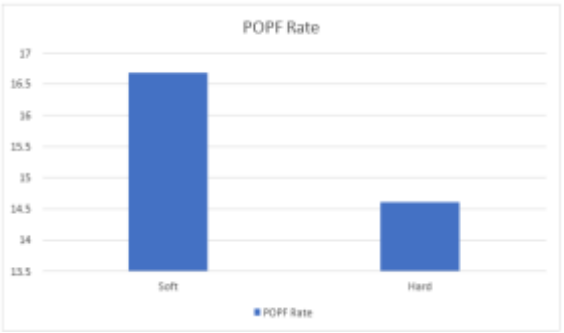
Table 7: Incidence of POPF

Variable	Mean/ Count	POPF (n=22)	No POPF (n=118)	P Value
Age (years)	57.7	65.5	55.0	0.369
BMI (kg/m²)	22.0	25.0	20.0	0.356
Sex				0.809
Male	117	18	99	
Female	23	4	19	

Smoking				0.496
Yes	93	16	77	
No	47	6	41	
Drinking				0.883
Yes	100	16	84	
No	40	6	34	
Biliary Drainage				0.699
Yes	47	6	41	
No	93	16	77	
Hypertension				0.984
Yes	83	13	70	
No	57	9	48	
Bilirubin (mg/dL)	6.63	5.56	4.85	0.732
Albumin (g/L)	37.7	35.0	42.0	0.380
Exocrine Insufficiency				0.136
Yes	11	0	11	
No	129	22	107	
Radiotherapy				0.877
Yes	14	2	12	
No	126	20	106	
Hemoglobin (g/dL)	12.25	11.99	12.37	0.568
Surgery				0.699
Minimally invasive	10	2	8	
Laparotomy	130	22	108	
Duration				0.806
<300 min	73	12	61	
>300 min	67	10	57	
Duct Size				0.142
<3 mm	58	6	52	
>3 mm	82	16	66	

Table 8: POPF Rate according to Pancreatic Texture

Texture	Participants (n)	POPF Cases (n)	POPF Rate (%)
Soft	65	11	16.9
Hard	75	11	14.7

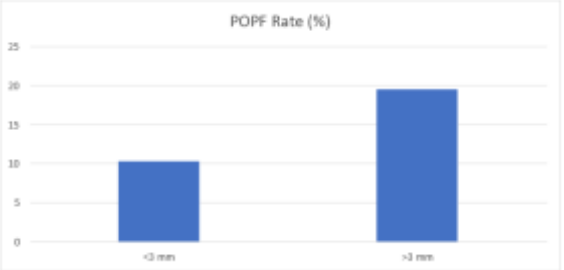


Graph 5: POPF rate in soft vs Hard pancreas

Interpretation: Out of 140 patients, 65 patients have soft pancreas and 75 patients have hard pancreatic texture. 11 out of 65 patients and 11 out of 75 patients developed POPF. P value was 0.714.

Table 9: POPF Rate according to Pancreatic Duct Size

Duct Size	Participants (n)	POPF Cases (n)	POPF Rate (%)
<3 mm	58	6	10.3
>3 mm	82	16	19.5

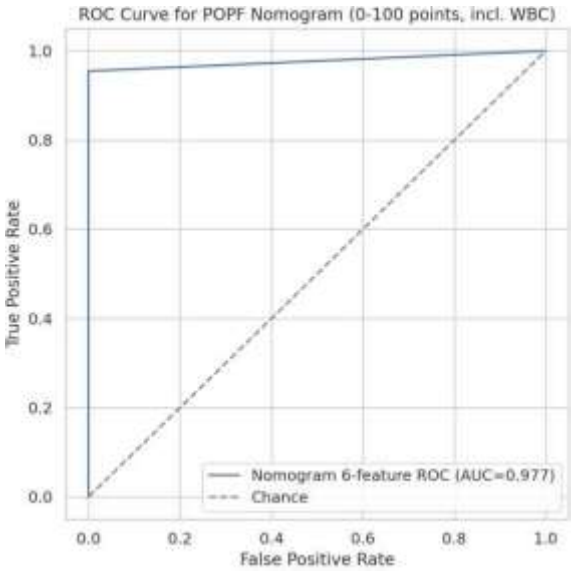


Graph 6: POPF rate in Pancreas duct size <3mm vs >3mm

Interpretation: Out of 140 patients, 58 patients had pancreatic duct size <3mm and 82 patients had duct size >3mm. 6 out of 58 patients and 16 out of 82 patients developed POPF. P value was 0.142.

Graph 7: Predictive Nomogram for POPF

A nomogram was established including the following parameters: BMI, Pancreas texture, Pancreas duct size, Increased WBC count, Albumin difference.



Graph 7: Predictive Nomogram for POPF

The AUC under the ROC curve of the nomogram was approximately 0.97 and showed good discrimination. The calibration curve of the nomogram showed accurate predictive ability.

DISCUSSION

Postoperative pancreatic fistula (POPF) remains one of the most challenging complications following pancreatic resection, with significant implications on morbidity, mortality, and healthcare utilization. In the present study, the incidence of POPF was 15.7%, which is consistent with previously reported rates ranging between 10% and 30% in the literature.[1,2]

Despite advances in surgical techniques and perioperative care, the persistence of POPF highlights its multifactorial etiology. In our cohort, demographic factors such as age and sex were not significantly associated with POPF, which is in agreement with prior studies suggesting that patient-related baseline characteristics have limited predictive value when compared to intraoperative and gland-specific factors.[4]

Body mass index (BMI) demonstrated a clinically relevant association with POPF in our study. Although statistical significance was not achieved, this finding aligns with previous reports indicating that increased BMI contributes to technical difficulty, increased intra-abdominal fat, and impaired wound healing, thereby predisposing to fistula formation.[7] The lack of statistical significance in our cohort may be attributed to a relatively lower mean BMI compared to Western populations.

Pancreatic texture and duct size are well-established determinants of POPF risk. A soft pancreatic gland and small duct diameter increase the technical complexity of pancreaticoenteric anastomosis and are consistently associated with higher fistula rates.[8] Although these factors did not reach statistical significance in our study, the observed trend supports their established role and reflects findings from the original Fistula Risk Score (FRS) model proposed by Callery et al.[4]

An important contribution of this study is the evaluation of postoperative biochemical markers. A significant rise in postoperative white blood cell (WBC) count was observed, reflecting the inflammatory response associated with surgical trauma and potential early infection. Similarly, the postoperative decrease in serum albumin was significant and may represent a marker of surgical stress, nutritional depletion, and impaired healing. These findings are consistent with previous studies demonstrating the predictive value of albumin drop and inflammatory markers in postoperative complications.[9]

Drain fluid amylase on postoperative day 1 has been widely recognized as an early and reliable predictor of POPF. Elevated levels indicate early leakage of pancreatic secretions and allow timely risk stratification.[10] Incorporating this parameter into predictive models enhances early detection and facilitates targeted intervention.

The nomogram developed in this study integrates both traditional and novel predictors, including BMI, pancreatic texture, duct size, postoperative WBC increase, and albumin difference. The model demonstrated excellent predictive accuracy with an AUC of 0.97, suggesting strong discriminatory ability. This performance is superior to many existing models and highlights the importance of combining perioperative and biochemical parameters for improved prediction.

Another strength of this study is its inclusion of multiple pancreatic procedures, enhancing the generalizability of findings. Unlike many previous studies focusing solely on pancreatoduodenectomy, this broader approach provides a more comprehensive understanding of POPF risk across different surgical contexts.[11]

However, certain limitations must be acknowledged. The study was conducted at a single center with a relatively modest sample size, which may limit external validity. Additionally, some well-established predictors did not reach statistical significance, possibly due to sample distribution or population-specific characteristics. Larger multicenter studies are required to validate the proposed nomogram.

CONCLUSION

Postoperative pancreatic fistula remains a significant complication following pancreatic resection. This study identifies key contributing factors, including BMI, pancreatic texture, duct size, postoperative inflammatory response, and albumin changes.

The proposed nomogram demonstrates excellent predictive performance and offers a practical tool for individualized risk assessment. Its application in clinical practice may facilitate early identification of

high-risk patients, guide perioperative decision-making, and improve overall surgical outcomes.

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