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ORIGINAL RESEARCH

# Clinical Outcomes of Diabetes Mellitus on Moderately Severe Acute Pancreatitis and Severe Acute Pancreatitis

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**Objective:** To analyze the influence of diabetes mellitus on the clinical outcomes of moderately severe acute pancreatitis (MSAP) and severe acute pancreatitis (SAP).

**Methods:** This retrospective study included patients diagnosed with MSAP and SAP at Shanxi Bethune Hospital from January 1, 2017, to December 31, 2021. Clinical data were collected, including patient demographics, 24-hour laboratory indicators, and inflammation indices. Propensity score matching (PSM) was used to compare outcomes before and after matching. Patients were randomized into training and validation sets (7:3) to develop and validate a clinical prediction model for infected pancreatic necrosis (IPN).

**Results:** Among 421 patients, 79 had diabetes at admission. Before PSM, diabetic patients had higher incidences of peripancreatic fluid (71% vs 47%, p<0.001) and IPN (48% vs 10%, p<0.001), higher surgical intervention rates (24% vs 12%, p=0.008), and significant differences in abdominocentesis (22% vs 11%, p=0.014). After PSM, 174 patients were matched, and the diabetes group still showed higher incidences of peripancreatic fluid (69% vs 47%, p=0.008), IPN (48% vs 11%, p<0.001), and surgical intervention rates (27% vs 13%, p=0.037). Diabetes, modified CT severity index (MCTSI), serum calcium, and HDL-c were identified as independent risk factors for IPN. The prediction model demonstrated good predictive value.

**Conclusion:** In MSAP and SAP patients, diabetes mellitus can exert an influence on their clinical outcome and is an independent risk factor for IPN. The alignment diagram and web calculator constructed on the basis of diabetes mellitus, modified CT severity index (MCTSI), serum calcium and high-density lipoprotein cholesterol (HDL-c) have good predictive value and clinical guidance for the occurrence of IPN in MSAP and SAP.

**Keywords:** acute pancreatitis, diabetes, propensity score matching, predictive model

## Introduction

Acute pancreatitis (AP) is a common acute abdominal condition in the gastrointestinal system. Global reports suggest that the incidence of AP ranges from 4.9 to 73.4 cases per 100,000 individuals.[1] In recent times, there has been a 3.07% annual increase in the incidence of AP, likely attributed to improved living standards.[2] This statistical trend underscores the significant health risks associated with acute pancreatitis. Diabetes, a prevalent endocrine disorder, has shown a significant increase in global prevalence since 1980.[3] Diabetes can exacerbate the body's inflammatory response and increase susceptibility to infectious diseases.[4] Diabetes plays a significant role in the clinical outcomes of pancreatitis. It increases the risk of local complications, renal failure rates, and ICU admission rates in patients with pancreatitis, and also raises the mortality rate of AP.[5–7] Diabetes significantly impacts the severity of pancreatitis, with patients suffering

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from acute pancreatitis and diabetes having a higher incidence of severe acute pancreatitis compared to those without diabetes.[8] Magnetic resonance imaging (MRI) findings indicate that diabetic patients are more prone to developing severe pancreatitis.[9] Additionally, patients with moderate to severe pancreatitis and concurrent diabetes have higher CTSI scores and pancreatic inflammation scores.[10]

In moderately severe acute pancreatitis (MSAP) and severe acute pancreatitis (SAP), infected pancreatic necrosis (IPN) is a common severe local complication, which includes early acute necrotic collection (ANC) with infection and late walled-off necrosis (WON) with infection.[11] 10% to 70% of patients with severe acute pancreatitis (SAP) may develop infected pancreatic necrosis (IPN),[12] leading to severe systemic complications like sepsis and multiple organ failure, with a mortality rate ranging from 20% to 30%.[13] It is evident that IPN has a significant impact on the prognosis of acute pancreatitis and is a major cause of late death in patients with this condition.[14] Therefore, early and accurate prediction of IPN is crucial in clinical diagnosis and treatment. Currently, early prediction methods for IPN mainly include various clinical scoring systems and laboratory markers such as C-reactive protein and procalcitonin as inflammatory markers.[15–17] Recent study has also suggested that the neutrophil CD64 index has good predictive value for IPN.[18] However, there is limited research specifically addressing the relationship between diabetes and IPN. Currently, it is inconclusive whether diabetes can predict the occurrence of IPN.

In recent years, research on the impact of diabetes on the clinical outcomes of acute pancreatitis has mostly consisted of retrospective studies, which are easily influenced by confounding factors and lack sufficient evidence strength. Propensity score matching (PSM) can address disparities in the distribution of factors that significantly affect prognosis between groups, and enhance statistical power.[19,20] This study initially employed propensity score matching to mitigate the influence of pertinent biases on the outcomes. It investigated the association between diabetes and the prognosis of MSAP and SAP. Subsequently, diabetes was identified as an independent risk factor for IPN through univariate and multivariate logistic regression analysis. Finally, a clinical prediction model for the simultaneous occurrence of IPN in MSAP and SAP patients was developed.

# Materials and Methods

## Patients

We collected the clinical data of 511 patients diagnosed with MSAP and SAP at Shanxi Bethune Hospital from January 1, 2017, to December 31, 2021. By including and excluding criteria, the clinical data of 421 patients were included in this study. This study was conducted in accordance with the ethical standards of the 1964 helsinki declaration and its later amendments or comparable ethical standards. The Ethics Committee of Shanxi Medical University Affiliated Bethune Hospital reviewed and approved the study protocol.(Approval No: YXLL-2023-237). Given the retrospective nature of the study, the Ethics Committee waived the requirement for informed consent. Patient data confidentiality was strictly maintained, and all data were anonymized to protect patient privacy.

Exclusions were made for: (1) incomplete clinical data or missing medical records; (2) non-first-time hospitalizations; (3) chronic pancreatitis, trauma, or pregnancy-related pancreatitis; (4) patients with tumors; (5) patients diagnosed with severe heart, brain, lung, kidney, or other organ dysfunction before onset; (6) age under 18 years old.

## Data Collection

Including general information such as age, gender, body mass index (BMI), etiology, smoking, drinking, presence of hypertension, hyperlipidemia, fatty liver, and other chronic diseases; clinical data encompassing the incidence of systemic inflammatory response syndrome (SIRS), multiple organ failure, local complications, whether surgical intervention was conducted, placement of a feeding tube, length of hospital stay, ICU admissions, and mortality rates.

Laboratory Parameters Within 24 hours of Hospital Admission: Alanine Aminotransferase (ALT), Aspartate Aminotransferase (AST), Albumin (ALB), Total Bilirubin (TBIL), Direct Bilirubin (DBIL), Triglycerides (TG), High-Density Lipoprotein Cholesterol (HDL-C), Low-Density Lipoprotein Cholesterol (LDL-C), Urea, Creatinine(SCr), Blood Glucose (Glu), Amylase (AMY), Lipase (LPS), Potassium (K), Sodium (Na), Chloride (Cl), Inorganic Phosphate (P), Magnesium (Mg), Calcium (Ca), Prothrombin Time (PT), Prothrombin Activity (PT%), Activated Partial

Thromboplastin Time (APTT), Thrombin Time (TT), Fibrinogen (FIB), D-Dimer, White Blood Cell Count (WBC), Neutrophil Count (NEUT), Lymphocyte Count (LYMPH), Monocyte Count (MONO), Red Blood Cell Count (RBC), Hemoglobin (HGB), Hematocrit (HCT), Mean Corpuscular Volume (MCV), Mean Corpuscular Hemoglobin (MCH), Mean Corpuscular Hemoglobin Concentration (MCHC), Red Cell Distribution Width (RDW), Platelet Crit (PCT), Platelet Count (PLT), Platelet Distribution Width (PDW), Mean Platelet Volume (MPV).

Inflammatory Indices and Clinical Scoring Parameters in Acute Pancreatitis: Platelet-to-Lymphocyte Ratio (PLR), Neutrophil-to-Lymphocyte Ratio (NLR), Onodera Prognostic Nutritional Index (OPNI), Modified CT Severity Index (MCTSI), Bedside Index for Severity in Acute Pancreatitis (BISAP). PLR, NLR, and OPNI are calculated based on laboratory parameters within 24 hours of hospital admission. BISAP is determined based on the patient's consciousness status and clinical indicators recorded in the electronic medical records within the first 24 hours of hospitalization. MCTSI is assessed using CT or contrast-enhanced CT scans within 48 hours of admission.

## Define

Diagnosis and Severity Classification in Acute Pancreatitis:

The diagnostic criteria for acute pancreatitis align with the revised 2012 Atlanta classification: (1) Persistent upper abdominal pain. (2) Serum amylase and/or lipase levels exceeding three times the upper limit of normal. (3) Abdominal imaging showing characteristic changes indicative of acute pancreatitis. Diagnosis of acute pancreatitis (AP) requires meeting at least two of these criteria.

Severity classification in acute pancreatitis refers to the revised Atlanta classification (RAC): (1) Mild Acute Pancreatitis (MAP): No organ dysfunction or local/systemic complications. (2) Moderately Severe Acute Pancreatitis (MSAP): Transient (≤48 hours) organ dysfunction and/or local complications. (3) Severe Acute Pancreatitis (SAP): Persistent (>48 hours) organ dysfunction.

Diabetes Definition: Diabetes refers to diagnosed type 1 or type 2 diabetes before treatment initiation. Diagnostic criteria include typical diabetes symptoms plus: random blood glucose ≥11.1 mmol/L, or fasting blood glucose ≥7.0 mmol/L, or 2-hour post-oral glucose tolerance test (OGTT) blood glucose ≥11.1 mmol/L, or glycated hemoglobin (HbA1c) ≥6.5%.[21]

Organ Failure Diagnosis: Organ failure is defined based on the modified Marshall scoring system, with any organ score ≥2 indicating organ failure.

Modified Computed Tomography Severity Index (MCTSI):

MCTSI includes three components: (1) Pancreatic inflammation response. (2) Pancreatic necrosis. (3) Extrapancreatic complications. MCTSI score = Inflammation score + Necrosis score + Extrapancreatic complications score. All AP patients undergo abdominal and pelvic CT scans within 48 hours of symptom onset. Two experienced radiologists independently assess pancreatic morphology changes, local complications, and extrapancreatic complications while ensuring patient anonymity.

Infectious Pancreatic Necrosis Diagnosis: Diagnosis of infectious pancreatic necrosis is based on CT findings showing the "bubble sign".

BISAP Score: Introduced in 2008, the BISAP score includes five key clinical parameters: (1) Blood urea nitrogen (BUN). (2) Glasgow Coma Scale score. (3) Systemic inflammatory response syndrome (SIRS). (4) Age. (5) Pleural effusion. Each parameter present contributes 1 point, with a total score ranging from 0 to 5.

SIRS Criteria: SIRS is defined by meeting two or more of the following criteria: (1) Heart rate >90 beats/minute. (2) Body temperature <36°C or >38°C. (3) White blood cell count (WBC) <4x10^9/L or >12x10^9/L. (4) Respiratory rate >20 breaths/minute or partial pressure of carbon dioxide (PaCO2) <32 mmHg.

Onodera Prognostic Nutritional Index (OPNI): OPNI = Serum albumin level (g/L) + 5 × peripheral lymphocyte count × 10^9/L.

Surgical Intervention: Refers to the "Step-up" approach for peripancreatic fluid and pancreatic necrosis management, involving sequential percutaneous drainage, video-assisted debridement, and open surgery for patients with inadequate drainage response.

## Data Processing and Statistical Analysis

Statistical analysis was performed using SPSS 26.0 and R 4.3.2 software. For normally distributed continuous data, descriptive statistics are presented as mean ± standard deviation (mean ± s), and independent sample *t*-tests were used for group comparisons. For non-normally distributed continuous data, median and interquartile range (IQR, represented as M (P25, P75)) were used, and group comparisons were conducted using the Mann–Whitney rank-sum test. Categorical data were summarized using counts and percentages, and group comparisons were assessed using the chi-square test. A significance level of $p<0.05$ was considered statistically significant.

We will implement propensity score matching (PSM) using the R package MatchIt. The grouping will be based on whether individuals had diabetes at the time of admission. Covariates considered for matching include gender, age, BMI, smoking, alcohol consumption, hypertension, hyperlipidemia, fatty liver, other chronic diseases, and etiology. We will use a 1:2 nearest neighbor matching method, where each individual in the diabetes group will be matched with two control group individuals having the most similar propensity score values. To ensure the quality of the matching results, a caliper value of 0.02 will be defined.

Next, we will incorporate significant variables from the univariate analysis into a binary logistic regression equation for multivariable analysis. The results will be used to construct predictive models for the occurrence of postoperative infectious pancreatic necrosis (IPN) in both MSAP and SAP cases. Receiver operating characteristic (ROC) curves will be used to determine the area under the curve (AUC) for the predictive models in the training and validation groups, along with 95% confidence intervals. Additionally, calibration curves and decision curve analysis (DCA) will be plotted.

# Results

A total of 511 patients with severe and critically severe acute pancreatitis were collected. Among them, 90 cases were excluded, and a final total of 421 patients were included in the study (Figure 1).

## To Study the Effect of Diabetes on the Clinical Outcomes of MSAP and SAP Based on PSM

### Comparison of Clinical Characteristics Between the Two Groups Before PSM

In a cohort of 421 enrolled patients, 79 were diagnosed with diabetes, accounting for 18.8%.

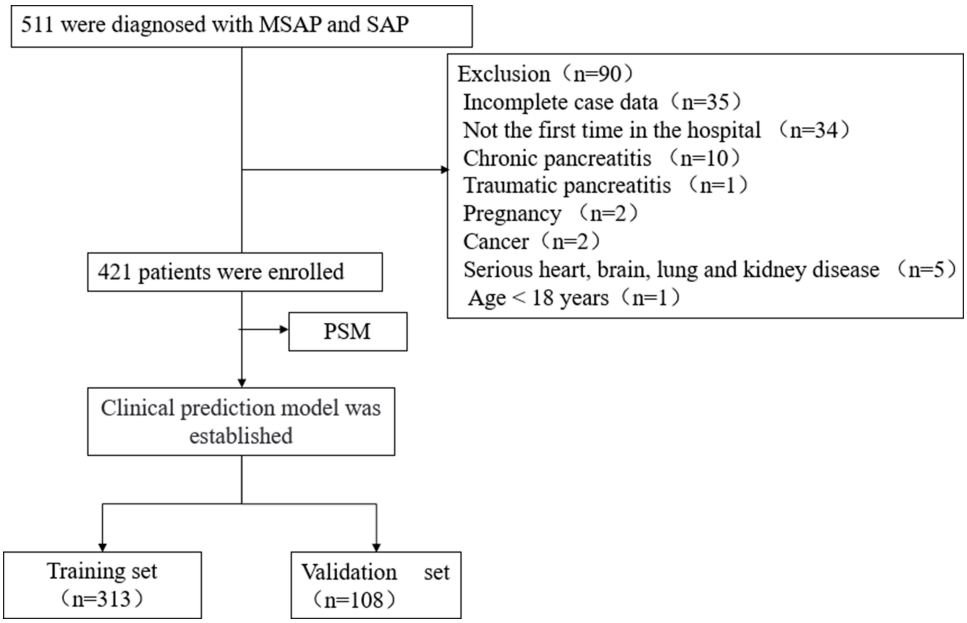


**Figure 1** Flowchart of patient enrollment.

Table 1 reveals that, upon admission, diabetic patients exhibited higher BMI (27.78 vs 25.56, p<0.001), a greater prevalence of hypertension (32% vs 16%, p=0.002), and a higher incidence of hyperlipidemia (32% vs 16%, p=0.002) compared to non-diabetic patients. However, there were no significant differences between the two groups in terms of gender, age, etiology, smoking history, alcohol consumption, fatty liver, or other chronic diseases.

**Table 1** Before PSM, the Difference of Basic Clinical Characteristics at Admission Between the Two Groups in Patients with or Without DM

| | **Total (n = 421)** | **No-DM (n = 342)** | **DM (n = 79)** | ***p*** |
|---|---|---|---|---|
| Sex, n (%) | | | | 1 |
| Female | 155 (37) | 126 (37) | 29 (37) | |
| Male | 266 (63) | 216 (63) | 50 (63) | |
| Age, M(P25,P75) | 52 (38, 67) | 52 (38, 67) | 46 (37, 63) | 0.097 |
| Days, M(P25,P75) | 16 (10, 24) | 15 (10, 23) | 17 (11, 26.5) | 0.078 |
| BMI, M(P25,P75) | 25.71 (23.12, 29.37) | 25.56 (22.92, 28.72) | 27.78 (24.84, 30.76) | < 0.001 |
| Pathogeny, n (%) | | | | 0.083 |
| Biliary | 224 (53) | 187 (55) | 37 (47) | |
| Hypertriglyceridemia | 33 (8) | 22 (6) | 11 (14) | |
| Alcoholic | 68 (16) | 58 (17) | 10 (13) | |
| Others | 96 (23) | 75 (22) | 21 (27) | |
| Smoking, n (%) | | | | 0.118 |
| No | 269 (64) | 212 (62) | 57 (72) | |
| Yes | 152 (36) | 130 (38) | 22 (28) | |
| Drinking, n (%) | | | | 0.2 |
| No | 264 (63) | 209 (61) | 55 (70) | |
| Yes | 157 (37) | 133 (39) | 24 (30) | |
| HTN, n (%) | | | | 0.002 |
| No | 342 (81) | 288 (84) | 54 (68) | |
| Yes | 79 (19) | 54 (16) | 25 (32) | |
| HPL, n (%) | | | | 0.002 |
| No | 342 (81) | 288 (84) | 54 (68) | |
| Yes | 79 (19) | 54 (16) | 25 (32) | |
| Fatty Liver, n (%) | | | | 0.247 |
| No | 327 (78) | 270 (79) | 57 (72) | |
| Yes | 94 (22) | 72 (21) | 22 (28) | |
| Other chronic diseases, n (%) | | | | 0.46 |
| No | 325 (77) | 267 (78) | 58 (73) | |
| Yes | 96 (23) | 75 (22) | 21 (27) | |

Regarding clinical outcomes (Table 2), diabetic patients had a higher incidence of peripancreatic fluid collection (71% vs 47%, p<0.001) and infected pancreatic necrosis (48% vs 10%, p<0.001). Additionally, they had a higher rate of surgical interventions (24% vs 12%, p=0.008) and showed significant differences in the use of percutaneous catheter drainage (22% vs 11%, p=0.014). However, there were no significant differences between the two groups in other clinical outcomes, including

**Table 2** Before PSM, the Difference of Clinical Outcomes Between the Two Groups in Patients with or Without DM

| | Total (n = 421) | No-DM (n = 342) | DM (n = 79) | *p* |
|---|---|---|---|---|
| SIRS, n (%) | | | | 0.843 |
| No | 113 (27) | 93 (27) | 20 (25) | |
| Yes | 308 (73) | 249 (73) | 59 (75) | |
| MODS, n (%) | | | | 0.619 |
| No | 146 (35) | 121 (35) | 25 (32) | |
| Yes | 275 (65) | 221 (65) | 54 (68) | |
| Peripancreatic Effusion, n (%) | | | | < 0.001 |
| No | 203 (48) | 180 (53) | 23 (29) | |
| Yes | 218 (52) | 162 (47) | 56 (71) | |
| IPN | | | | < 0.001 |
| No | 348 (83) | 307 (90) | 41 (52) | |
| Yes | 73 (17) | 35 (10) | 38 (48) | |
| Hydrothorax, n (%) | | | | 0.337 |
| No | 199 (47) | 166 (49) | 33 (42) | |
| Yes | 222 (53) | 176 (51) | 46 (58) | |
| Seroperitoneum, n (%) | | | | 0.283 |
| No | 228 (54) | 190 (56) | 38 (48) | |
| Yes | 193 (46) | 152 (44) | 41 (52) | |
| Surgical Intervention, n (%) | | | | 0.008 |
| No | 362 (86) | 302 (88) | 60 (76) | |
| Yes | 59 (14) | 40 (12) | 19 (24) | |
| Thoracocentesis, n (%) | | | | 0.336 |
| No | 404 (96) | 330 (96) | 74 (94) | |
| Yes | 17 (4) | 12 (4) | 5 (6) | |
| Abdominocentesis, n (%) | | | | 0.014 |
| No | 368 (87) | 306 (89) | 62 (78) | |
| Yes | 53 (13) | 36 (11) | 17 (22) | |

(*Continued*)

**Table 2** (Continued).

| | Total (n = 421) | No-DM (n = 342) | DM (n = 79) | *p* |
|---|---|---|---|---|
| Operative Treatment, n(%) | | | | 0.166 |
| Peripancreatic debridement | 17 (4) | 11 (3) | 6 (8) | |
| LC | 53 (13) | 47 (14) | 6 (8) | |
| ERCP | 3 (1) | 3 (1) | 0 (0) | |
| Bile duct exploration | 6 (1) | 6 (2) | 0 (0) | |
| No | 342 (81) | 275 (80) | 67 (85) | |
| Enteral Nutrition, n (%) | | | | 0.766 |
| No | 312 (74) | 255 (75) | 57 (72) | |
| Yes | 109 (26) | 87 (25) | 22 (28) | |
| ICU admission, n (%) | | | | 1 |
| No | 392 (93) | 318 (93) | 74 (94) | |
| Yes | 29 (7) | 24 (7) | 5 (6) | |
| Length of hospital stay, M(P25,P75) | 16 (10, 24) | 15 (10, 23) | 17 (11, 26.5) | 0.078 |
| Mortality, n (%) | | | | 0.75 |
| No | 404 (96) | 327 (96) | 77 (97) | |
| Yes | 17 (4) | 15 (4) | 2 (3) | |

systemic inflammatory response syndrome (SIRS), organ dysfunction, pleural effusion, intra-abdominal fluid accumulation, use of thoracic drainage, surgical treatment, enteral nutrition, ICU admission rate, length of hospital stay, or mortality.

## Comparison of Clinical Characteristics Between the Two Groups After PSM

Considering those differences in BMI, blood pressure, and lipid levels between the first two patient groups may impact clinical outcomes differently, we employed propensity score matching to mitigate confounding factors. Using a 1:2 nearest neighbor matching approach with a caliper value of 0.02, we matched diabetic patients as the reference group. The controlled covariates included gender, age, BMI, etiology, smoking, alcohol consumption, hypertension, hyperlipidemia, fatty liver, and other chronic diseases. Due to sample size limitations, some individuals could not be successfully matched, resulting in a final cohort of 174 matched cases (Table 3). The histogram of propensity scores is depicted in Figure 2, where 'Raw' represents pre-matching scores, showing substantial differences between the two groups, while 'Matched' indicates post-matching scores, suggesting good matching.

Supplementary Table 1 reveals that there were no significant differences ($p>0.05$) in baseline characteristics between the two groups after matching.

However, Table 3 demonstrates that post-matching, the diabetic group still exhibited a higher incidence of peripancreatic fluid collection (69% vs 47%, $p=0.008$) and infected pancreatic necrosis (48% vs 11%, $p<0.001$). Additionally, diabetic patients maintained a higher rate of surgical interventions (27% vs 13%, $p=0.037$), although there were no significant differences specifically in percutaneous catheter drainage between the two groups.

Based on the propensity score matching results, it appears that diabetic patients admitted with MSAP and SAP are more likely to develop infectious pancreatic necrosis during disease progression. To accurately assess the relationship between diabetes and infectious pancreatic necrosis, a predictive model for early diagnosis of IPN in MSAP and SAP patients can be established.

**Table 3** After PSM, the Difference of Clinical Outcomes Between the Two Groups in Patients with or Without DM

| | Total (n = 174) | No-DM (n = 112) | DM (n = 62) | *p* |
|---|---|---|---|---|
| SIRS, n (%) | | | | 0.843 |
| No | 42 (24) | 26 (23) | 16 (26) | |
| Yes | 132 (76) | 86 (77) | 46 (74) | |
| MODS, n (%) | | | | 0.74 |
| No | 66 (38) | 44 (39) | 22 (35) | |
| Yes | 108 (62) | 68 (61) | 40 (65) | |
| Peripancreatic Effusion, n (%) | | | | 0.008 |
| No | 78 (45) | 59 (53) | 19 (31) | |
| Yes | 96 (55) | 53 (47) | 43 (69) | |
| IPN | | | | < 0.001 |
| No | 132 (76) | 100 (89) | 32 (52) | |
| Yes | 42 (24) | 12 (11) | 30 (48) | |
| Hydrothorax, n (%) | | | | 0.903 |
| No | 67 (39) | 44 (39) | 23 (37) | |
| Yes | 107 (61) | 68 (61) | 39 (63) | |
| Seroperitoneum, n (%) | | | | 0.542 |
| No | 91 (52) | 61 (54) | 30 (48) | |
| Yes | 83 (48) | 51 (46) | 32 (52) | |
| Surgical Intervention, n (%) | | | | 0.037 |
| No | 142 (82) | 97 (87) | 45 (73) | |
| Yes | 32 (18) | 15 (13) | 17 (27) | |
| Thoracocentesis, n (%) | | | | 0.746 |
| No | 164 (94) | 106 (95) | 58 (94) | |
| Yes | 10 (6) | 6 (5) | 4 (6) | |
| Abdominocentesis, n (%) | | | | 0.077 |
| No | 145 (83) | 98 (88) | 47 (76) | |
| Yes | 29 (17) | 14 (12) | 15 (24) | |
| Operative Treatment, n(%) | | | | 0.266 |
| Peripancreatic debridement | 10 (6) | 4 (4) | 6 (10) | |
| LC | 19 (11) | 13 (12) | 6 (10) | |
| Bile duct exploration | 3 (2) | 3 (3) | 0 (0) | |
| No | 142 (82) | 92 (82) | 50 (81) | |

(*Continued*)

**Table 3** (Continued).

| | Total (n = 174) | No-DM (n = 112) | DM (n = 62) | *p* |
|---|---|---|---|---|
| Enteral Nutrition, n (%) | | | | 0.929 |
| No | 120 (69) | 78 (70) | 42 (68) | |
| Yes | 54 (31) | 34 (30) | 20 (32) | |
| ICU admission, n (%) | | | | 1 |
| No | 163 (94) | 105 (94) | 58 (94) | |
| Yes | 11 (6) | 7 (6) | 4 (6) | |
| Length of hospital stay, M(P25,P75) | 17 (11.25, 25) | 17.5 (11, 24.25) | 17 (12, 28.5) | 0.31 |
| Mortality, n (%) | | | | 0.424 |
| No | 168 (97) | 107 (96) | 61 (98) | |
| Yes | 6 (3) | 5 (4) | 1 (2) | |

## Establishment of a Clinical Prediction Model for Infected Pancreatic Necrosis

In a study involving 421 enrolled patients with moderately acute pancreatitis (MSAP) and severe acute pancreatitis (SAP), a random allocation of 7:3 was applied to create training and validation sets. The training cohort consisted of 313 patients, while the validation cohort comprised 108 patients. Notably, there were no statistically significant differences in basic clinical characteristics and laboratory findings between the training and validation sets.

Based on the training dataset, we developed a clinical prediction model for infectious pancreatic necrosis (IPN). IPN is a severe complication of acute pancreatitis, and early identification is crucial for improving patient outcomes. The model leveraged relevant clinical features and laboratory parameters to predict the occurrence of IPN. Our goal was to enhance medical resource allocation and patient management by providing an effective risk assessment tool.

### Comparison Basic Characteristics and Clinical Parameters of Patients Grouped by IPN

In the training cohort of 313 enrolled patients, we categorized them based on the occurrence of infectious pancreatic necrosis (IPN). The IPN group consisted of 52 patients, while the non-IPN group included 261 patients (Table 4). We compared basic characteristics, laboratory parameters, inflammatory indices, and clinical scoring between these two groups.

Table 4 reveals that, upon admission, there were no significant differences (all $p>0.05$) in basic characteristics (gender, age, BMI, etiology, smoking, alcohol consumption, hypertension, hyperlipidemia, fatty liver, and other chronic diseases) between the two groups. However, regarding diabetes, 50% of the IPN group had diabetes at admission, whereas only 12% of the non-IPN group had diabetes, resulting in a significant difference ($p<0.001$).

Supplementary Table 2 demonstrates that in terms of laboratory parameters, the IPN group exhibited lower levels of albumin, high-density lipoprotein cholesterol, low-density lipoprotein cholesterol, serum calcium, and prothrombin activity compared to the non-IPN group. Conversely, the IPN group had higher levels of serum magnesium, prothrombin time, D-dimer, and monocyte count (all with statistical significance at $p<0.05$). Other laboratory indices showed no significant differences between the two groups.

Table 5 indicates that in terms of inflammatory indices and clinical scoring, the two groups significantly differed in the Modified Computed Tomography Severity Index (MCTSI) ($p<0.001$). However, there were no significant differences in Platelet-to-Lymphocyte Ratio (PLR), Neutrophil-to-Lymphocyte Ratio (NLR), Organ Failure Predictive Nomogram Index (OPNI), Japanese Severity Score (JSS), or Bedside Index for Severity in Acute Pancreatitis (BISAP).

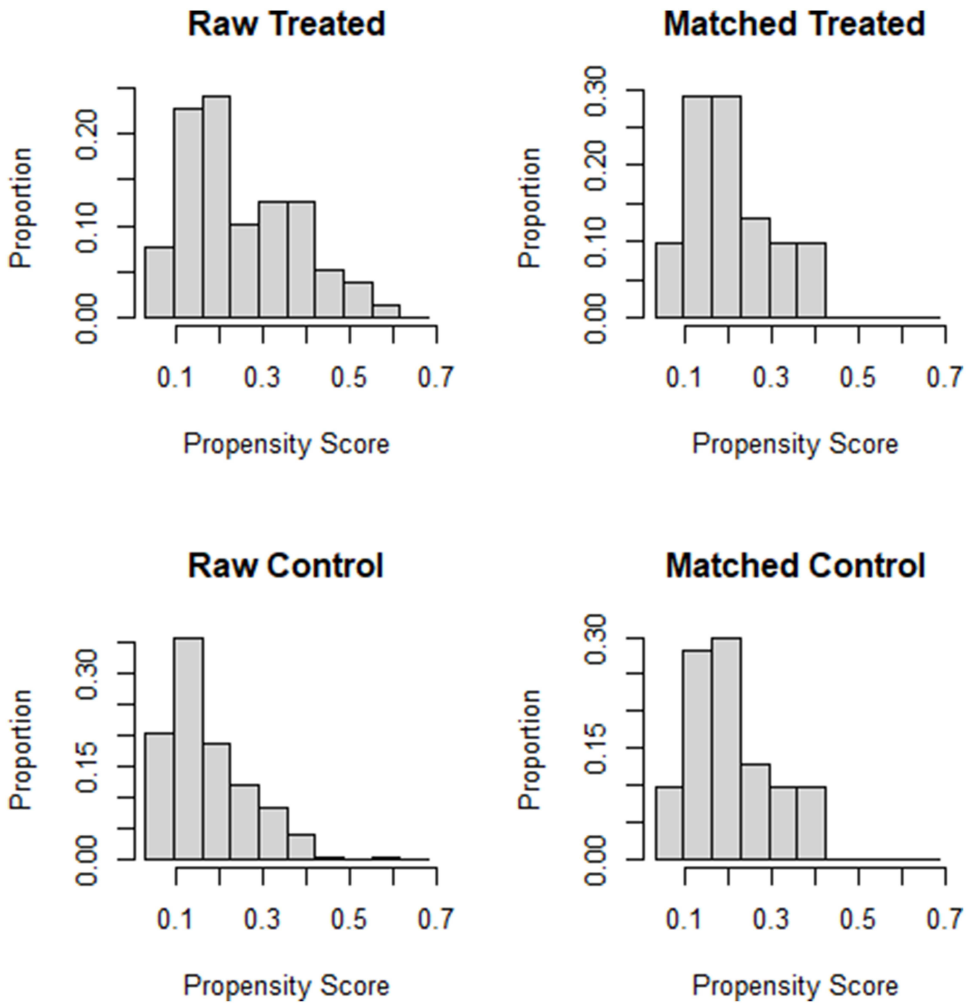


**Figure 2** Histogram of propensity score distribution before and after matching.

## Building Predictive Models

In the logistic regression analysis, we examined the indicators that showed differences between the two compared groups. The results are summarized in Table 6. Diabetes, Modified Computed Tomography Severity Index (MCTSI), high-density lipoprotein cholesterol, and serum calcium were identified as independent risk factors for predicting the

**Table 4** The Difference of Basic Clinical Characteristics at Admission Between the Two Groups in Patients with or Without IPN

| | **Total (n = 313)** | **No-IPN (n = 261)** | **IPN (n = 52)** | ***p*** |
|---|---|---|---|---|
| Sex, n (%) | | | | 0.726 |
| Female | 112 (36) | 95 (36) | 17 (33) | |
| Male | 201 (64) | 166 (64) | 35 (67) | |
| Age, M(P25,P75) | 52 (38, 68) | 53 (38, 68) | 48.5 (36.75, 61.25) | 0.185 |
| BMI, M(P25,P75) | 26.12 (23.44, 29.41) | 25.71 (23.31, 29.38) | 27.91 (23.83, 30.69) | 0.077 |

(*Continued*)

**Table 4** (Continued).

| | Total (n = 313) | No-IPN (n = 261) | IPN (n = 52) | *p* |
|---|---|---|---|---|
| Pathogeny, n (%) | | | | 0.944 |
| Biliary | 168 (54) | 140 (54) | 28 (54) | |
| Hypertriglyceridemia | 24 (8) | 21 (8) | 3 (6) | |
| Alcoholic | 47 (15) | 38 (15) | 9 (17) | |
| Others | 74 (24) | 62 (24) | 12 (23) | |
| Smoking, n (%) | | | | 0.451 |
| No | 198 (63) | 168 (64) | 30 (58) | |
| Yes | 115 (37) | 93 (36) | 22 (42) | |
| Drinking, n (%) | | | | 0.808 |
| No | 197 (63) | 163 (62) | 34 (65) | |
| Yes | 116 (37) | 98 (38) | 18 (35) | |
| DM, n (%) | | | | < 0.001 |
| No-DM | 255 (81) | 229 (88) | 26 (50) | |
| DM | 58 (19) | 32 (12) | 26 (50) | |
| HTN, n (%) | | | | 0.943 |
| No | 215 (69) | 180 (69) | 35 (67) | |
| Yes | 98 (31) | 81 (31) | 17 (33) | |
| HPL, n (%) | | | | 0.243 |
| No | 256 (82) | 210 (80) | 46 (88) | |
| Yes | 57 (18) | 51 (20) | 6 (12) | |
| Fatty Liver, n (%) | | | | 1 |
| No | 239 (76) | 199 (76) | 40 (77) | |
| Yes | 74 (24) | 62 (24) | 12 (23) | |
| Other chronic diseases, n (%) | | | | 1 |
| No | 239 (76) | 199 (76) | 40 (77) | |
| Yes | 74 (24) | 62 (24) | 12 (23) | |

occurrence of infected pancreatic necrosis (IPN) in patients with moderately acute pancreatitis (MSAP) and severe acute pancreatitis (SAP). Based on these findings, we constructed a predictive model represented as nomogram (Figure 3). Each indicator in the graph corresponds to its test result, allowing for the determination of the corresponding predictive score. By aggregating scores from various indicators, the total predictive score provides an estimate of the probability of IPN.

**Table 5** The Difference of Inflammatory Indices and Clinical Scoring Parameters Between the Two Groups in Patients with or Without IPN

| | Total (n = 313) | No-IPN (n = 261) | IPN (n = 52) | *p* |
|---|---|---|---|---|
| PLR, (Q1,Q3) | 196.05 (141.93, 291.95) | 197.01 (141.93, 294.9) | 187.55 (143.44, 278.33) | 0.84 |
| NLR, (Q1,Q3) | 11.17 (6.73, 17.5) | 11.23 (6.67, 17.27) | 10.66 (6.97, 17.53) | 0.979 |
| OPNI, (Q1,Q3) | 39.55 (33.05, 45.05) | 40.1 (33.55, 45.45) | 36.3 (32.12, 42.18) | 0.051 |
| MCTSI, n (%) | | | | < 0.001 |
| 0 | 3 (1) | 2 (1) | 1 (2) | |
| 2 | 103 (33) | 86 (33) | 17 (33) | |
| 4 | 78 (25) | 70 (27) | 8 (15) | |
| 6 | 117 (37) | 103 (39) | 14 (27) | |
| 8 | 12 (4) | 0 (0) | 12 (23) | |
| BISAP, n (%) | | | | 0.24 |
| 0 | 68 (22) | 53 (20) | 15 (29) | |
| 1 | 144 (46) | 125 (48) | 19 (37) | |
| 2 | 82 (26) | 69 (26) | 13 (25) | |
| 3 | 19 (6) | 14 (5) | 5 (10) | |

**Table 6** Univariate and Multivariate Logistic Regression Analysis of Infected Pancreatic Necrosis

| | Univariable | | Multivariable | |
|---|---|---|---|---|
| | OR (95% CI) | *p* | OR (95% CI) | *P* |
| DM | 7.16 (3.72–13.92) | <0.001 | 10.15 (4.63–23.34) | <0.001 |
| MCTSI | 1.20 (1.02–1.42) | 0.028 | 1.25 (1.04–1.52) | 0.019 |
| Alb | 0.97 (0.94–1.00) | 0.038 | 0.97 (0.92–1.00) | 0.152 |
| HDL-C | 0.63 (0.39–0.90) | 0.027 | 0.56 (0.31–0.97) | 0.044 |
| LDL-C | 0.97 (0.95–0.99) | 0.024 | 1.00 (0.95–1.05) | 0.922 |
| Mg | 6.55 (1.29–37.01) | 0.024 | 4.80 (0.64–43.72) | 0.147 |
| Ca | 0.14 (0.04–0.41) | <0.001 | 0.10 (0.02–0.46) | 0.004 |
| PT-S | 1.11 (0.98–1.27) | 0.082 | 0.88 (0.54–1.24) | 0.527 |
| PT(%) | 0.97 (0.95–0.99) | 0.005 | 0.96 (0.89–1.01) | 0.173 |
| D-Dimer | 1.00 (1.00–1.00) | 0.914 | 1.00 (1.00–1.00) | 0.544 |
| MONO | 2.06 (1.15–3.77) | 0.016 | 1.89 (0.96–3.75) | 0.061 |

## Evaluation of Model Predictive Performance

Validation of the model was performed using the validation dataset. We evaluated its performance in terms of discrimination, calibration, and clinical utility.

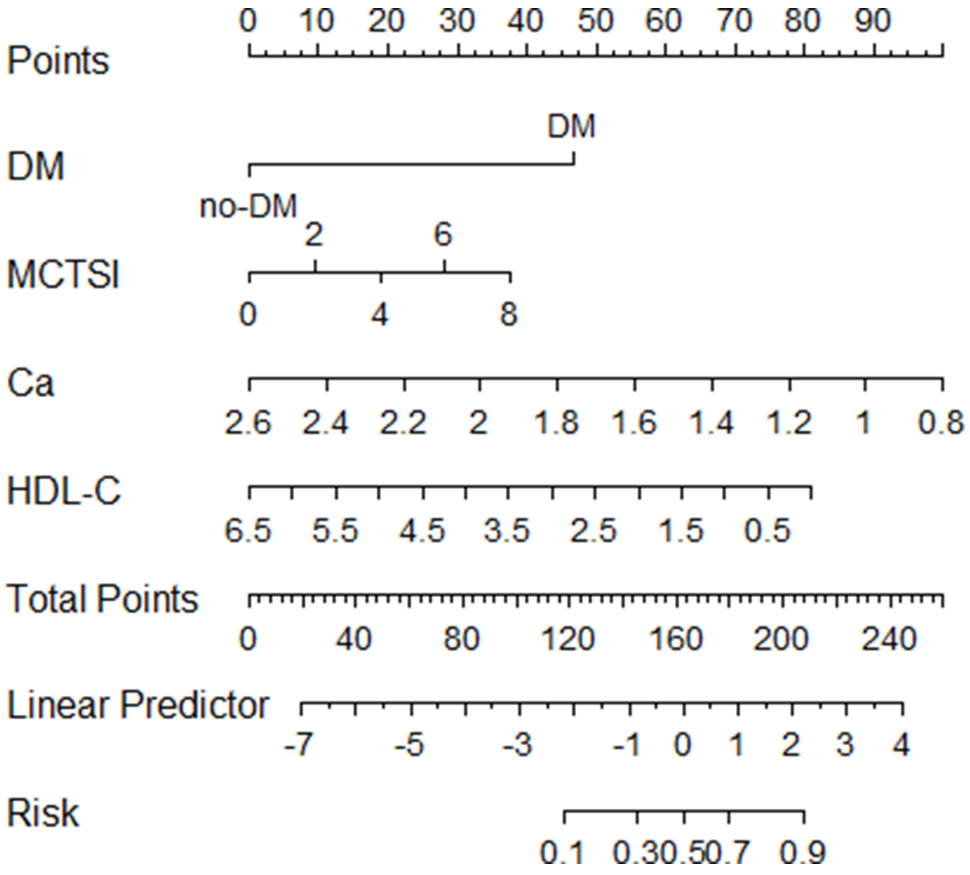


**Figure 3** Nomogram for predicting whether patients with MSAP and SAP will develop IPN.

As shown in Figure 4A (training set) and 4B (validation set), the ROC curves demonstrated an area under the curve (AUC) of 0.819 (95% CI: 0.756–0.882) for the training set and 0.833 (95% CI: 0.726–0.939) for the validation set. These results indicate that the model effectively discriminates between the IPN group and the non-IPN group.

Following internal validation using bootstrap resampling, the calibration curves (Figure 4C for training set and 4D for validation set) were generated. In these curves, the 'Ideal' line represents perfect alignment between predicted and actual probabilities, the 'Apparent' line reflects the model's performance without calibration, and the "Bias-corrected" line represents the model's performance after resampling. The closer the "Bias-corrected" line is to the "Ideal" line, the better the model predicts the probability of event occurrence. Figures 4C and D demonstrate the high predictive value of this model.

To further elucidate the clinical utility, we plotted decision curve analysis (DCA) curves (Figure 4E for training set and 4F for validation set). The "All" line represents scenarios where all samples receive intervention, while the "None" line represents no intervention. The solid red line represents net benefit at different risk thresholds, reflecting the net gain from taking intervention based on model predictions compared to taking no action. Figure 4E and F highlight the significant clinical net benefit provided by this model.

In summary, performance evaluation confirms that this model effectively predicts whether MSAP and SAP patients will develop IPN and has practical implications when applied in a clinical setting.

## Web Calculator

For ease of calculation and obtaining specific test results, a user-friendly web calculator based on the nomogram model has been developed (available at this link: https://xjl-123.shinyapps.io/DynNomapp/). Users can adjust the numerical sliders on the left, input their test results, and then click "Predict" to obtain precise predictions (Figure 5).

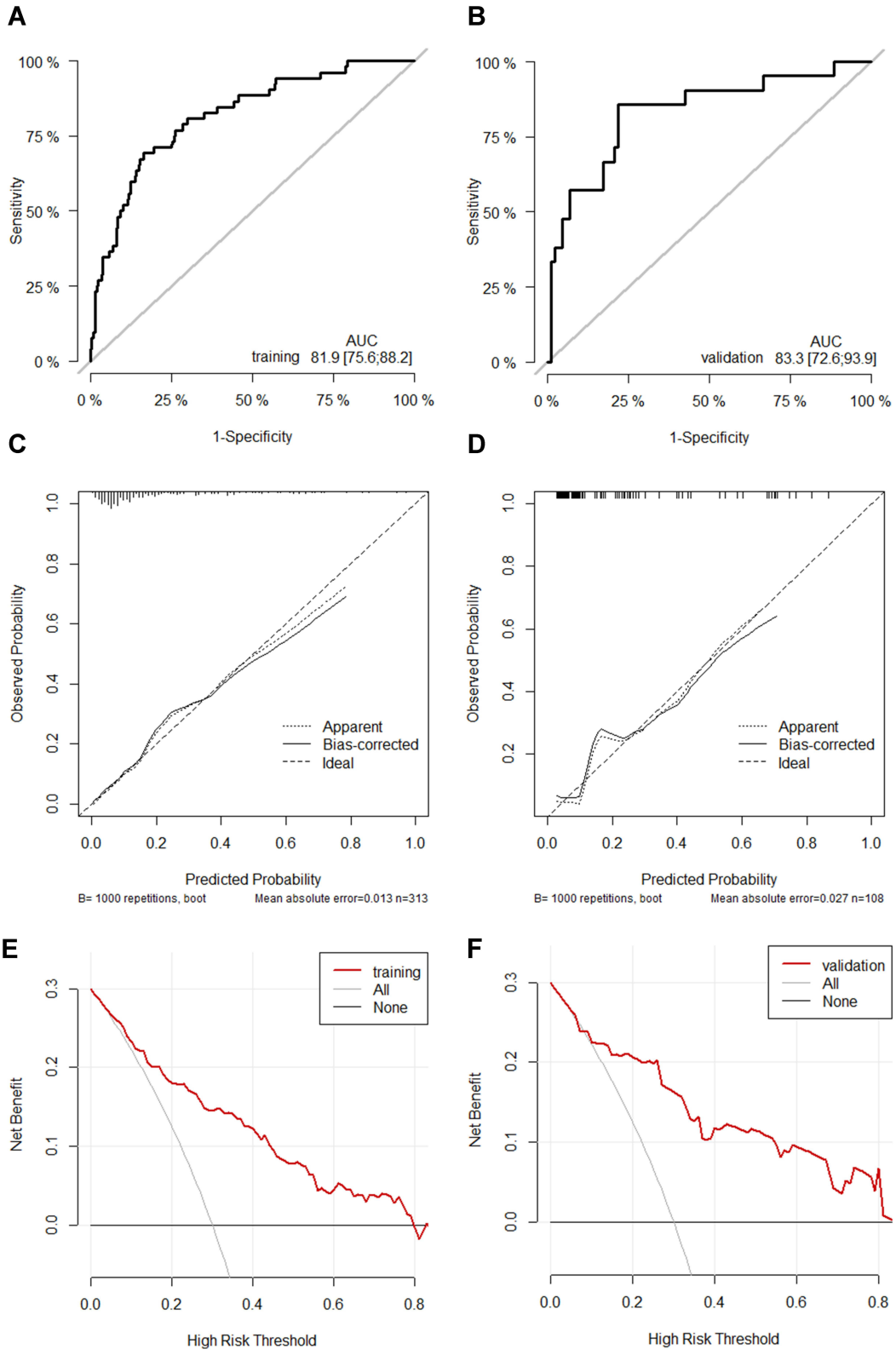


**Figure 4** Nomogram performance. ROC curves of the model for predicting IPN probabilities in the training cohort (**A**) and validation cohort (**B**). Calibration plots for predicting POF probabilities in the training cohort (**C**) and validation cohort (**D**). The closer the Bias-corrected line is to the Idea l line, the better the predictive ability of the model is. Decision curves for the training cohort (**E**) and validation cohort (**F**). The abscissa is the threshold probability, and the ordinate is the net benefit rate, when the red dashed line is above the two solid lines, it indicates that the model provides a net benefit.

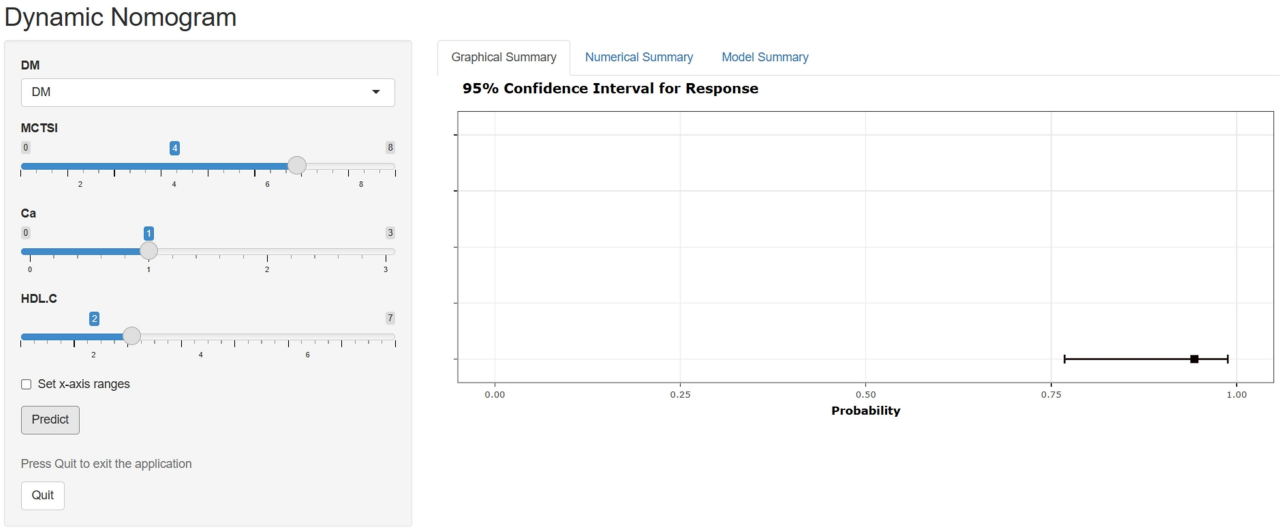


**Figure 5** Dynamic web calculator to predict whether patients with MSAP and SAP will develop IPN. The left band inputs variable values, Graphical Summary shows the probability and confidence interval of IPN occurrence in the form of pictures.

## Discussion

This study focuses on investigating the impact of concurrent diabetes at admission on clinical outcomes in patients with moderately acute pancreatitis (MSAP) and severe acute pancreatitis (SAP). Through logistic regression, this study confirmed diabetes as an independent risk factor for IPN, leading to the development of a clinical prediction model for IPN in MSAP and SAP patients. Beyond diabetes, modified CT severity index, serum calcium, and high-density lipoprotein cholesterol were also identified as independent risk factors for IPN.

In existing research, the impact of diabetes on clinical outcomes in acute pancreatitis remains a topic of debate. Some studies suggest that diabetes increases the incidence of renal failure in pancreatitis patients,[6,10] elevates the risk of necrosis and local complications,[7] and contributes to higher mortality rates in pancreatitis patients.[22] However, contrasting conclusions have been proposed. Durmuş et al found that although the diabetes group differed from the non-diabetes group in terms of local complications, there were no significant differences in organ failure between the two groups.[7] Furthermore, diabetes was not associated with increased mortality in pancreatitis patients.[23,24] Generally, it is believed that diabetes may impact non-malignant outcomes in pancreatitis, possibly related to insulin use. Our study results lean toward adverse outcomes associated with diabetes in pancreatitis. Mechanistically, hyperglycemia in diabetic patients can increase intracellular reactive oxygen species (ROS),[25] disrupt calcium homeostasis, damage mitochondria, and ultimately lead to pancreatic cell apoptosis.[26] Additionally, diabetes enhances Notch signaling, promoting polarization of macrophages toward the M1 phenotype.[27] It also suppresses the production of the anti-inflammatory protein REG3β during pancreatitis, resulting in increased inflammation, edema formation, and cell death.[28] Conversely, insulin may exert acute anti-inflammatory effects by reducing intracellular NF- κB and ROS in monocytes.[29]

The Modified Computed Tomography Severity Index (MCTSI) provides a visually intuitive reflection of pancreatic inflammation through radiological features, aiding in the assessment of pancreatitis severity. In our study, MCTSI emerged as an independent risk factor for infectious pancreatic necrosis (IPN), aligning with previous research where MCTSI was also identified as an independent risk factor for complications in acute pancreatitis. Zhao et al found that MCTSI was an independent risk factor for pancreatitis complicated by pancreatic portal hypertension.[30] Zhang et al demonstrated that an automated machine learning model combining MCTSI with serum markers effectively predicted severe acute pancreatitis (SAP) early.[31] Additionally, Xu et al showed that MCTSI combined with low muscle mass (LMSS) better predicted the severity of hyperlipidemic pancreatitis.[32] These findings underscore the high clinical utility of MCTSI in pancreatitis assessment.

Serum calcium has been consistently associated with pancreatitis outcomes in multiple studies.[8,33,34] Our research further confirms that serum calcium is an independent risk factor for IPN. The progression of pancreatitis is closely

linked to calcium ions. Abnormal calcium ion activation can lead to pancreatic enzyme hyperactivity, triggering autodigestion of the pancreas.[35] Intracellular calcium ions can also cause mitochondrial damage and endoplasmic reticulum stress, exacerbating cellular injury.[36] During pancreatitis, intracellular calcium overload and the binding of extracellular free fatty acids (FFAs) with calcium ions can result in decreased blood calcium levels.[37]

High-density lipoprotein cholesterol (HDL-C) has also been implicated in pancreatitis prognosis across various studies. HDL-C has early predictive value for sustained organ failure in acute pancreatitis patients and serves as an independent predictor of pancreatic necrosis and mortality rates.[38,39] FFAs during pancreatitis exert lipotoxic effects on human pancreatic β cells, leading to dysfunction and cell death.[40] HDL plays a central role in FFA clearance and reverse cholesterol transport, offering antioxidant, antithrombotic, and anti-apoptotic functions.[41] Therefore, reduced HDL-C during pancreatitis elevates FFAs, creating an acidic environment that damages acinar cells and ultimately increases the likelihood of peripancreatic necrosis.

It's worth noting that although several studies have highlighted the predictive value of inflammatory markers such as C-reactive protein (CRP), procalcitonin (PCT), interleukin-6 (IL-6), neutrophil-to-lymphocyte ratio (NLR), and platelet-to-lymphocyte ratio (PLR) for pancreatitis outcomes,[16,17,42,43] our study did not find statistically significant associations with these markers. This discrepancy may be due to the fact that non-mild pancreatitis patients often experience sterile inflammation-induced systemic inflammatory response syndrome (SIRS) early in their hospitalization, while IPN typically occurs later in the disease course.[12] Additionally, missing data for CRP, PCT, IL-6, and other markers in our study may have influenced their statistical significance, despite their established predictive value in prior research.

Additionally, we explored the relationship between diabetes and clinical outcomes in MSAP and SAP patients using propensity score matching at the beginning of this study. Prior to matching, diabetic patients exhibited higher rates of peripancreatic fluid collection, infectious pancreatic necrosis (IPN), and surgical interventions, primarily involving percutaneous catheter drainage. Post-matching results indicated that diabetic patients still had elevated rates of peripancreatic fluid collection and IPN, suggesting a persistent association between diabetes and local complications in MSAP and SAP after accounting for confounding factors. This further confirms the impact of diabetes on clinical outcomes. However, there was no significant difference in percutaneous catheter drainage between the two groups after matching. Potential bias factors, such as higher BMI and hyperlipidemia in pancreatitis patients, may contribute to this lack of difference, potentially necessitating more frequent or earlier clinical surgical interventions.[44] Additionally, the timing of abdominal drainage procedures often relies on the treating physician's clinical judgment, introducing subjectivity that could influence pre- and post-matching results.

The predictive model developed in this study is presented using column line graphs and a web-based calculator, facilitating its practical application in clinical diagnosis and treatment. Based on the results of this study, we recommend that in future clinical practice, physicians should place greater emphasis on regulating blood glucose levels and enhance patient education regarding blood glucose control. However, there are still some limitations to consider. Although propensity score matching partially mitigates bias, unknown covariates may still influence the results. Additionally, this study is based on a single-center retrospective design, necessitating future validation with multi-center studies and larger sample datasets to confirm our findings.

## Conclusion

In moderately to severe acute pancreatitis (MSAP and SAP), diabetes can significantly impact clinical outcomes and serves as an independent risk factor for infectious pancreatic necrosis (IPN). The column line graph and web-based calculator, constructed based on diabetes, Modified Computed Tomography Severity Index (MCTSI), serum calcium, and high-density lipoprotein cholesterol (HDL-C), demonstrate excellent predictive value and clinical guidance for IPN occurrence in MSAP and SAP.

## Disclosure

The authors report no conflicts of interest in this work.

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