

Development and Validation of a Multivariate Nomogram for Predicting Post-ERCP Pancreatitis: A Retrospective Cohort Study

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AIM: To identify predictors of post-endoscopic retrograde cholangiopancreatography (ERCP) pancreatitis (PEP) and to develop a multivariate prediction model by comprehensively evaluating clinical characteristics, procedure-related factors, and inflammatory biomarkers, including C-reactive protein (CRP)-to-lymphocyte ratio (CLR).

METHODS: A total of 335 patients who underwent endoscopic retrograde cholangiopancreatography (ERCP) at Zhejiang Jinhua Guangfu Cancer Hospital from December 2022 to December 2025 were retrospectively analyzed. Patients were divided into the PEP group ($n = 52$) and the non-PEP group ($n = 283$) according to whether PEP occurred. Demographic characteristics, comorbidities, ERCP-related procedural factors, and preoperative laboratory indices were collected and evaluated. Univariate and multivariate logistic regression analyses were performed to identify independent predictors of PEP. A nomogram was subsequently developed based on the identified independent predictors. The discriminative ability, calibration, and clinical utility of the model were evaluated using the receiver operating characteristic (ROC) curve, Hosmer–Lemeshow test, and decision curve analysis, respectively.

RESULTS: Compared with the non-PEP group, patients who developed PEP exhibited significantly higher CLR levels and a higher prevalence of periampullary diverticulum, pancreatic duct cannulation, and pancreatic duct guidewire passage ≥ 2 times (all $p < 0.05$). Multivariate logistic regression analysis revealed that a history of acute pancreatitis (odds ratio [OR] = 3.43, 95% confidence interval [CI]: 1.32–8.93), periampullary diverticulum (OR = 4.10, 95% CI: 2.00–8.39), pancreatic duct cannulation (OR = 3.11, 95% CI: 1.46–6.64), and CLR (OR = 1.11, 95% CI: 1.04–1.19) were independent predictors of PEP. The nomogram incorporating these independent predictors demonstrated satisfactory discriminative ability (area under the curve [AUC] = 0.80, 95% CI: 0.73–0.87). The Hosmer–Lemeshow test indicated good model calibration ($p = 0.239$), and the decision curve analysis showed that the model provided a net clinical benefit within the threshold probability range of 0.2–0.7.

CONCLUSIONS: The multivariate nomogram incorporating CLR and other independent predictors demonstrated good discriminative ability and calibration, and may serve as a practical tool for facilitating individualized risk assessment and guiding preventive strategies in patients undergoing ERCP.

Keywords: ERCP; post-ERCP pancreatitis; C-reactive protein-to-lymphocyte ratio; prediction model

Introduction

Endoscopic retrograde cholangiopancreatography (ERCP) is a minimally invasive technique that combines endoscopy and fluoroscopy for the diagnosis and treatment of biliary and pancreatic diseases, including common bile duct stones, benign biliary strictures, and periampullary diverticula [1]. Over the past two decades, advances in technology and the expansion of clinical indications have driven the rapid development of therapeutic ERCP worldwide, and as a result,

it has gradually replaced certain traditional surgical procedures, becoming the first-line interventional approach for most biliopancreatic diseases [2]. However, ERCP-related complications remain a significant concern. Among them, post-ERCP pancreatitis (PEP) is the most common adverse event with potentially serious consequences. Its overall incidence is approximately 2%–10% and can reach 30%–50% in high-risk populations [3]. The typical clinical manifestation of PEP is acute abdominal pain occurring within 24 hours after the procedure, often accompanied by nausea, vomiting, and fever. It not only prolongs hospital stay but also increases medical costs and patient mortality [4]. Therefore, early identification of high-risk patients, accurate prediction of PEP occurrence, and the development of efficient preoperative prediction tools are of critical importance for improving patient prognosis and guiding preventive strategies.

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The pathogenesis of PEP is complex, involving the synergistic effects of multiple factors such as mechanical injury, chemical stimulation, elevated intrapancreatic duct pressure, abnormal activation of zymogens, and thermal injury. Repeated cannulation attempts and pancreatic duct opacification can lead to pancreatic duct epithelial injury and impaired drainage, thereby triggering a local inflammatory response that amplifies into a systemic inflammatory cascade [5]. Various predictors of PEP, primarily including patient-related and procedure-related factors, have been confirmed in several systematic reviews [6,7]. Although these factors provide important references for clinical risk assessment, they have obvious limitations: (i) patient-related factors are mostly non-modifiable, static, inherent characteristics that are difficult to reflect the real-time physiological status of patients before ERCP; (ii) procedure-related factors can only be determined intraoperatively and cannot achieve effective preoperative stratification of patients; and (iii) these factors largely reflect risk from the perspectives of anatomical features or technical difficulty, without evaluating the pathophysiological aspect from the angle of the patient's intrinsic inflammatory response capacity to injury. Therefore, these limitations call for the exploration of biological markers that can be conveniently obtained before operation and objectively quantify the host's inflammatory and immune status, and the development of a multifactorial prediction model that integrates the newly characterized factors with traditional predictors to facilitate early identification and individualized prevention of PEP.

In recent years, inflammation-related biomarkers derived from peripheral blood have been widely applied in risk assessment for various diseases due to their convenient acquisition, low cost, and good reproducibility. For example, C-reactive protein (CRP), as a classic acute-phase reactant, has been shown to possess important predictive value in pancreatic diseases, including the assessment of disease risk and severity [8]. However, single inflammatory markers are relatively limited in reflecting the complex inflammatory response and immune status of patients. To improve the accuracy of risk assessment, composite inflammatory indices have gradually gained attention. The CRP-to-lymphocyte ratio (CLR), as a novel composite index, integrates parameters related to inflammatory response and immune function, thereby providing a more comprehensive reflection of the body's inflammatory and immune balance. A previous study has indicated that CLR is closely associated with the occurrence and progression of acute pancreatitis [9]. Further research has also confirmed that CLR is significantly associated with the risk of moderate-to-severe and severe acute pancreatitis, demonstrating superior predictive performance over other inflammatory markers [10]. In view of this, CLR may serve as a useful inflammatory biomarker that complements conventional clinical predictors. Therefore, incorporating CLR into a multivariate prediction model may provide additional information for pre-

operative risk stratification in patients undergoing ERCP. Accordingly, this study aimed to identify factors associated with PEP by comprehensively evaluating patient characteristics, procedure-related factors, and laboratory biomarkers, and to develop a multivariate prediction model based on the independently associated factors. A nomogram was subsequently constructed and evaluated in terms of discrimination, calibration, and clinical utility to facilitate individualized risk stratification in patients undergoing ERCP.

Methods

Study Population

This study employed a single-center retrospective cohort design. Consecutive patients who underwent ERCP at Zhejiang Jinhua Guangfu Cancer Hospital between December 2022 and December 2025 were included. The study protocol was approved by the by the Ethics Committee of Zhejiang Jinhua Guangfu Cancer Hospital (approval number 2026-003-01). Since this retrospective study involved no patient-identifiable information and ensured complete anonymization, the ethics review board waived the requirement for informed consent.

Inclusion and Exclusion Criteria

Inclusion criteria: (1) Patients meeting the indications for ERCP; (2) Age ≥ 18 years; (3) Availability of complete clinical data; (4) For patients who underwent only one ERCP during the study period, or for those who underwent multiple procedures, only data from the first ERCP were included.

Exclusion criteria: (1) Patients with a preoperative diagnosis of acute pancreatitis or acute cholangitis; (2) Patients with hematologic malignancies, autoimmune diseases, immunodeficiency disorders, or systemic infections; (3) Patients with coagulopathy or those who had taken anticoagulant drugs within 7 days before the procedure; (4) Patients with severe hepatic or renal insufficiency; (5) Patients who underwent palliative ERCP solely due to advanced malignant tumors; (6) Patients with a history of biliary or pancreatic duct stent placement or removal.

Clinical Manifestations and Diagnostic Criteria of PEP

The primary outcome of this study was the occurrence of post-ERCP pancreatitis (PEP). The typical clinical manifestations of PEP include abdominal pain occurring within 24 hours after the procedure, often accompanied by symptoms such as nausea, vomiting, and fever. Diagnosis is primarily based on clinical manifestations combined with imaging findings, where computed tomography (CT) or ultrasound can confirm pancreatic inflammatory changes. According to the clinical practice guideline [11], the diagnostic criteria for PEP are as follows: new or worsened abdominal pain within 24–48 hours after ERCP, accompanied by serum amylase or lipase levels elevated to more than three times the upper limit of normal, or imaging findings sug-

gestive of pancreatic swelling or fluid collection, and these manifestations must result in prolongation of hospital stay.

Data Collection

Clinical data of patients were retrospectively retrieved from the hospital electronic medical record system. All laboratory indices were measured within 24 hours before ERCP. The collected data cover the following:

Demographic characteristics: age, sex, and body mass index (BMI).

Comorbidities: diabetes mellitus, hypertension, coronary heart disease, etc.

Previous medical and surgical history: history of acute pancreatitis, history of cholecystectomy.

Indications for ERCP: choledocholithiasis, malignant obstruction, benign biliary stricture, and others.

Procedure-related and imaging factors: periampullary diverticulum, extrahepatic bile duct dilation, pancreatic duct cannulation, and the number of pancreatic duct guidewire passages. Periampullary diverticulum was defined as a duodenal diverticulum located within 2–3 cm of the major duodenal papilla and was identified from ERCP procedure reports based on endoscopic findings. Extrahepatic bile duct dilatation was assessed using preoperative CT or MRCP and was defined as a common bile duct diameter ≥ 7 mm in patients with the gallbladder in situ or ≥ 10 mm in patients with a history of cholecystectomy [12].

Laboratory indices: white blood cell count, neutrophil count, lymphocyte count (LYM), monocyte count, hemoglobin, platelet count, and CRP level. The CRP-to-lymphocyte ratio (CLR) was calculated using the formula in the following:

$$\text{CLR} = \frac{\text{CRP}(\text{mg/L})}{\text{LYM}(10^9/\text{L})}$$

Imaging-related information was obtained from preoperative abdominal CT or magnetic resonance cholangiopancreatography reports. Data extraction was performed independently and cross-checked by two researchers. Any discrepancies were resolved by reviewing the original medical records for confirmation.

Statistical Analysis

All statistical analyses were performed using R software version 4.5.2 (R Foundation for Statistical Computing, Vienna, Austria). The normality of continuous variables was assessed using the Shapiro–Wilk test. Continuous variables following a normal distribution were expressed as mean $\pm$ standard deviation (SD), and comparisons between groups were conducted using the independent samples *t*-test. Continuous variables with a non-normal distribution were expressed as median and interquartile range (IQR), and comparisons between groups were performed using the

Mann–Whitney *U* test. Categorical variables were presented as frequencies and percentages, and comparisons between groups were conducted using the chi-square test or Fisher's exact test. All tests were two-sided, and a *p*-value < 0.05 was considered statistically significant.

To evaluate the relationship between various indicators and the risk of PEP, univariate logistic regression analysis was first performed to screen variables significantly associated with PEP. Variables with $p < 0.05$ in the univariate analysis were considered candidate variables and subsequently included in a multivariate logistic regression model to identify independent predictors of PEP. Only variables that remained statistically significant in the multivariate analysis were incorporated into the final nomogram model. Results were expressed as odds ratios (ORs) with 95% confidence intervals (CIs). Based on the results of the multivariate analysis, a nomogram for PEP risk prediction was constructed. The discriminative ability of the model was assessed using the receiver operating characteristic (ROC) curve, with the area under the curve (AUC) and 95% CI calculated. The Hosmer–Lemeshow goodness-of-fit test was used to evaluate the calibration of the model. Internal validation was performed using 1000 bootstrap resamples, and calibration curves were plotted to assess the consistency between predicted and actual probabilities. In addition, decision curve analysis (DCA) was employed to evaluate the net clinical benefit of the model at different threshold probabilities.

Results

Baseline Characteristics of the Study Population

This study enrolled a total of 335 eligible patients undergoing ERCP, among whom 52 developed PEP, corresponding to a PEP incidence of 15.5%. Baseline characteristics of the patients are summarized in Table 1. With regard to medical history, the proportion of patients with a history of acute pancreatitis was significantly higher in the PEP group than in the non-PEP group ($p < 0.05$). Regarding procedure-related and imaging factors, the proportions of patients with periampullary diverticulum, pancreatic duct cannulation, extrahepatic bile duct dilatation, and ≥ 2 pancreatic duct guidewire passages were all significantly higher in the PEP group than in the non-PEP group (all $p < 0.05$). Compared with patients without PEP, patients who developed PEP exhibited significantly lower lymphocyte count but significantly higher CRP levels and CLR (all $p < 0.05$).

Univariate and Multivariate Analysis of PEP Predictors

Variables that showed significant differences between groups in the baseline comparison were included in the univariate logistic regression analysis (Supplementary Table 1). The results of the univariate analysis revealed that a history of acute pancreatitis, periampullary diverticulum, pancreatic duct cannulation, extrahepatic bile duct dilation, pancreatic duct guidewire passage ≥ 2 times, lymphocyte

Table 1. Baseline characteristics of the study population.

Variables	Non-PEP group (n = 283)	PEP group (n = 52)	Statistic	p-value
Age (years), median (IQR)	55.00 (52.00, 59.00)	56.50 (51.00, 64.00)	Z = -0.94	0.348
Female, n (%)	147 (51.94)	25 (48.08)	$\chi^2 = 0.26$	0.608
BMI (kg/m ²), median (IQR)	26.80 (23.80, 29.60)	26.20 (23.35, 29.52)	Z = -0.96	0.337
Diabetes mellitus, n (%)	43 (15.19)	9 (17.31)	$\chi^2 = 0.15$	0.699
Hypertension, n (%)	80 (28.27)	13 (25.00)	$\chi^2 = 0.23$	0.629
Coronary heart disease, n (%)	24 (8.48)	6 (11.54)	$\chi^2 = 0.20$	0.656
Indications for ERCP, n (%)			Fisher	1.000
Choledocholithiasis	203 (71.73)	38 (73.08)		
Malignant obstruction	54 (19.08)	10 (19.23)		
Benign biliary stricture	12 (4.24)	2 (3.85)		
Others	14 (4.95)	2 (3.85)		
History of cholecystectomy, n (%)	49 (17.31)	13 (25.00)	$\chi^2 = 1.72$	0.190
History of acute pancreatitis, n (%)	25 (8.83)	11 (21.15)	$\chi^2 = 6.95$	0.008
Periampullary diverticulum, n (%)	55 (19.43)	24 (46.15)	$\chi^2 = 17.40$	<0.001
Pancreatic duct cannulation, n (%)	61 (21.55)	28 (53.85)	$\chi^2 = 23.48$	<0.001
Extrahepatic bile duct dilatation, n (%)	41 (14.49)	14 (26.92)	$\chi^2 = 4.95$	0.026
Pancreatic duct guidewire passage, n (%)			$\chi^2 = 16.02$	<0.001
<2 times	265 (93.64)	39 (75.00)		
≥2 times	18 (6.36)	13 (25.00)		
Laboratory parameters				
White blood cell ($\times 10^9/L$), mean $\pm$ SD	8.54 $\pm$ 2.05	8.87 $\pm$ 1.47	t = -1.41	0.161
Neutrophil ($\times 10^9/L$), median (IQR)	5.77 (4.38, 7.23)	6.39 (5.42, 7.16)	Z = -1.75	0.080
Lymphocyte ($\times 10^9/L$), median (IQR)	1.83 (1.50, 2.45)	1.56 (1.30, 2.09)	Z = -3.30	<0.001
Monocyte ($\times 10^9/L$), median (IQR)	0.50 (0.38, 0.64)	0.55 (0.41, 0.72)	Z = -1.43	0.151
Hemoglobin (g/L), mean $\pm$ SD	131.44 $\pm$ 11.78	132.37 $\pm$ 10.81	t = -0.53	0.598
CRP (mg/L), median (IQR)	11.80 (7.60, 15.80)	16.80 (9.10, 22.33)	Z = -3.79	<0.001
Platelet ($\times 10^9/L$), median (IQR)	235.00 (203.00, 263.50)	237.50 (202.00, 272.50)	Z = -0.17	0.868
CLR, median (IQR)	5.63 (3.61, 8.81)	9.23 (6.15, 13.94)	Z = -4.66	<0.001

Abbreviations: BMI, body mass index; CLR, CRP-to-lymphocyte ratio; CRP, C-reactive protein; PEP, post-ERCP pancreatitis; ERCP, endoscopic retrograde cholangiopancreatography; SD, standard deviation; IQR, interquartile range.

count, CRP, and CLR were all significantly associated with the occurrence of PEP (all $p < 0.05$).

Given that CLR is derived from CRP and lymphocyte count, to avoid the influence of multicollinearity on model stability, only CLR was included as the composite inflammatory marker in the multivariate analysis, while CRP and lymphocyte count were excluded. The remaining variables with $p < 0.05$ in the univariate analysis were entered into the multivariate logistic regression model. As shown in Table 2, a history of acute pancreatitis, periampullary diverticulum, pancreatic duct cannulation, and CLR were independent predictors of PEP occurrence (all $p < 0.05$).

Construction and Validation of a Prediction Model for PEP

Based on the results of the multivariate logistic regression analysis, the independent predictors of PEP—including history of acute pancreatitis, periampullary diverticulum, pancreatic duct cannulation, and CLR—were incorporated to construct a nomogram for PEP risk prediction (Fig. 1A).

The Hosmer–Lemeshow test yielded a p -value of 0.239, suggesting no significant difference between the predicted and actual probabilities, and the calibration curve demonstrated good agreement between them (Fig. 1B). The discriminative ability of the model was assessed using the ROC curve. The AUC for predicting PEP was 0.80 (95% CI: 0.73–0.87), indicating good discriminative performance (Fig. 1C). Decision curve analysis (DCA) indicated that, within the threshold probability range of 0.2–0.7, the prediction model provided a higher net benefit compared with the “treat all” or “treat none” strategies, suggesting good clinical application potential within a certain risk threshold range (Fig. 1D).

Discussion

In this single-center retrospective cohort study, preoperative clinical characteristics, procedure-related factors, and inflammatory biomarkers were comprehensively evaluated, with the ultimate goal of developing and internally validating a multivariate nomogram for PEP risk prediction.

Table 2. Multivariate logistic regression analysis of PEP predictors.

Variables	β	S.E.	Z	p	OR (95% CI)
History of acute pancreatitis	1.23	0.49	2.52	0.012	3.43 (1.32–8.93)
Periampullary diverticulum	1.41	0.37	3.86	<0.001	4.10 (2.00–8.39)
Pancreatic duct cannulation	1.14	0.39	2.93	0.003	3.11 (1.46–6.64)
Extrahepatic bile duct dilatation	0.62	0.42	1.46	0.145	1.85 (0.81–4.25)
Pancreatic duct guidewire passage	0.85	0.50	1.68	0.093	2.33 (0.87–6.25)
CLR	0.11	0.03	3.02	0.003	1.11 (1.04–1.19)

Abbreviations: OR, odds ratio; CI, confidence interval; S.E., standard error.

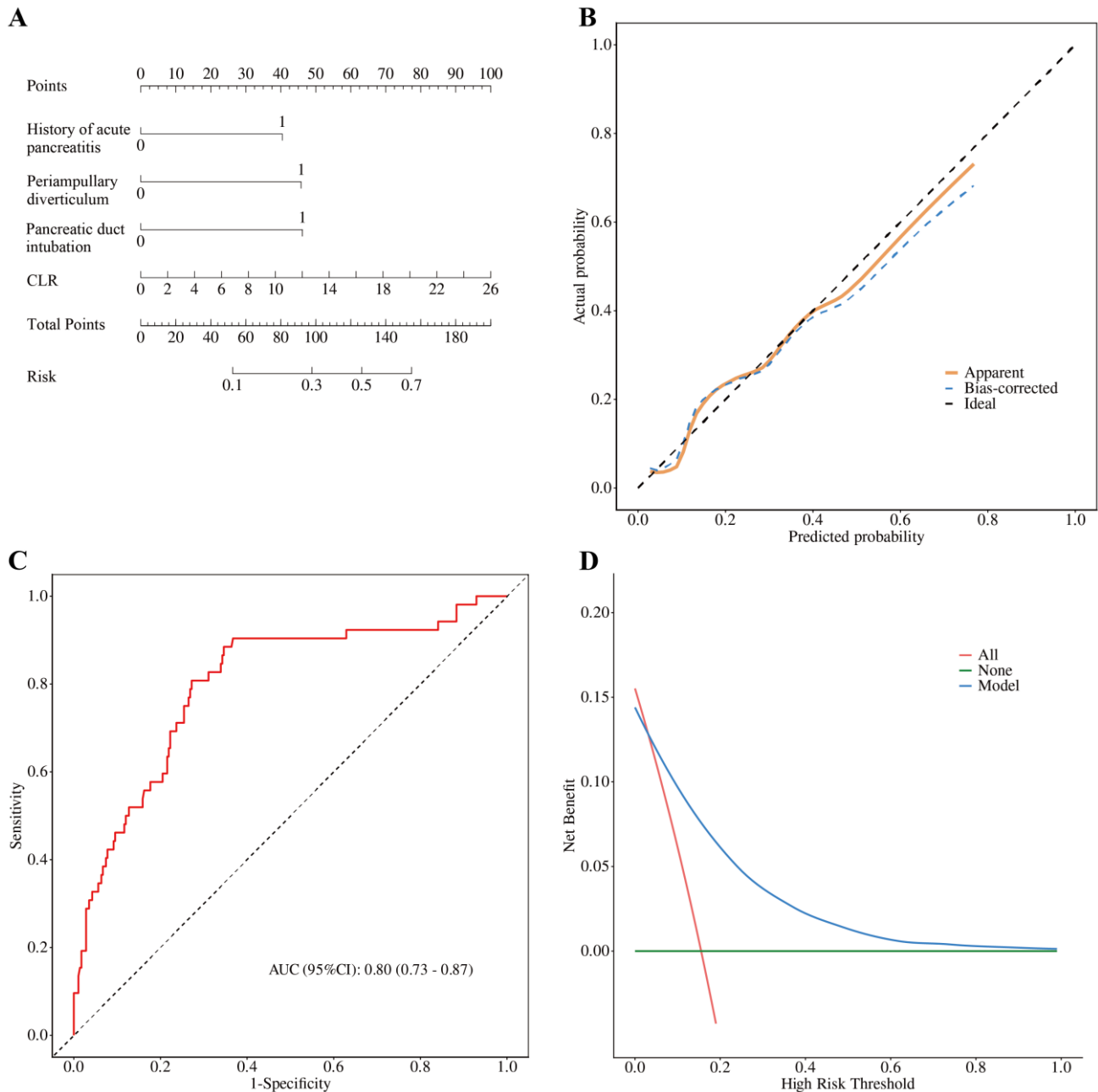


Fig. 1. Nomogram for predicting post-ERCP pancreatitis and its performance evaluation. (A) Nomogram for PEP risk prediction. (B) Calibration curve (Hosmer–Lemeshow test). (C) ROC curve of the nomogram. (D) Decision curve analysis of the nomogram. Abbreviations: CLR, CRP-to-lymphocyte ratio; PEP, post-ERCP pancreatitis; ROC, receiver operating characteristic curve.

The results showed that a history of acute pancreatitis, periampullary diverticulum, pancreatic duct cannulation, and CLR were identified as independent predictors of PEP and were subsequently incorporated into the final nomogram. Internal validation confirmed that the model exhibited good discriminative ability and calibration, suggesting its potential clinical value in risk assessment.

According to the European Society of Gastrointestinal Endoscopy guideline, a history of pancreatitis is an important risk factor for PEP [13]. Patients with a history of pancreatitis may have underlying injury to the pancreatobiliary system, such as a persistent low-grade inflammatory state, rendering them more susceptible to ERCP-related manipulations. Recurrent episodes of pancreatitis can lead to parenchymal damage and decreased exocrine function of the pancreas; therefore, the risk of PEP is significantly higher in these patients than in those without a history of pancreatitis [14]. The present study confirmed that a history of acute pancreatitis is an independent risk factor for PEP. Patients with such a history showed a 3.43-fold higher risk of developing PEP than those without, which is consistent with the conclusions of a systematic review [15]. Previous episodes of pancreatitis may result in residual pancreatic injury and persistent alterations in pancreatic structure or function, rendering the gland more susceptible to subsequent inflammatory insults during ERCP [16]. Therefore, patients with a history of acute pancreatitis should be regarded as a high-risk population and may benefit from more individualized preventive strategies and careful procedural planning.

Regarding procedure- and anatomy-related factors, this study confirmed that pancreatic duct cannulation is an independent risk factor for PEP. The mechanical stimulation of pancreatic duct epithelium during cannulation, along with chemical injury caused by contrast medium injection, can result in mucosal hyperemia, edema, and elevated intraductal pressure. These changes may further promote premature activation of pancreatic enzymes and local inflammatory responses, thereby contributing to the development of PEP. In addition, periampullary diverticulum was also confirmed to be independently associated with PEP, possibly by altering the normal anatomical structure of the duodenal papilla, increasing cannulation difficulty and raising procedural complexity, which indirectly elevates the risk of pancreatic duct injury [17]. These factors may subsequently increase pancreatic duct irritation and procedure-related pancreatic injury, ultimately contributing to the development of PEP. Collectively, these procedure- and anatomy-related factors reflect the technical complexity of ERCP and highlight the importance of careful identification of papillary anatomy, individualized design of cannulation strategies, and minimization of unnecessary pancreatic duct manipulation in high-risk patients.

In terms of inflammatory markers, this study revealed a significant association between CLR and the occurrence

of PEP. ERCP-induced pancreatic duct epithelial injury, elevated intraductal pressure, and abnormal activation of pancreatic enzymes can all trigger local inflammatory responses. Damaged acinar cells release damage-associated molecular patterns, which activate immune cells such as macrophages and neutrophils, thereby promoting the release of pro-inflammatory cytokines, including interleukin (IL)-6, tumor necrosis factor alpha (TNF- α), and IL-1 β [18]. These pro-inflammatory cytokines not only directly amplify the local inflammatory response but also enter the systemic circulation and exert dual effects: stimulating hepatic synthesis of CRP while inducing lymphocyte apoptosis and functional suppression [19]. As an acute-phase reactant, CRP directly reflects the inflammatory burden of the body, whereas a decrease in lymphocyte count indicates impaired immune regulation. Together, these two components constitute the core of CLR. Therefore, an elevated CLR may reflect an imbalance between inflammatory activation and immune status associated with the development of PEP. When elevated CRP levels coexist with reduced lymphocyte levels before ERCP, they may signify a state of inflammatory-immune imbalance, rendering the host more vulnerable to defensive barrier injury. Local damage caused by ERCP may further promote inflammatory responses and thereby contribute to an increased risk of PEP. By integrating information on both inflammatory burden and immune status, CLR may provide complementary information regarding the inflammatory-immune status of patients before ERCP. When incorporated together with other independent predictors, CLR may contribute to individualized preoperative risk stratification for PEP. All variables included in the model are derived from routine clinical data, conferring favorable accessibility and clinical applicability. In practical application, the model helps identify high-risk populations for PEP at an early stage, thereby guiding optimization of cannulation strategies, reduction of unnecessary pancreatic duct manipulations, and strengthening of perioperative management to achieve more targeted preventive interventions.

It is noteworthy that the incidence of PEP in this study was 15.5%, which is higher than the overall incidence rates reported in previous literature [20,21]. For patients who underwent multiple ERCP procedures during the study period, only the first procedure was included in the analysis. First-time procedures may involve greater technical difficulty and a higher risk of pancreatic duct injury during cannulation. Furthermore, the relatively high prevalence of risk factors, such as periampullary diverticulum and pancreatic duct cannulation, suggests that the study population had an inherently elevated baseline risk of PEP. These factors may account for the elevated incidence observed in this study.

This study has several limitations. First, as this is a single-center retrospective study, selection bias may exist. Second, the sample size was relatively limited, and some potential confounding factors, such as operator experience and

total cannulation time, were not included in the analysis. In addition, certain procedure-related variables, including endoscopic sphincterotomy and biliary stent insertion, were not systematically recorded in the retrospective database and therefore could not be further evaluated. Moreover, candidate predictors for the multivariate model were selected primarily on the basis of univariable p values, which may have excluded clinically relevant variables that were not statistically significant in univariable analysis and may have affected model stability. Future studies should consider alternative variable-selection strategies incorporating predefined clinically relevant predictors. Third, only preoperative CLR levels were evaluated, without analyzing the predictive value of its postoperative dynamic changes for PEP. In addition, the model was validated internally using only the bootstrap method without external validation; thus, its generalizability in other populations and settings requires further assessment. Future multicenter, large-scale prospective studies are needed to further validate the clinical value of CLR in PEP risk prediction.

Conclusions

This study identified preoperative CLR as one of the independent predictors of PEP. A multivariate nomogram incorporating CLR with a history of acute pancreatitis, periampullary diverticulum, and pancreatic duct cannulation demonstrated good discriminative ability and calibration, and may help identify patients at high risk of PEP before ERCP. Given its accessibility and clinical applicability, this model may provide a practical reference for facilitating individualized risk assessment and preventive decision-making. Future multicenter prospective studies are warranted to externally validate these findings.

Availability of Data and Materials

The data and materials in the current study are available from the corresponding author on reasonable request.

Author Contributions

Conception and design: XDZ and JYZ. Administrative support: XDZ. Provision of study materials: LW. Collection and assembly of data: JYZ and LW. Data analysis and interpretation: XDZ and JYZ. Manuscript writing: All authors. All authors contributed to the critical revision of the manuscript for important intellectual content. All authors read and approved the final manuscript. All authors have participated sufficiently in the work and agreed to be accountable for all aspects of the work.

Ethics Approval and Consent to Participate

This study was reviewed and approved by the Ethics Committee of Zhejiang Jinhua Guangfu Cancer Hospital (approval number: 2026-003-01). Since this retrospective study involved no patient-identifiable information and en-

sured complete anonymization, the ethics review board waived the requirement for informed consent. The study was conducted in accordance with the principles of the Declaration of Helsinki.

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Conflict of Interest

The authors declare no conflict of interest.

Supplementary Material

Supplementary material associated with this article can be found, in the online version, at <https://doi.org/10.62713/aic.4758>.

References

- [1] Craig E, Jimenez C, Bowles R, Martinez J, Cubas R. ERCP performed and described by surgical endoscopists. *Revista De La Facultad De Ciencias Medicas (Cordoba, Argentina)*. 2025; 82: 446–457. <https://doi.org/10.31053/1853.0605.v82.n2.45367>
- [2] Zakaria N, Tahseen MU, Niaz TS, Asim M, Yaseen A, Kadir S, et al. Endoscopic retrograde cholangiopancreatography in pediatric and adult populations: 17-year experience from Pakistan with trends, complications, and global comparison. *World Journal of Gastrointestinal Endoscopy*. 2025; 17: 109909. <https://doi.org/10.4253/wjge.v17.i11.109909>
- [3] Cahyadi O, Tehami N, de-Madaria E, Siau K. Post-ERCP Pancreatitis: Prevention, Diagnosis and Management. *Medicina (Kau-nas, Lithuania)*. 2022; 58: 1261. <https://doi.org/10.3390/medicina58091261>
- [4] Mutneja HR, Vohra I, Go A, Bhurwal A, Katiyar V, Palomera Tejada E, et al. Temporal trends and mortality of post-ERCP pancreatitis in the United States: a nationwide analysis. *Endoscopy*. 2021; 53: 357–366. <https://doi.org/10.1055/a-1220-2242>
- [5] Obeidat AE, Mahfouz R, Monti G, Kozai L, Darweesh M, Mansour MM, et al. Post-Endoscopic Retrograde Cholangiopancreatography Pancreatitis: What We Already Know. *Cureus*. 2022; 14: e21773. <https://doi.org/10.7759/cureus.21773>
- [6] Beran A, Aboursheid T, Ali AH, Nayfeh T, Albunni H, Vargas A, et al. Predictors of Post-endoscopic Retrograde Cholangiopancreatography Pancreatitis: A Comprehensive Systematic Review and Meta-analysis. *Clinical Gastroenterology and Hepatology : the Official Clinical Practice Journal of the American Gastroenterological Association*. 2025; 23: 1905–1916. <https://doi.org/10.1016/j.cgh.2024.11.014>
- [7] Xu XQ, Zhang JY, Diao HZ, Zhang P, Tian X, Wu HM. Risk Prediction Models for Post-Endoscopic Retrograde Cholangiopancreatography Pancreatitis: A Systematic Review and Meta-Analysis. *Pancreas*. 2026; 55: e431–e439. <https://doi.org/10.1097/MPA.0000000000002564>
- [8] Schlick K, Magnes T, Huemer F, Ratzinger L, Weiss L, Pichler M, et al. C-Reactive Protein and Neutrophil/Lymphocytes Ratio: Prognostic Indicator for Doubling overall survival Prediction in Pancreatic Cancer Patients. *Journal of Clinical Medicine*. 2019; 8: 1791. <https://doi.org/10.3390/jcm8111791>
- [9] Chen X, Lin Z, Chen Y, Lin C. C-reactive protein/lymphocyte ratio as a prognostic biomarker in acute pancreatitis: a cross-sectional

- study assessing disease severity. *International Journal of Surgery* (London, England). 2024; 110: 3223–3229. <https://doi.org/10.1097/JS9.0000000000001273>
- [10] Ma H, Li N, Zhang H, Shen Z, Yang J, Bi Q, et al. The association between inflammatory indices and acute pancreatitis severity: a retrospective cohort study. *Frontiers in Surgery*. 2026; 13: 1764029. <https://doi.org/10.3389/fsurg.2026.1764029>
- [11] Mukai S, Takeyama Y, Itoi T, Ikeura T, Irisawa A, Iwasaki E, et al. Clinical Practice Guidelines for post-ERCP pancreatitis 2023. *Digestive Endoscopy : Official Journal of the Japan Gastroenterological Endoscopy Society*. 2025; 37: 573–587. <https://doi.org/10.1111/den.15004>
- [12] Pausawasdi N, Hongsisuwan P, Kamani L, Maipang K, Charatcharoenwithaya P. Diagnostic Value of Endoscopic Ultrasonography for Common Bile Duct Dilatation without Identifiable Etiology Detected from Cross-Sectional Imaging. *Clinical Endoscopy*. 2022; 55: 122–127. <http://doi.org/10.5946/ce.2021.122>
- [13] Dumonceau JM, Kapral C, Aabakken L, Papanikolaou IS, Tringali A, Vanbiervliet G, et al. ERCP-related adverse events: European Society of Gastrointestinal Endoscopy (ESGE) Guideline. *Endoscopy*. 2020; 52: 127–149. <https://doi.org/10.1055/a-1075-4080>
- [14] Akshintala VS, Singh VK. Postendoscopic Retrograde Cholangiopancreatography Pancreatitis Pathophysiology and Prevention. *Gastrointestinal Endoscopy Clinics of North America*. 2023; 33: 771–787. <https://doi.org/10.1016/j.giec.2023.05.001>
- [15] Sperna Weiland CJ, Akshintala VS, Singh A, Buxbaum J, Choi JH, Elmunzer BJ, et al. Preventive Measures and Risk Factors for Post-ERCP Pancreatitis: A Systematic Review and Individual Patient Data Meta-Analysis. *Digestive Diseases and Sciences*. 2024; 69: 4476–4488. <https://doi.org/10.1007/s10620-024-08693-2>
- [16] Bejjani J, Ramsey ML, Lee PJ, Phillips AE, Singh VK, Yadav D, et al. Alterations in exocrine pancreatic function after acute pancreatitis. *Pancreatology*. 2024; 24: 505–510. <https://doi.org/10.1016/j.pan.2024.03.003>
- [17] Mu P, Yue P, Li F, Lin Y, Liu Y, Meng W, et al. Does periampullary diverticulum affect ERCP cannulation and post-procedure complications? an up-to-date meta-analysis. *The Turkish Journal of Gastroenterology : the Official Journal of Turkish Society of Gastroenterology*. 2020; 31: 193–204. <https://doi.org/10.5152/tjg.2020.19058>
- [18] Chen H, Wang Y, Zippi M, Fiorino S, Hong W. Oxidative stress, DAMPs, and immune cells in acute pancreatitis: molecular mechanisms and therapeutic prospects. *Frontiers in Immunology*. 2025; 16: 1608618. <https://doi.org/10.3389/fimmu.2025.1608618>
- [19] Castell JV, Gómez-Lechón MJ, David M, Andus T, Geiger T, Trullenque R, et al. Interleukin-6 is the major regulator of acute phase protein synthesis in adult human hepatocytes. *FEBS Letters*. 1989; 242: 237–239. [https://doi.org/10.1016/0014-5793\(89\)80476-4](https://doi.org/10.1016/0014-5793(89)80476-4)
- [20] Archibugi L, Ciarfaglia G, Cárdenas-Jaén K, Poropat G, Korpela T, Maisonneuve P, et al. Machine learning for the prediction of post-ERCP pancreatitis risk: A proof-of-concept study. *Digestive and Liver Disease : Official Journal of the Italian Society of Gastroenterology and the Italian Association for the Study of the Liver*. 2023; 55: 387–393. <https://doi.org/10.1016/j.dld.2022.10.005>
- [21] Yan C, Zheng J, Tang H, Fang C, Zhu J, Feng H, et al. Prediction for post-ERCP pancreatitis in non-elderly patients with common bile duct stones: a cross-sectional study at a major Chinese tertiary hospital (2015-2023). *BMC Medical Informatics and Decision Making*. 2024; 24: 143. <https://doi.org/10.1186/s12911-024-02541-z>

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