scientific reports

OPEN

Clinical significance of PCT, CRP, IL-6, NLR, and TyG Index in early diagnosis and severity assessment of acute pancreatitis: A retrospective analysis

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To evaluate the clinical utility of PCT, CRP, IL-6, NLR, and TyG index in improving the early diagnosis and severity assessment of acute pancreatitis (AP). This retrospective study included 137 AP patients and 30 healthy controls from Hunan Provincial People's Hospital (January 2021–September 2023). Univariate and multivariate logistic regression analyses assessed the associations between biomarkers and severe acute pancreatitis (SAP). Receiver operating characteristic (ROC) curves, DeLong test, and Bonferroni correction were used to evaluate predictive performance. Model robustness was validated via 5-fold cross-validation. PCT, CRP, IL-6, NLR, and TyG index levels were significantly elevated in AP patients compared to controls ($P<0.001$) and correlated with disease severity ($P<0.05$). CRP and NLR levels differed significantly among mild, moderate, and severe AP ($P<0.01$). Alcohol consumption and hyperlipidemia were significantly linked to AP severity (P for trend < 0.0001). Multivariate analysis identified hyperlipidemia (OR = 3.030, $P=0.040$), CRP (OR = 1.011, $P<0.001$), and NLR (OR = 1.078, $P=0.020$) as independent SAP predictors. The combined model of CRP + NLR + TyG achieved the highest AUC (0.882, sensitivity = 77.2%, specificity = 88.5%), though it was not significantly better than CRP + NLR or CRP + TyG models ($P>0.05$). 5-fold cross-validation confirmed consistent performance (mean AUC = 0.817 ± 0.118). PCT, CRP, IL-6, NLR, and TyG index are valuable in diagnosing and assessing AP prognosis. Hyperlipidemia, CRP, and NLR are reliable independent predictors of SAP. Combining multiple biomarkers enhances diagnostic precision and provides guidance for personalized treatment strategies in AP.

Keywords Acute Pancreatitis (AP), C-Reactive protein (CRP), Procalcitonin (PCT), Interleukin-6 (IL-6), Neutrophil-to-lymphocyte ratio (NLR), Triglyceride-glucose index (TyG Index)

Acute pancreatitis (AP) is a common and potentially life-threatening condition of the digestive system, characterized by sudden onset and rapid progression. It represents a significant clinical and public health challenge due to its relatively high prevalence and the risk of severe complications in a subset of patients[1]. The pathogenesis of AP involves the abnormal activation of pancreatic enzymes, leading to autodigestion of the pancreas and a systemic inflammatory response that may extend to surrounding tissues and organs[1]. The primary etiological factors include gallstones, hypertriglyceridemia, and excessive alcohol consumption, with gallstones being the leading cause in severe cases[2]. Based on its severity, AP is classified into mild (MAP), moderately severe (MSAP), and severe (SAP)[2]. Approximately 20% of AP cases progress to SAP, which is associated with organ failure and a mortality rate exceeding 20%[3].

Biomarkers play a crucial role in the early diagnosis and severity stratification of AP, guiding timely and appropriate clinical interventions. Among them, C-reactive protein (CRP) and procalcitonin (PCT) are well-established acute-phase proteins commonly used in clinical practice. CRP, a marker of systemic inflammation, rises rapidly in response to cytokine activation, with levels exceeding 150 mg/dL within 48 h of symptom onset

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strongly predictive of severe disease[4–7]. PCT, primarily associated with bacterial infections, is markedly elevated in SAP and has been proposed as a reliable early indicator of disease severity[8]. However, while CRP and PCT are valuable, their diagnostic and prognostic accuracy may be limited in certain clinical scenarios, particularly in non-infectious AP, underscoring the need for complementary biomarkers.

Beyond acute-phase proteins, cytokines such as interleukin-6 (IL-6) are pivotal in the inflammatory cascade of AP. IL-6 functions as both a pro-inflammatory and anti-inflammatory mediator, with elevated serum levels strongly associated with disease severity, particularly in the early stages of SAP[9]. Its dynamic profile, characterized by a peak during acute inflammation followed by a decline during resolution, makes it a promising biomarker for monitoring disease progression[10,11]. In addition to inflammatory markers, metabolic and immune-based indicators have gained attention for their roles in AP assessment. The triglyceride-glucose (TyG) index, a surrogate marker of insulin resistance and metabolic dysregulation, has demonstrated significant predictive value in identifying patients at risk of progression to SAP[12–16]. Similarly, the neutrophil-to-lymphocyte ratio (NLR), a simple yet effective marker of systemic immune activation, has shown utility in stratifying disease severity and predicting adverse outcomes[17]. Together, these markers provide a broader perspective on the inflammatory, metabolic, and immune mechanisms underlying AP.

While these biomarkers provide valuable insights, their individual predictive accuracy and sensitivity remain suboptimal when used in isolation. This highlights the potential benefits of combining multiple biomarkers to enhance diagnostic precision and prognostic reliability. This study aims to evaluate the clinical significance of PCT, CRP, IL-6, the TyG index, and NLR, both as standalone markers and in combination, to address the limitations of single biomarkers. By integrating markers that reflect distinct pathological processes—such as inflammation, immune response, and metabolic dysregulation—this study seeks to provide a more comprehensive approach to AP management. Ultimately, the findings are expected to improve the accuracy of early diagnosis and severity stratification, contributing to better clinical outcomes for patients with acute pancreatitis.

Methods

Study subjects

From January 2021 to September 2023, 137 patients diagnosed with acute pancreatitis (AP) were selected from Hunan Provincial People's Hospital based on inclusion and exclusion criteria. The cohort included 91 males with an average age of 42 years. The inclusion criteria were: (1) onset within 48 h, (2) serum amylase or lipase levels exceeding three times the upper normal limit, (3) Typical abdominal pain symptoms meeting the diagnostic criteria for acute pancreatitis, and (4) Imaging findings indicative of acute pancreatitis. Patients were included if they met at least two of the above criteria, as defined by the 2012 Revised Atlanta Classification.

Exclusion criteria were: Pre-treatment before onset, concurrent systemic infectious diseases (excluding biliary tract infections such as cholangitis), diabetic ketoacidosis, chronic pancreatitis, hematologic diseases or malignancies, lactation or pregnancy, mental disorders or intellectual disabilities, and incomplete clinical data. Based on the 2012 revised Atlanta classification, patients were further categorized into mild acute pancreatitis (MAP) ($n = 52$), moderately severe acute pancreatitis (MSAP) ($n = 28$), and severe acute pancreatitis (SAP) ($n = 57$). Additionally, 30 healthy individuals undergoing physical examinations during the same period were selected as the control group, consisting of 19 males with an average age of 43.5 years. Detailed clinical information for each group (MAP, MSAP, SAP, and healthy subjects), including age, sex distribution, and other demographic data, is provided in Supplementary Table S1.

The study protocol was approved by the Institutional Review Board (IRB) of Changsha Medical University (Number: X2023033). Since the data were extracted from existing de-identified datasets, informed consent was waived by the ethical committee. All experiments were conducted in accordance with the Declaration of Helsinki and Good Clinical Practice (GCP) guidelines.

Data collection

This was a retrospective study based on data from the electronic medical record system. Medical personnel conducted a systematic review of the treatment records of AP patients, examining case reports, nursing records, laboratory test results, and imaging characteristics. Data collected included demographic characteristics (e.g., gender and age), comorbidities (e.g., hypertension, diabetes, cerebrovascular diseases, and chronic liver disease), clinical manifestations, laboratory test results, treatment methods, and outcomes (discharge or death). Blood samples for laboratory data were collected as part of routine clinical care during the initial hospital presentation of the patients. According to available records, blood collection was typically performed prior to the initiation of therapeutic interventions such as fluid resuscitation or medication administration.

However, as this study was retrospective, it is possible that in some cases minimal supportive measures (e.g., initial hydration or pain management) may have been administered before sampling. Despite this, fasting was generally required for at least 8 h before sample collection, and glucose (GLU) values used in this study refer to fasting blood glucose. The laboratory data are considered to reflect the patients' baseline condition at admission. The collected serological indicators included PCT, CRP, neutrophil count (NEU), lymphocyte count (LY), IL-6, triglycerides (TG), and glucose (GLU). The TyG index was calculated using the formula: Ln [TG(mg/dL) * GLU(mg/dL) / 2]. According to the Hunan Provincial People's Hospital's test project manual and reagent instructions, the normal reference values for each indicator were: CRP 0–10 mg/L, PCT 0–0.25 μg/L, IL-6 0–7 pg/mL, TG 0.45–1.69 mmol/L, fasting glucose (GLU) 3.9–6.1 mmol/L, neutrophil count 1.9-8.0 × 10^9/L, and lymphocyte count 0.8–5.2 × 10^9/L.

Detection methods and quality control

Biochemical indicators (including PCT, CRP, TG, and GLU) were detected using a Hitachi automatic biochemical analyzer (Hitachi 7600, Hitachi High-Technologies Corporation, Tokyo, Japan). Blood routine items (including

NEU and LY) were measured using a Sysmex automatic blood analyzer (XN-2000, Sysmex Corporation, Kobe, Japan). IL-6 levels were detected using a flow cytometer (NovoCyte 3000, Agilent Technologies, Santa Clara, CA, USA).

To ensure the accuracy and reliability of the test results, all reagents were strictly performed according to the standard configurations provided by the companies. Samples were collected using sterile blood collection tubes, and venous blood samples from patients were immediately centrifuged to separate serum or plasma. Reagent preparation and instrument calibration and quality control steps were conducted according to the standard operating procedures (SOP) in the reagent kit instructions, with regular use of calibration products for instrument calibration. Quality control was performed before and after each test using control products to ensure the stability of the detection process and the accuracy of the results. Additionally, sample handling time and storage conditions were strictly controlled to avoid interference factors such as lipemia and hemolysis. All operations were performed by professionally trained laboratory technicians, and detailed operation logs were recorded during each test to ensure the traceability and reliability of the data.

Data statistical analysis

Data processing was conducted using SPSS 26.0. For quantitative data, normality tests were first performed; all data in this study were found to be non-normally distributed and were compared between groups using non-parametric rank-sum tests, with results presented as median (M) and interquartile range (P25, P75). For count data, comparisons were made using the chi-square test, expressed as number of cases (n) and percentage (%). To explore the relationship between independent variables and SAP, SAP was assigned a value of 1 and non-SAP a value of 0. Independent variables included PCT, CRP, IL-6, NLR, and TyG index. Logistic regression models were used for univariate and multivariate analyses to assess the association between each independent variable and SAP. Finally, receiver operating characteristic (ROC) curves were employed to evaluate the predictive performance of each indicator for disease severity. To validate the robustness of predictive models, a 5-fold cross-validation was performed. In this method, the dataset was split into five folds, with four folds used for training and one fold for testing in each iteration, ensuring that all data points were tested exactly once. The mean AUC values across the folds were reported to evaluate the consistency of model performance. A P-value < 0.05 was considered statistically significant.

Results

Comparison between healthy control group and AP group

As shown in Table 1, the levels of PCT, CRP, IL-6, NLR, and TyG index in the AP group were significantly higher than those in the healthy control group, with statistically significant differences ($P < 0.001$). These results indicate that patients with acute pancreatitis have significantly elevated levels of these biomarkers compared to healthy individuals, suggesting that these indicators may have important clinical value in reflecting the systemic inflammatory response in acute pancreatitis and potentially assisting in the assessment of its severity.

Comparison among different severity levels of AP

Table 2 shows that the levels of PCT, CRP, IL-6, NLR, and TyG index significantly increase with AP severity (MAP, MSAP, SAP), with highly significant differences observed for PCT ($P < 0.001$), CRP ($P < 0.001$), IL-6 ($P = 0.001$), NLR ($P = 0.010$), and TyG index ($P = 0.040$). Pairwise comparisons in Supplementary Table S2 further confirmed these trends, demonstrating significant differences across severity groups for PCT, CRP, NLR, and TyG index after Bonferroni correction ($P < 0.05$). These findings reinforce the progressive increase in these biomarkers with disease severity, highlighting their potential clinical value.

To provide a clearer understanding of the underlying factors associated with AP severity, we analyzed the etiologies of AP in our cohort. The results (Table 3) showed that gallstone-induced AP accounted for 35.0% of the total cohort and 47.4% of the SAP subgroup, making it the most common cause in both groups. Alcohol-induced AP accounted for 20.4% of the total cohort and 26.3% of the SAP subgroup. Hypertriglyceridemia-induced AP comprised 17.5% of the total cohort and was disproportionately represented in the SAP subgroup, making up 19.3% of cases. This suggests that hypertriglyceridemia-induced AP tends to present more severely, which may partly explain the association between TyG index and SAP.

In addition to etiology, we compared the clinical characteristics of patients across different severity levels. There were no significant differences among the three groups in smoking, alcohol consumption, hypertension, or diabetes (smoking: $P = 1.000$, alcohol consumption: $P = 0.690$, hypertension: $P = 0.547$, diabetes: $P = 0.835$). However, hyperlipidemia differed significantly across groups ($P = 0.003$) (Table 4).The Cochran-Armitage

	Control Group ($n = 30$)	AP Group($n = 137$)	Z	P
PCT	0.08(0.04,0.16)	0.26(0.07,1.31)	4.162	< 0.001
CRP	6.60(3.64,8.76)	96.80(35.91,186.77)	7.312	< 0.001
IL-6	4.59(2.45,6.34)	50.72(20.07,127.78)	7.100	< 0.001
NLR	3.88(2.37,5.58)	8.67(5.62,13.55)	5.666	< 0.001
TyG Index	1.04(0.70,1.22)	2.59(1.66,4.02)	6.815	< 0.001

Table 1. Comparison between Healthy Control Group and AP Group [M(P25, P75)] Notes:1. Data are presented as median (interquartile range). 2. Mann-Whitney non-parametric test was used to compare differences between the two groups. 3. $P < 0.001$ indicates a high level of statistical significance.

	MAP	MSAP	SAP	H	*P*
n	52	28	57	-	-
PCT	0.08 (0.05, 0.43)	0.18 (0.08, 0.55)	0.61 (0.23, 3.35)	24.545	< 0.001
CRP	47.01 (19.14, 78.31)	67.69 (31.81, 165.00)	172.00 (107.52, 260.15)	41.103	< 0.001
IL–6	28.46 (8.42, 120.50)	30.34 (19.28, 60.66)	77.63 (43.18, 167.05)	15.627	0.001
NLR	7.29 (5.46, 10.27)	8.24 (4.64, 13.28)	9.77 (7.21, 16.64)	9.242	0.010
TyG Index	2.38 (1.37, 3.82)	2.82 (1.58, 3.87)	3.02 (2.08, 4.59)	6.425	0.040

Table 2. Comparison of Serological indicators in patients with different degrees of Acute pancreatitis [M(P25, P75)] Notes: (1) Data are presented as median (interquartile range). (2) Kruskal-Wallis H test was used to compare differences among the three groups. (3) $P < 0.05$ indicates statistical significance.

Etiology	Total ($n = 137$)	SAP ($n = 57$)	Total (%)	SAP (%)
Gallstone	48	27	35.0	47.4
Alcohol	28	15	20.4	26.3
Hyertriglyceridemia	24	11	17.5	19.3
Idiopathic	23	4	16.8	7.0
others	14	0	10.2	0.0

Table 3. Etiology of Acute Pancreatitis in the Cohort and SAP Subgroup. Notes: (1) Hypertriglyceridemia-induced AP was disproportionately represented in the SAP subgroup, making up 19.3% of SAP cases, compared to 17.5% in the total cohort. (2) Gallstone-induced AP was the most common cause in both the total cohort and the SAP subgroup.

	MAP(%)	MSAP(%)	SAP(%)	Odds Ratio	*P*
n	52	28	57	-	-
Smoking	12(23.08)	2(7.14)	17(29.82)	1.042	1.000
Drinking	15(28.85)	1(3.57)	20(35.09)	1.236	0.690
Hypertension	15(28.85)	6(21.43)	14(24.56)	1.318	0.547
Diabetes	11(21.15)	5(17.86)	15(26.32)	0.872	0.835
Hyperlipidemia	18(34.62)	12(42.86)	40(70.18)	0.336	**0.003**

Table 4. Comparison of General data in patients with different degrees of AP [n(%)] Notes: (1) Data are presented as the number of patients (percentage). (2) Fisher's Exact Test was used to compare differences among the three groups. 3.Smoking: Defined as active smoking at the time of hospital admission or a history of regular smoking within the past year. Drinking: Defined as regular alcohol consumption of more than 20 g/day for females or 30 g/day for males over the past year. Hypertension: Defined as a documented history of hypertension or meeting the diagnostic criteria of systolic blood pressure ≥ 140 mmHg and/or diastolic blood pressure ≥ 90 mmHg. Hyperlipidemia: Defined as fasting triglycerides ≥ 1.7 mmol/L, total cholesterol ≥ 5.2 mmol/L, or a documented diagnosis of hyperlipidemia in the patient's medical history. 4. $P < 0.05$ indicates statistical significance.

trend test showed a significant upward trend in hyperlipidemia prevalence with increasing severity of AP (P for trend < 0.0001). The prevalence increased progressively from 34.62% in MAP to 42.86% in MSAP and 70.18% in SAP (Table 5).

To further explore the relationship between TyG index and SAP severity, a subgroup analysis was performed by excluding cases of hypertriglyceridemia-induced AP (TG > 11.3 mmol/L). As shown in Table 6, the TyG index remained higher in the severe group (mean TyG = 2.468 ± 0.15) compared to the mild (mean TyG = 1.986 ± 0.12) and moderate groups (mean TyG = 1.965 ± 0.10). However, the differences across groups did not reach statistical significance ($P = 0.069$). This observation suggests that the association between TyG index and SAP severity is not solely driven by hypertriglyceridemia-induced AP but may reflect broader metabolic disturbances, including systemic insulin resistance and dysregulated glucose-lipid metabolism, which are exacerbated with increasing AP severity.

Severity Level	*n*	Hyperlipidemia (%)	Z	*P* for trend
MAP	52	18(34.62)		
MSAP	28	12(42.86)		
SAP	57	40(70.18)	3.64	< 0.0001

Table 5. Cochran-Armitage Trend Test results for Hyperlipidemia. Notes: (1) Data are presented as the number of patients (percentage). (2) Trend analysis was performed using Cochran-Armitage test, indicating a significant increase in the hyperlipidemia rate with increasing severity of AP (P for trend < 0.0001).

AP Severity Level	Including Hypertriglyceridemia	Excluding Hypertriglyceridemia	*P*
Mild	2.538 ± 0.15	1.986 ± 0.12	
Moderate	2.650 ± 0.12	1.965 ± 0.10	
Severe	3.320 ± 0.18	2.468 ± 0.15	0.069

Table 6. Comparison of TyG Index Across AP Severity Levels, including and excluding Hypertriglyceridemia (Mean ± SE). Notes: (1) Data presentation: Values are expressed as mean ± standard error (SE). (2) Statistical analysis: Differences in TyG Index between groups were analyzed using the Mann-Whitney U test with Bonferroni correction for multiple comparisons. (3) Interpretation: The P-value refers to the statistical significance of the difference between the "Including Hypertriglyceridemia" and "Excluding Hypertriglyceridemia" groups for the severe AP subgroup.

	Univariate Analysis		Multivariate Analysis	
	OR(95%CI)	*P*	OR(95%CI)	*P*
Smoking	2.004(0.892–4.500)	0.092		
Drinking	2.162(0.999–4.679)	0.050		
Hypertension	0.915(0.418–2.000)	0.823		
Diabetes	1.429(0.639–3.195)	0.385		
Hyperlipidemia	3.922(1.898–8.104)	< 0.001	3.030(1.053–8.720)	0.040
PCT	1.300(1.083–1.561)	0.005	1.035(0.926–1.157)	0.545
CRP	1.013(1.008–1.018)	< 0.001	1.011(1.005–1.016)	< 0.001
IL−6	1.002(1.000–1.004)	0.036	1.002(1.000–1.004)	0.112
NLR	1.084(1.026–1.145)	0.004	1.078(1.012–1.148)	0.020
TyG Index	1.369(1.088–1.722)	0.007	0.996(0.712–1.394)	0.982

Table 7. Logistic regression analysis results for each Indicator.

Logistic regression analysis of risk factors for SAP

In the univariate analysis (Table 7), hyperlipidemia (OR = 3.922, 95% CI: 1.898–8.104, $P < 0.001$), PCT (OR = 1.300, 95% CI: 1.083–1.561, $P = 0.005$), CRP (OR = 1.013, 95% CI: 1.008–1.018, $P < 0.001$), IL-6 (OR = 1.002, 95% CI: 1.000-1.004, $P = 0.036$), and NLR (OR = 1.084, 95% CI: 1.026–1.145, $P = 0.004$), and TyG Index (OR = 1.369, 95% CI: 1.088–1.722, $P = 0.007$) were significantly associated with outcomes.

In the multivariate analysis, hyperlipidemia (OR = 3.030, 95% CI: 1.053–8.720, $P = 0.040$), C-reactive protein (CRP, OR = 1.011, 95% CI: 1.005–1.016, $P < 0.001$), and NLR (OR = 1.078, 95% CI: 1.012–1.148, $P = 0.020$) continued to show significant independent associations. However, PCT and IL-6 no longer showed significance in the multivariate model ($P = 0.545$ and $P = 0.112$, respectively). These results suggest that hyperlipidemia, CRP, and NLR may be more reliable independent predictors when assessing the risk of SAP.

To evaluate the predictive value of the biomarkers, a Random Forest classification model was developed using quartile-transformed variables. The model achieved an AUC of 0.748, indicating moderate discriminative ability in predicting SAP (Supplementary Figure S1). Feature importance analysis (Supplementary Table S3) identified CRP (relative importance: 0.308), IL-6 (0.268), and PCT (0.195) as the most significant contributors, consistent with their roles in systemic inflammation. The metabolic markers TyG index (0.118) and NLR (0.111) showed lower importance in the model. These findings highlight the dominant contribution of inflammatory biomarkers in predicting SAP compared to metabolic markers.

Clinical value of PCT, CRP, IL-6, NLR, and TyG Index in AP

We analyzed the receiver operating characteristic (ROC) curves for CRP, NLR, and TyG in predicting SAP. As shown in Table 8, CRP was the most effective single biomarker, with an AUC of 0.854 (95% CI: 0.783–0.925), sensitivity of 87.7%, and specificity of 75%, outperforming NLR (AUC = 0.660, 95% CI: 0.558–0.762) and TyG (AUC = 0.637, 95% CI: 0.533–0.741). Among dual combinations, CRP + NLR achieved the highest AUC (0.873,

	Best Threshold	Sensitivity (%)	Specificity (%)	AUC	*P*	95%CI
CRP	72.18	87.7	75	**0.854**	< 0.001	0.783–0.925
NLR	10.53	49.1	78.8	0.660	0.004	0.558–0.762
TyG	1.003	100	21.2	0.637	0.014	0.533–0.741
CRP + NLR	0.335	89.5	73.1	**0.873**	< 0.001	0.807–0.938
CRP + TyG	0.313	93	69.2	**0.871**	< 0.001	0.805–0.938
NLR + TyG	0.599	43.9	84.6	0.685	0.001	0.587–0.784
CRP + NLR + TyG	0.539	77.2	88.5	**0.882**	< 0.001	0.819–0.945

Table 8. ROC Analysis results for Predicting SAP with Indicator.

Fold	AUC	Sensitivity	Specificity
1	0.82	0.89	0.74
2	0.83	0.88	0.75
3	0.80	0.85	0.78
4	0.81	0.87	0.76
5	0.80	0.83	0.80

Table 9. Cross-validation results.

95% CI: 0.807–0.938), followed closely by CRP + TyG (AUC = 0.871, 95% CI: 0.805–0.938), both showing modest improvements over CRP alone. The three-marker combination, CRP + NLR + TyG, provided the highest AUC (0.882, 95% CI: 0.823–0.949), with a specificity of 88.5% and sensitivity of 77.2%.

To evaluate the statistical significance of these differences, pairwise comparisons of AUC values (0.854, 0.873, 0.871, and 0.882) were conducted using the DeLong test with Bonferroni correction. Although the combined models slightly improved AUC values, the differences were not statistically significant (all Bonferroni-corrected $P > 0.05$). These findings suggest that while combining biomarkers enhances predictive performance, the improvements are incremental and lack statistical significance.

Internal validation through cross-validation

To evaluate the internal validity and robustness of the prediction models, a 5-fold cross-validation was performed using the current dataset. The analysis yielded an average AUC of 0.812 (range: 0.80–0.83), with sensitivity ranging from 0.83 to 0.89 and specificity from 0.74 to 0.80 across folds (Table 9). The ROC curves for each fold, presented in Fig. 1, illustrate consistent model performance with minimal variation across data splits. These results confirm the stability and reliability of the prediction models within the study population, supporting their potential for broader application in similar cohorts.

Discussion

AP is a multifactorial acute digestive system disease characterized by rapid progression. Early diagnosis and accurate assessment of the severity of the condition are crucial for improving patient prognosis[1–3,18]. Current clinical diagnosis primarily relies on clinical symptoms, laboratory tests, and imaging studies, but these methods have limitations in terms of sensitivity and specificity for early diagnosis and severity assessment[19]. Therefore, identifying reliable biomarkers to enhance the accuracy of early diagnosis and severity assessment of AP has become a research focus.

This study explored the clinical significance of various biomarkers (PCT, CRP, IL-6, NLR, and TyG index) in acute pancreatitis. The results showed that the levels of PCT, CRP, IL-6, NLR, and TyG index in patients with AP were significantly higher than those in the healthy control group ($P < 0.001$). As shown in Table 2, these indicators further increased with the severity of the condition (CRP: $P < 0.001$, NLR: $P = 0.010$, TyG index: $P = 0.040$), demonstrating that systemic inflammation and metabolic dysregulation worsen as AP progresses. Furthermore, hyperlipidemia, as shown in Table 5 ($P = 0.003$) and its trend analysis (P for trend < 0.0001), also showed significant associations with AP severity. These findings suggest that both inflammatory and metabolic processes play crucial roles in the progression of AP.

CRP is an acute-phase protein that can rapidly reflect systemic inflammatory responses, with its levels rising quickly during inflammation[20]. Previous studies have indicated that elevated CRP levels in AP are closely related to the severity of the condition[21], consistent with our findings. CRP`s high AUC in this study further emphasizes its potential as a reliable single biomarker for predicting SAP, demonstrating a balance between sensitivity and specificity.

This study focuses on simple blood test indicators, such as CRP, NLR, and TyG index, for early severity assessment of acute pancreatitis. While established scoring systems like BISAP and HAPS provide comprehensive evaluations, certain parameters required for these scores, such as BUN levels and SIRS criteria, were unavailable in our dataset. Compared to these scoring systems, our approach offers the advantage of simplicity and

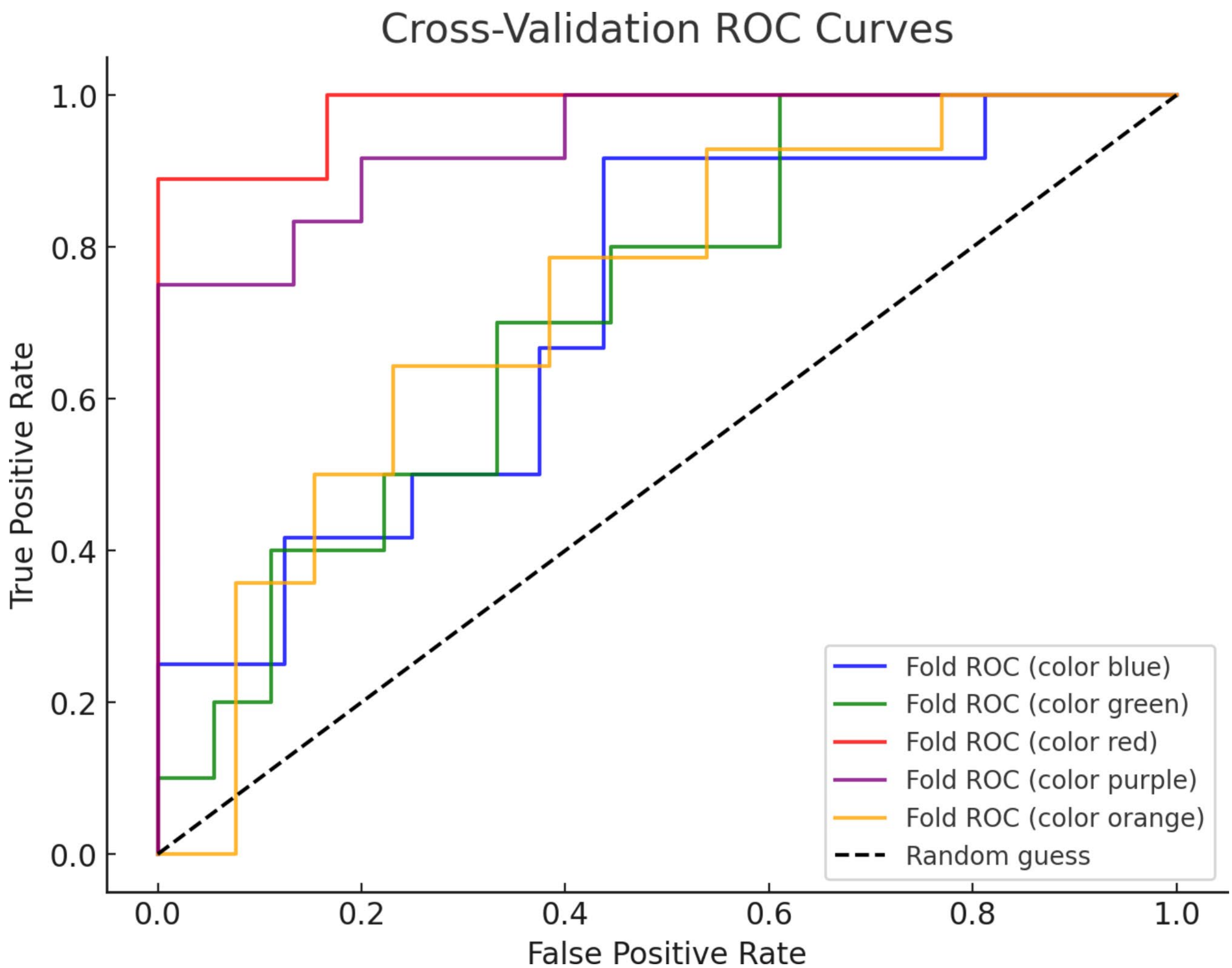

Fig. 1. Cross-validation ROC curves for the prediction model. Each colored line represents the ROC curve for a single fold in the 5-fold cross-validation (Blue: Fold 1, Green: Fold 2, Red: Fold 3, Purple: Fold 4, Orange: Fold 5). The black dashed line represents the random guess baseline (AUC = 0.5).

accessibility, particularly in resource-limited settings. However, future studies should incorporate BISAP and HAPS scores for direct comparison and further validation of our findings.

PCT, a specific marker for bacterial infection, also showed significant elevation in AP, reflecting pancreatic tissue damage and systemic inflammatory responses[22]. Other studies have supported the application of PCT in the early diagnosis of AP, but its significance in multivariate models is lower, suggesting it may be influenced by other factors[23]. IL-6, a multifunctional cytokine, plays a key role in acute inflammatory responses, with its levels closely related to disease severity[12]. Similarly, IL-6 did not retain statistical significance in the multivariate model, indicating it may act as a secondary marker rather than a primary independent predictor, which may limit its standalone clinical value.

NLR is a simple and effective inflammatory marker widely used to assess the prognosis of various diseases[24]. Studies have shown that NLR is significantly elevated in AP patients and is related to the severity of the condition[25,26], which is also supported by our study. The TyG index reflects insulin resistance and the state of metabolic syndrome[27], and studies have shown its significant elevation in AP patients, suggesting its important role in assessing the metabolic state and severity of AP. However, its relatively lower AUC and dependence on specific metabolic conditions, such as hypertriglyceridemia, highlight the need for caution when using TyG as a standalone predictive marker for SAP. The subgroup analysis excluding hypertriglyceridemia-induced AP cases (Fig. 1) showed that the TyG index remained higher in SAP patients but without statistical significance ($P = 0.069$), suggesting that its predictive role may extend beyond hypertriglyceridemia-related AP.

Further analysis in our study, including univariate and multivariate logistic regression analyses, showed that hyperlipidemia (OR = 3.030, $P = 0.040$), CRP (OR = 1.011, $P < 0.001$), and NLR (OR = 1.078, $P = 0.020$) are independent predictors of SAP. This finding reinforces the importance of combining metabolic and inflammatory markers for comprehensive severity assessment, particularly highlighting hyperlipidemia as a unique contributor to SAP risk.

The results of the Random Forest analysis highlight the importance of CRP, IL-6, and PCT as potential predictors of SAP, consistent with their roles in systemic inflammation and metabolic regulation. The relatively high importance of CRP further emphasizes its utility as a reliable biomarker for reflecting inflammatory responses in AP patients. IL-6 and PCT, both closely associated with the inflammatory cascade and tissue injury, also emerged as significant contributors. While the ROC-AUC of the Random Forest model (0.748) indicates moderate predictive performance, it underscores the potential value of combining multiple biomarkers to achieve more accurate severity assessment. These findings suggest that incorporating serological and clinical data into composite models may enhance the prediction of SAP in clinical practice.

The combined prediction model analysis showed that the combination of CRP and NLR performed best among the dual-indicator models, with an AUC of 0.873, sensitivity of 89.5%, and specificity of 73.1%. Additionally, the combination of CRP and TyG (AUC = 0.871) also demonstrated high predictive capabilities. Although the three-indicator combination (CRP, NLR, TyG) showed an improved AUC (0.882), the lack of statistical significance underscores the challenges in balancing model complexity and clinical utility.

Previous studies have also indicated that the diagnostic performance of a single biomarker is limited, and combining multiple markers can improve diagnostic accuracy, but practical application should consider operational complexity and cost[28]. Given the comparable performance of CRP alone, clinicians may prioritize single-biomarker models when cost and simplicity are critical considerations.

Despite providing important insights into the clinical value of various biomarkers in the diagnosis and assessment of AP, this study has some limitations. Firstly, the sample size is relatively small, which may affect the generalizability of the results. Secondly, the variability of the biomarkers and individual differences may affect the precision of their clinical application. Future studies should expand the sample size and further validate these biomarkers in different populations. Additionally, other potential biomarkers should be explored to improve the accuracy of AP diagnosis and assessment. Integration of multi-dimensional data such as genomics and metabolomics could offer promising avenues for personalized diagnosis and treatment strategies[29–31].

In terms of clinical application, although the combined prediction of CRP, NLR, and TyG performed well, its practical application still needs to consider cost and operational complexity. Developing rapid and cost-effective methods for detecting these biomarkers could enhance their clinical adoption and facilitate their integration into routine practice. Additionally, further studies should investigate the performance of these biomarkers in different AP subtypes and their potential role in treatment monitoring.

In summary, this study shows that CRP, NLR, and TyG have important clinical significance in the diagnosis and assessment of AP, especially the combined prediction model of CRP, NLR, and TyG, which performed best (AUC = 0.882). These results are consistent with previous studies, further validating the clinical application value of these biomarkers. Future research should focus on optimizing their clinical applicability and exploring novel biomarkers to refine the diagnostic and prognostic framework for AP.

Data availability
The data that support the findings of this study are available from the corresponding author, [Lin Zhou], upon reasonable request.

Received: 8 October 2024; Accepted: 13 January 2025
Published online: 23 January 2025

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Acknowledgements
Not applicable.

Author contributions
Xu Xinyu and Zhou Jiang were responsible for the conceptualization and methodology of the study, as well as data curation, formal analysis, and the initial drafting of the manuscript. They also collected data and conducted investigations. Ai Qing and Li Lihua developed the methodology and software, and validated the results. Liu Xiehong and Zhou Lin provided resources, managed the project, and reviewed and edited the manuscript. All authors have read and approved the final manuscript.

Funding
Not applicable.

Declarations

Competing interests
The authors declare no competing interests.

Informed consent
Not applicable.

Ethical approval
Not applicable.

Additional information
Supplementary Information The online version contains supplementary material available at https://doi.org/10.1038/s41598-025-86664-x.

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