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Original Article

Diagnostic value of inflammatory indices and triglycerides in hyperlipidemic acute pancreatitis

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Abstract: Objective: High triglyceride (TG) levels complicate the diagnosis of acute pancreatitis (AP) due to delayed lipid testing. This study evaluates the diagnostic value of inflammatory indices, particularly the platelet-to-lymphocyte ratio (PLR) and systemic inflammation response index (SIRI), for identifying hyperlipidemic acute pancreatitis (HLAP). Methods: A retrospective cohort study analyzed 140 AP patients (59 HLAP, 81 non-HLAP) admitted between January 2023 and December 2024. The HLAP group was further stratified into gray-zone (HLAP-G) and typical (HLAP-S) subgroups. Healthy controls (HC, n=80) and individuals with simple hypertriglyceridemia (HTG, n=80) were included for comparison. Inflammatory indices (PLR, SIRI, NLR, MLR, SII) were calculated from admission blood counts. Diagnostic performance was assessed using ROC analysis, and a combined model (PLR+SIRI+TG) was developed and validated in an external cohort. Dynamic changes of PLR and SIRI were evaluated at 1, 6, and 12 hours post-admission. Results: PLR, SIRI, and other indices were significantly higher in the HLAP group than in the non-HLAP, HTG, and HC groups (all $P < 0.01$), showing a stepwise increase from HC to HLAP-S. SIRI demonstrated the highest diagnostic efficacy for HLAP (AUC=0.973, sensitivity =91.5%, specificity =96.3%), followed by PLR (AUC=0.960). The combined model achieved the highest AUC (0.988), with external validation confirming generalizability (AUC=0.845). Dynamic profiles revealed peak PLR and SIRI at 6 hours post-admission. Multivariate analysis identified PLR and SIRI as independent risk factors for HLAP. Conclusions: PLR and SIRI are valuable, easily accessible tools for early HLAP diagnosis. Their high diagnostic accuracy, particularly when combined with TG, provides a robust method for prompt identification and targeted therapy.

Keywords: Hyperlipidemic acute pancreatitis, platelet-to-lymphocyte ratio, systemic inflammation response index, diagnostic value, inflammatory index

Introduction

Acute Pancreatitis (AP) is a common, critical condition in clinical practice, often requiring intensive treatment in the Intensive Care Unit (ICU) due to its rapid progression, high complication risk, and serious threat to patient health [1, 2]. Key etiological factors include biliary diseases, elevated blood lipids, and excessive alcohol consumption [3]. With the westernization of lifestyles and dietary habits in China, the incidence of Hyperlipidemic Acute Pancreatitis (HLAP) has steadily increased [4]. Recent reports indicate HLAP has now replaced alcoholic pancreatitis as the second leading cause of AP, with its share of AP cases significantly rising. This suggests an urgent need for clinical prevention and control [5, 6].

HLAP diagnosis requires clear biochemical and clinical criteria: fasting serum triglyceride (TG) levels > 11.3 mmol/L, or TG levels between 5.65 and 11.3 mmol/L with detectable chylomicrons in serum [7, 8]. HLAP is primarily observed in young patients, often presenting with more severe clinical manifestations [9]. These include progression to severe pancreatitis, higher pancreatic cyst incidence, longer hospital stays, and an increased recurrence risk compared to non-HLAP. Early-stage HLAP often presents subtly, lacking specific symptoms, and can deteriorate rapidly, leading to higher mortality [5].

Currently, HLAP treatment focuses on quickly lowering serum TG levels and controlling systemic inflammation. Early differentiation from

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non-H LAP is essential for initiating targeted treatment and assessing disease severity and prognosis [1].

However, clinical diagnosis is challenging due to factors such as the effect of fasting on TG levels, and delays in diagnosis. Studies have shown that lipid testing, and variations in serum amylase levels, which may be below the diagnostic threshold for AP, can complicate early identification [12, 13]. Furthermore, high serum TG levels correlate with increased mortality and complications in AP, making the identification of accessible differential markers for HLAP a critical clinical issue [2].

In recent years, inflammatory indices derived from routine blood values have gained attention in AP research [3]. Indicators such as neutrophils, lymphocytes, and monocytes can be used to calculate indices like Systemic Immune-Inflammation Index (SII), Systemic Inflammation Response Index (SIRI), Neutrophil/Lymphocyte Ratio (NLR), Platelet/Lymphocyte Ratio (PLR), and Monocyte/Lymphocyte Ratio (MLR) [4]. SIRI, introduced in 2016, has been used to predict survival outcomes in pancreatic cancer patients, while NLR and PLR are validated markers for AP severity [5]. However, research on the use of these indices for differentiating HLAP from non-HLAP is limited [6].

This study aims to analyze clinical data from AP patients, focusing on serum TG levels and routine blood values. It will calculate SII, SIRI, NLR, PLR, and MLR, assessing their diagnostic efficacy for distinguishing HLAP from non-HLAP through Receiver Operating Characteristic (ROC) curve analysis. The aim is to provide a cost-effective, accessible, and rapid tool for HLAP differentiation, aiding in early diagnosis and precise treatment of AP.

Materials and methods

Study design and general information

This was a retrospective cohort study conducted at Lishui Municipal People's Hospital, including AP patients admitted between January 2023 and December 2024. A total of 140 eligible AP patients were identified through the hospital's electronic medical record system, with clinical data (demographic characteristics, laboratory results, and diagnostic records) extracted by trained physicians following a standardized protocol to ensure completeness, accuracy, and traceability. An external multicenter validation cohort was also included to verify the generalizability of findings.

The study was approved by the Ethics Committee of Lishui Municipal People's Hospital. Informed consent was waived due to the retrospective nature of the study and the use of de-identified data. All procedures adhered to the 2013 revised Declaration of Helsinki.

Study participants and grouping

Study groups: Four groups were included in the study, with detailed definitions and grouping criteria as follows:

AP patient cohort (n=140): Patients were grouped based on AP etiology as documented in electronic medical records: (1) Hyperlipidemic AP (HLAP) group (n=59): Met the diagnostic criteria for HLAP and had hypertriglyceridemia as the confirmed etiology. Further subdivided into: Gray-zone subgroup (HLAP-G): TG 5.65-11.3 mmol/L with serum chylomicronemia. Typical subgroup (HLAP-S): Fasting serum TG ≥ 11.3 mmol/L. (2) Non-hyperlipidemic AP (non-HLAP) group (n=81): AP attributed to other etiologies (biliary, alcoholic, idiopathic), excluding hypertriglyceridemia.

Healthy Control (HC) group: Recruited from the hospital's Health Examination Center during the same period (n=80). Eligibility required no history of pancreatic disease, severe systemic illness, acute/chronic inflammation, malignancy, or abnormal liver/renal function, with normal laboratory indices (complete blood count, lipid profiles).

Hypertriglyceridemia (HTG) group: Selected from the health examination cohort, defined as individuals with simple hypertriglyceridemia (serum TG ≥ 2.26 mmol/L) but no evidence of AP. They met the same exclusion criteria as the HC group, except for elevated TG levels.

External validation cohort (n=120): This included 60 HLAP and 60 non-HLAP patients from three tertiary hospitals across diverse economic regions in China, with a 1:1 ratio of HLAP to non-HLAP. HLAP patients were subdivided into HLAP-G (n=28, 46.7%) and HLAP-S (n=32, 53.3%). Inclusion, exclusion, and diagnostic standards were identical to the original AP cohort.

Inclusion and exclusion criteria

Inclusion criteria: For AP patients: (1) Met the 2012 revised Atlanta criteria for AP diagnosis, requiring at least two of the following: Clinical symptoms consistent with AP (e.g., sudden-onset severe upper abdominal pain radiating to the back); Serum amylase and/or lipase activity > 3 times the upper limit of normal; Characteristic imaging findings of AP on contrast-enhanced CT, MRI, or ultrasound. (2) Complete blood counts and serum biochemical parameters collected within 1 hour of admission, with available clinical and laboratory data. (3) For HC and HTG groups: Eligibility based on health status and laboratory indices as specified before.

Diagnostic criteria for HLAP: On the basis of AP diagnosis, HLAP was confirmed after excluding other etiologies (biliary, alcoholic, drug-induced, traumatic) and meeting one of the following lipid criteria: Fasting serum TG ≥ 11.3 mmol/L; or TG 5.65-11.3 mmol/L with serum chylomicronemia.

Exclusion criteria (applicable to all groups): Patients/individuals were excluded if they had: (1) A history of malignancy (solid or hematological); (2) Thalassemia or other types of anemia; (3) Inflammatory bowel diseases (e.g., Crohn's disease, ulcerative colitis); (4) Concurrent acute inflammatory diseases (e.g., pneumonia, urinary tract infections); (5) Pregnancy (confirmed by medical records or laboratory tests); (6) Admission delay (> 24 hours from symptom onset); (7) Incomplete data due to failure to complete CBC and serum biochemical tests within 1 hour of admission.

Data collection

A standardized data extraction form was used to retrospectively collect relevant patient information from the hospital's electronic medical record system. The collected data included: (1) Demographic characteristics: age (years), gender (male/female), and body mass index (BMI, kg/m^2, calculated as body weight in kg divided by height in m^2); (2) History of underlying diseases: diabetes mellitus was defined as a diagnosis in previous medical records or a fasting blood glucose level ≥ 7.0 mmol/L at admission; hypertension was defined as a documented diagnosis or a systolic blood pressure ≥ 140 mmHg and/or diastolic blood pressure ≥ 90 mmHg at admission; (3) Lifestyle habits: smoking history was defined as smoking ≥100 cigarettes for ≥ 6 months, self-reported by the patient. All information was extracted and verified by researchers to ensure data accuracy and consistency.

Collection of laboratory indicators and calculation of inflammatory indices

To ensure consistency in the primary diagnostic comparison, only laboratory test results obtained within 1 hour of patient admission were used to calculate primary inflammatory indices (NLR, PLR, MLR, SIRI, SII) and serum TG levels. These data were retrieved from the hospital's Laboratory Information System (LIS).

For secondary and exploratory analyses, additional data were collected: Dynamic Monitoring: Complete blood counts were extracted from the LIS at 6 and 12 hours after admission for a subset of patients to analyze early dynamic changes in PLR and SIRI.

Disease severity scores: Clinical data for calculatingacute physiology and chronic health evaluation II (APACHE II), Ranson, bedside index for severity in acute pancreatitis (BISAP), and computed tomography severity index (CTSI) scores were collected retrospectively for the entire hospitalization period, since these scores require data from the first 24-48 hours or imaging findings.

The collected indicators comprised routine blood tests and serum biochemical items. Routine blood indicators included white blood cell count (WBC, $\times 10^9$/L), neutrophil count (N, $\times 10^9$/L), lymphocyte count (L, $\times 10^9$/L), monocyte count (M, $\times 10^9$/L), platelet count (P, $\times 10^9$/L), and hemoglobin (Hb, g/L). Serum biochemical indicators included serum triglycerides (TG, mmol/L). Using the aforementioned routine blood data, the following inflammation-related indices were calculated: neutrophil-to-lymphocyte ratio (NLR) = N/L; platelet-to-lymphocyte ratio (PLR) = P/L; monocyte-to-lymphocyte ratio (MLR) = M/L; systemic inflammatory response index (SIRI) = (N×M)/L; and systemic immune-inflammation index (SII) = (N×P)/L. All inflammatory indices were uniformly calculated by researchers and used for subsequent corre-

Table 1. Baseline demographic and laboratory features in patients with HLAP and non-HLAP

Variable	HLAP (n=59)	non-HLAP (n=81)	t/χ^2	*P*-value
Age	51.10 ± 11.25	52.22 ± 10.18	0.404	0.687
BMI	27.31 ± 4.56	27.29 ± 4.30	3.681	0.982
Gender				
Male	34 (57.6)	45 (55.6)	0.098	0.754
Female	25 (42.4)	36 (44.4)		
Diabetes				
Yes	34 (57.6)	45 (55.6)	0.098	0.754
No	25 (42.4)	36 (44.4)		
Hypertension				
Yes	38 (64.4)	51 (63.0)	0.032	0.858
No	21 (35.6)	30 (37.0)		
Smoking				
Yes	40 (67.8)	54 (66.7)	0.025	0.874
No	19 (32.2)	27 (33.3)		
WBC ($\times10^9$/L)	7.02 ± 1.53	6.88 ± 1.61	0.541	0.590
Neutrophil ($\times10^9$/L)	4.25 ± 1.12	4.16 ± 1.18	0.467	0.641
Lymphocyte ($\times10^9$/L)	2.08 ± 0.61	2.01 ± 0.59	0.722	0.472
Monocyte ($\times10^9$/L)	0.58 ± 0.19	0.55 ± 0.17	0.935	0.351
Platelet ($\times10^9$/L)	198.40 ± 46.20	203.60 ± 44.80	-0.682	0.496
Hemoglobin (g/L)	139.20 ± 12.60	137.90 ± 12.10	0.618	0.537

BMI, Body Mass Index; WBC, White Blood Cell Count.

lation analysis, diagnostic efficacy evaluation, and risk factor analysis.

Statistical analysis

SPSS 26.0 software was used for statistical analysis of the retrospectively collected data. Appropriate statistical methods were selected based on data type and distribution. For continuous variables, normality was first evaluated using the Shapiro-Wilk test. Variables conforming to a normal distribution (e.g., age, BMI) were expressed as mean ± standard deviation and compared between groups using the independent samples t-test. Non-normally distributed variables (e.g., serum triglycerides, NLR, PLR, MLR, SIRI, SII, WBC, lymphocyte count) were expressed as median and interquartile range [M (P25, P75)], with group comparisons conducted using the Mann-Whitney U test. Categorical variables (e.g., gender, history of diabetes, smoking history) were presented as counts and percentages [n (%)], with inter-group comparisons done using the Chi-square test.

Pearson correlation analysis was applied to explore the relationship between serum TG levels and the five inflammatory indices in HLAP patients. Receiver operating characteristic (ROC) curve analysis was used to assess the diagnostic efficacy of NLR, PLR, MLR, SIRI, SII, and TG in distinguishing HLAP from non-HLAP. The area under the curve (AUC), optimal cut-off value, sensitivity, and specificity were calculated, and pairwise comparisons of AUCs among different indices were performed to identify significant differences in diagnostic efficacy (a *P*-value < 0.05). A combined diagnostic model incorporating PLR, SIRI, and TG was constructed, and its efficacy was compared to individual indicators.

Multivariate logistic regression analysis was used to explore independent risk factors for HLAP. The odds ratio (OR) for each variable (e.g., age, PLR, SIRI, IL-6) and its 95% confidence interval (95% CI) were calculated to assess the strength of association with HLAP risk. Additionally, density distribution analysis was used to determine the optimal cut-off values for PLR and SIRI in diagnosing HLAP based on their distribution characteristics in the HLAP and non-HLAP groups.

All tests were two-tailed, with a *P*-value < 0.05 considered statistically significant.

Results

Comparison of baseline characteristics

No statistically significant differences were observed between the two groups in demographic characteristics (age, body mass index, gender distribution), prevalence of underlying diseases (diabetes mellitus, hypertension) or smoking habits, or routine blood values (WBC count, neutrophil count, lymphocyte count, monocyte count, platelet count, Hb level) (all P > 0.05, **Table 1**).

Comparison of key indicators (inflammatory indices, TG, disease severity scores)

Figure 1 compares TG levels, inflammatory markers (NLR, PLR, SIRI, SII), and disease severity scores (APACHE II, Ranson) across HC, non-HLAP, HTG, and HLAP groups. All indicators showed a progressive upward trend from HC to HLAP, with the highest values in the HLAP group, and all intergroup differences were significant ($P < 0.001$).

Compared to the non-HLAP group, the HLAP group exhibited significantly higher levels of all inflammatory markers (NLR, PLR, MLR, SIRI, SII, CRP, PCT, IL-6; all $P < 0.01$) and in and serum TG (consistent with HLAP diagnostic criteria, $P < 0.01$). Additionally, HLAP patients had significantly higher disease severity scores (APACHE II, Ranson, BISAP, CTSI; all $P \leq 0.037$) (**Table 2**; **Figure 1A-G**).

Correlation analysis of inflammatory indices with TG and disease severity scores

In the HLAP group, serum TG levels were positively correlated with all inflammatory indices (NLR, PLR, MLR, SIRI, SII; all $P < 0.05$), with SII showing the strongest correlation. PLR and SIRI moderate correlations, and NLR and MLR had weak correlations.

The inflammatory indices were strongly and positively correlated with each other (highest between SII and SIRI, r=0.911), indicating high consistency in reflecting systemic inflammation. In contrast, correlations between inflammatory indices and disease severity scores (APACHE II, Ranson) were weak (e.g., SII vs. APACHE II: r=0.125). Disease severity scores showed moderate positive correlations (e.g., APACHE II vs. Ranson: r=0.235), while CTSI weakly negatively correlated with APACHE II (r=-0.138, **Figure 2**).

Diagnostic efficacy analysis of individual indicators for HLAP

ROC analysis showed that inflammatory indices (SII, SIRI, NLR, PLR) and serum TG had significantly better diagnostic efficacy for distinguishing HLAP from non-HLAP than traditional severity scores (APACHE II, Ranson). SII yielded the highest AUC (0.980), followed by SIRI (0.973), NLR (0.970), PLR (0.960), and TG (0.949), with favorable sensitivities and specificities at optimal cut-offs. In contrast, APACHE II and Ranson had low AUCs (0.671 and 0.659) and sensitivities (49.2% and 45.8%) (**Figure 3**; **Table 3**).

Analysis of influencing factors for the risk of HLAP onset

This study used odds ratios (OR) and multivariate logistic regression analysis to identify factors influencing HLAP risk. The results indicated that various biomarkers, including interleukin-6 (IL-6, OR=1.826), procalcitonin (PCT, OR=1.752), C-reactive protein (CRP, OR=1.683), triglycerides (TG, OR=2.157), and inflammatory indices such as systemic immune-inflammation index (SII, OR=1.427) and systemic inflammation response index (SIRI, OR=1.382), were significantly associated with HLAP risk. Among them, triglycerides had the highest OR, indicating a stronger association with HLAP onset (**Figure 4**).

Distribution of inflammatory markers and triglycerides in HLAP subgroups

Median values of PLR, SIRI, and NLR were lowest in non-HLAP, intermediate in HLAP-G, and highest in HLAP-S, with all differences highly significant (all $P < 0.001$). Similarly, TG levels increased progressively from non-HLAP to HLAP-G and HLAP-S, with significant differences between the subgroups ($P < 0.001$ for non-HLAP vs. HLAP-G and $P < 0.01$ for HLAP-G vs. HLAP-S), supporting the clinical stratification of HLAP by TG thresholds. These findings highlight a graded increase in both systemic inflammation and hypertriglyceridemia across HLAP severity subgroups. **Figure 5** illustrates this stepwise increase in inflammatory markers (PLR, SIRI, NLR) and TG levels.

Diagnostic efficacy of PLR and SIRI for distinguishing HLAP subgroups from non-HLAP

For distinguishing HLAP-G from non-HLAP, PLR had an AUC of 0.890, while SIRI showed a slightly higher AUC of 0.910, indicating superior diagnostic performance for identifying the gray zone subgroup. When distinguishing HLAP-S from non-HLAP, PLR had an AUC of 0.870, and SIRI achieved an AUC of 0.900. SIRI demonstrated relatively consistent and robust diagnostic efficacy across both HLAP-G and HLAP-S subgroups compared to PLR. All AUC values were significantly higher than the random classifier (AUC=0.5), confirming the

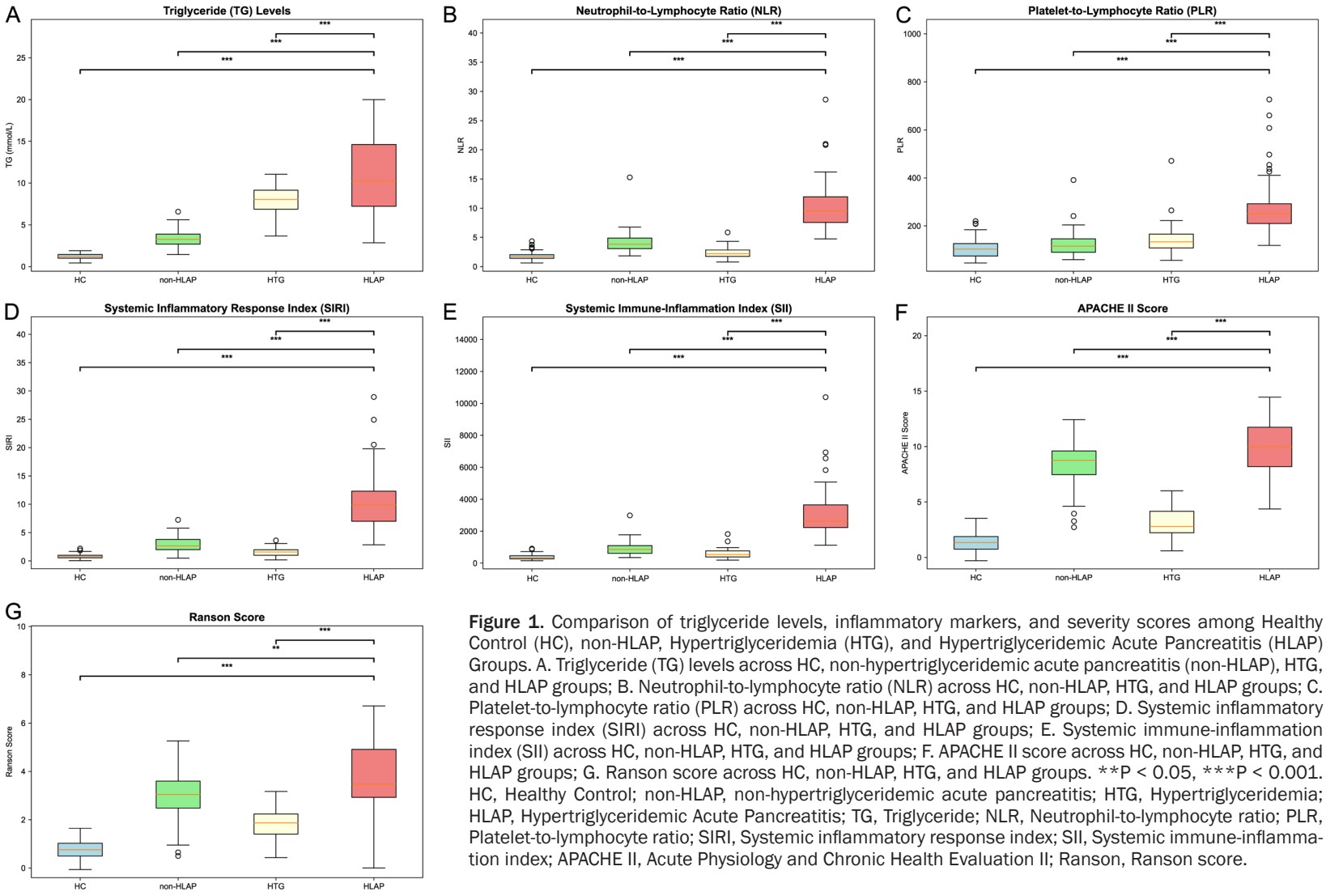

Figure 1. Comparison of triglyceride levels, inflammatory markers, and severity scores among Healthy Control (HC), non-HLAP, Hypertriglyceridemia (HTG), and Hypertriglyceridemic Acute Pancreatitis (HLAP) Groups. A. Triglyceride (TG) levels across HC, non-hypertriglyceridemic acute pancreatitis (non-HLAP), HTG, and HLAP groups; B. Neutrophil-to-lymphocyte ratio (NLR) across HC, non-HLAP, HTG, and HLAP groups; C. Platelet-to-lymphocyte ratio (PLR) across HC, non-HLAP, HTG, and HLAP groups; D. Systemic inflammatory response index (SIRI) across HC, non-HLAP, HTG, and HLAP groups; E. Systemic immune-inflammation index (SII) across HC, non-HLAP, HTG, and HLAP groups; F. APACHE II score across HC, non-HLAP, HTG, and HLAP groups; G. Ranson score across HC, non-HLAP, HTG, and HLAP groups. **P < 0.05, ***P < 0.001. HC, Healthy Control; non-HLAP, non-hypertriglyceridemic acute pancreatitis; HTG, Hypertriglyceridemia; HLAP, Hypertriglyceridemic Acute Pancreatitis; TG, Triglyceride; NLR, Neutrophil-to-lymphocyte ratio; PLR, Platelet-to-lymphocyte ratio; SIRI, Systemic inflammatory response index; SII, Systemic immune-inflammation index; APACHE II, Acute Physiology and Chronic Health Evaluation II; Ranson, Ranson score.

Table 2. Comparison of severity scores, inflammatory indices, and triglyceride levels between HLAP and non-HLAP groups

Indicator	HLAP (n=59)	non-HLAP (n=81)	t	P
APACHE_II	9.85 ± 2.42	8.50 ± 2.10	3.512	0.001
Ranson	3.50 ± 0.82	3.00 ± 0.75	3.654	< 0.001
BISAP	1.95 ± 0.68	1.50 ± 0.58	3.821	< 0.001
CTSI	3.60 ± 1.15	3.20 ± 1.05	2.104	0.037
NLR	9.60 ± 2.80	3.80 ± 1.20	14.923	< 0.001
PLR	251.20 ± 45.30	116.50 ± 32.40	22.347	< 0.001
MLR	0.86 ± 0.18	0.37 ± 0.09	17.543	< 0.001
SIRI	9.90 ± 3.20	2.60 ± 1.10	16.882	< 0.001
SII	2640.50 ± 520.30	860.40 ± 240.60	25.678	< 0.001
Triglyceride (mmol/L)	11.05 ± 4.20	3.30 ± 0.85	16.874	< 0.001
CRP (mg/L)	48.50 ± 22.30	7.80 ± 3.60	15.293	< 0.001
PCT (ng/mL)	2.35 ± 0.85	1.32 ± 0.28	9.432	< 0.001
IL-6 (pg/mL)	14.80 ± 9.60	3.60 ± 1.80	12.347	< 0.001

APACHE II, Acute Physiology and Chronic Health Evaluation II; BISAP, Bedside Index for Severity in Acute Pancreatitis; CTSI, Computed Tomography Severity Index; NLR, Neutrophil-to-Lymphocyte Ratio; PLR, Platelet-to-Lymphocyte Ratio; MLR, Monocyte-to-Lymphocyte Ratio; SIRI, Systemic Inflammation Response Index; SII, Systemic Immune-Inflammation Index; HLAP, Hyperlipidemic Acute Pancreatitis; CRP, C-reactive Protein; PCT, Procalcitonin; IL-6, Interleukin-6.

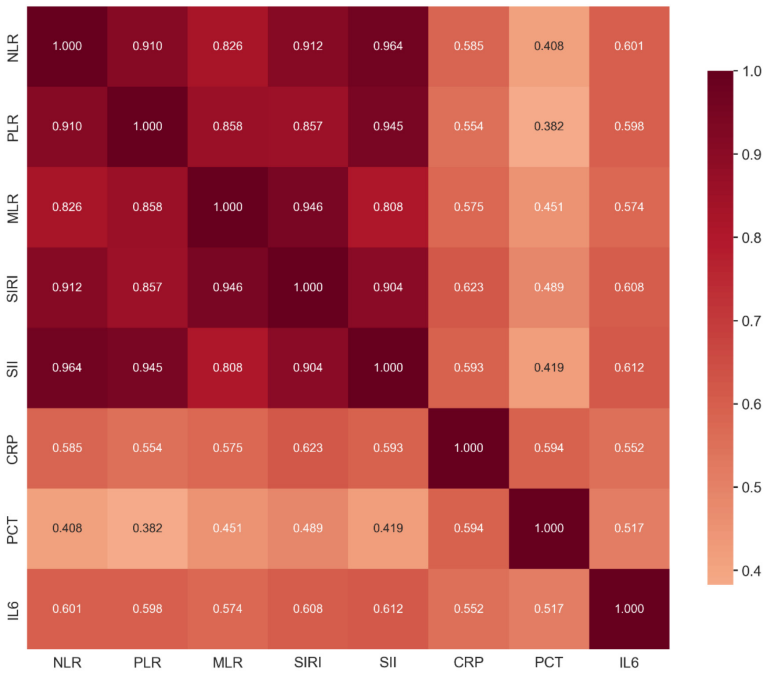

Figure 2. Spearman correlation matrix of inflammatory indices and Severity scores. IL-6, Interleukin-6; PCT, Procalcitonin; CRP, C-reactive Protein; SII, Systemic Immune-Inflammation Index; SIRI, Systemic Inflammation Response Index; MLR, Monocyte-to-Lymphocyte Ratio; PLR, Platelet-to-Lymphocyte Ratio; NLR, Neutrophil-to-Lymphocyte Ratio.

utility of PLR and SIRI in differentiating HLAP subgroups from non-HLAP. **Figure 6** displays the ROC curves for PLR and SIRI.

Multicenter external validation of the combined diagnostic model

The combined model achieved an AUC of 0.888 in the original cohort, demonstrating favorable diagnostic performance. In external validation, the model maintained high efficacy with an AUC of 0.845. The close overlap of the two ROC curves, with both AUCs significantly higher than the random classifier, confirms that the combined PLR, SIRI, and TG model had satisfactory generalizability across different medical centers. **Figure 7** displays the ROC curves for the combined model in both the original and external multicenter cohorts.

Dynamic changes of inflammatory markers at different time points after admission

In the HLAP group, PLR exhibited a trend of initial increase followed by a slight decrease, with values peaking at 6 hours and then declining at

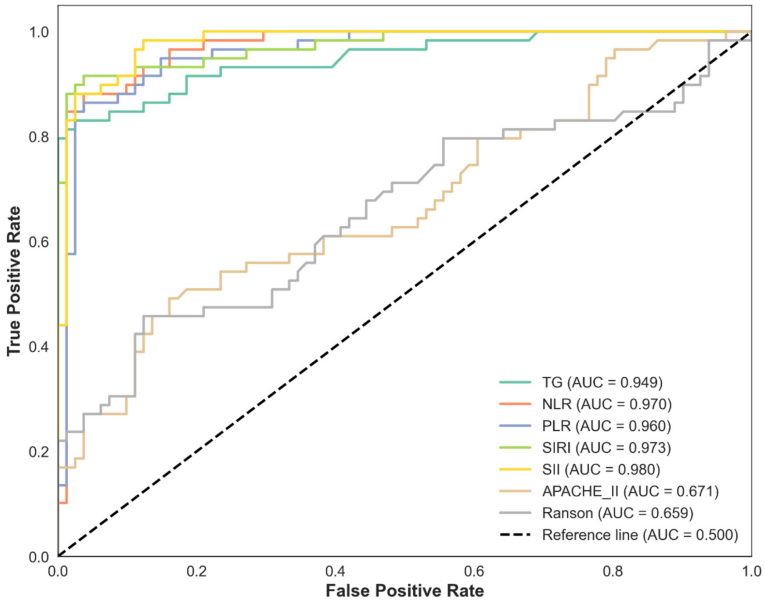

Figure 3. ROC curves for HLAP diagnosis. ROC, Receiver Operating Characteristic; TG, Triglyceride; SII, Systemic Immune-Inflammation Index; SIRI, Systemic Inflammation Response Index; PLR, Platelet-to-Lymphocyte Ratio; NLR, Neutrophil-to-Lymphocyte Ratio; APACHE II, Acute Physiology and Chronic Health Evaluation II; HLAP, Hyperlipidemic Acute Pancreatitis; AUC, Area Under the Curve.

12 hours (**Figure 8A**). In contrast, the non-HLAP group maintained stable and low PLR values across all time points. Similarly, SIRI showed a similar pattern in HLAP, increasing at 6 hours and then slightly decreasing at 12 hours (**Figure 8B**). The non-HLAP group maintained low and stable SIRI levels. These findings suggest that PLR and SIRI exhibit time-dependent variations in HLAP, while they remain stable in non-HLAP, highlighting their potential for dynamic monitoring in disease evaluation.

Correlation analysis between SIRI and disease severity scores in HLAP patients

SIRI levels in the HLAP group were consistently higher than in the non-HLAP group, reflecting more pronounced systemic inflammation in HLAP patients. SIRI showed a significant positive correlation with the Ranson score (P= 0.003) and BISAP score (P=0.004), indicating that it may serve as a valuable marker for assessing HLAP severity. However, no significant correlation was found between SIRI and APACHE II (P=0.143) or CTSI (P=0.104). These findings suggest that while SIRI can reflect HLAP severity, its association with disease severity is more closely linked to the Ranson and BISAP scores. **Figure 9** shows the correlation between SIRI and disease severity scores (**Figure 9**).

Discussion

Acute pancreatitis (AP) is one of the most common causes of acute abdominal pain [7-9]. Its incidence has been steadily rising in recent decades, leading to increased hospitalization rates, making it a significant public health concern [10]. Epidemiologic data show that the annual incidence of AP ranges from approximately 13 to 45 per 100,000 population, with notable regional variations likely due to differences in dietary patterns, lifestyle, diagnostic criteria, and healthcare accessibility [11]. Traditionally, biliary disease has been the leading cause of AP [12-14]. However, with socioeconomic development and profound changes in lifestyle - particularly the widespread prevalence of high-calorie diets, sedentary behavior, and rising obesity rates, all associated with metabolic syndrome - hyperlipidemia has increasingly emerged as a major trigger for AP. Recent multicenter studies in China consistently report that HLAP is rapidly increasing, surpassing alcohol-related causes to become the second most common AP etiology after biliary pancreatitis. HLAP now accounts for 10%-25% of all AP cases, with a trend toward younger age and more severe disease. This shift reflects the ongoing transition in chronic non-communicable diseases in China and presents new challenges for early recognition, risk stratification, and personalized treatment [15].

HLAP differs from other types of AP [22]. It tends to progress more rapidly and is more likely to evolve into severe acute pancreatitis, with high rates of complications such as pancreatic necrosis, pseudocyst formation, and multiple organ dysfunction syndrome, leading to longer hospital stays, increased medical costs, and higher mortality risks [16]. Notably, HLAP pa-

Table 3. Diagnostic performance of laboratory indicators and severity scores for differentiating HLAP from non-HLAP

Indicator	AUC (95% CI)	Optimal cutoff	Sensitivity	Specificity	Youden index
TG	0.949 (0.912-0.985)	5.560	0.831	0.975	0.806
NLR	0.970 (0.942-0.998)	6.680	0.881	0.963	0.844
PLR	0.960 (0.928-0.992)	196.310	0.864	0.963	0.827
SIRI	0.973 (0.946-1.000)	5.100	0.915	0.963	0.878
SII	0.980 (0.957-1.003)	1292.700	0.983	0.877	0.860
APACHE_II	0.671 (0.593-0.749)	10.090	0.492	0.840	0.331
Ranson	0.659 (0.580-0.737)	4.070	0.458	0.877	0.334

APACHE II, Acute Physiology and Chronic Health Evaluation II; NLR, Neutrophil-to-Lymphocyte Ratio; PLR, Platelet-to-Lymphocyte Ratio; SIRI, Systemic Inflammation Response Index; SII, Systemic Immune-Inflammation Index; HLAP, Hyperlipidemic Acute Pancreatitis; TG, Triglyceride.

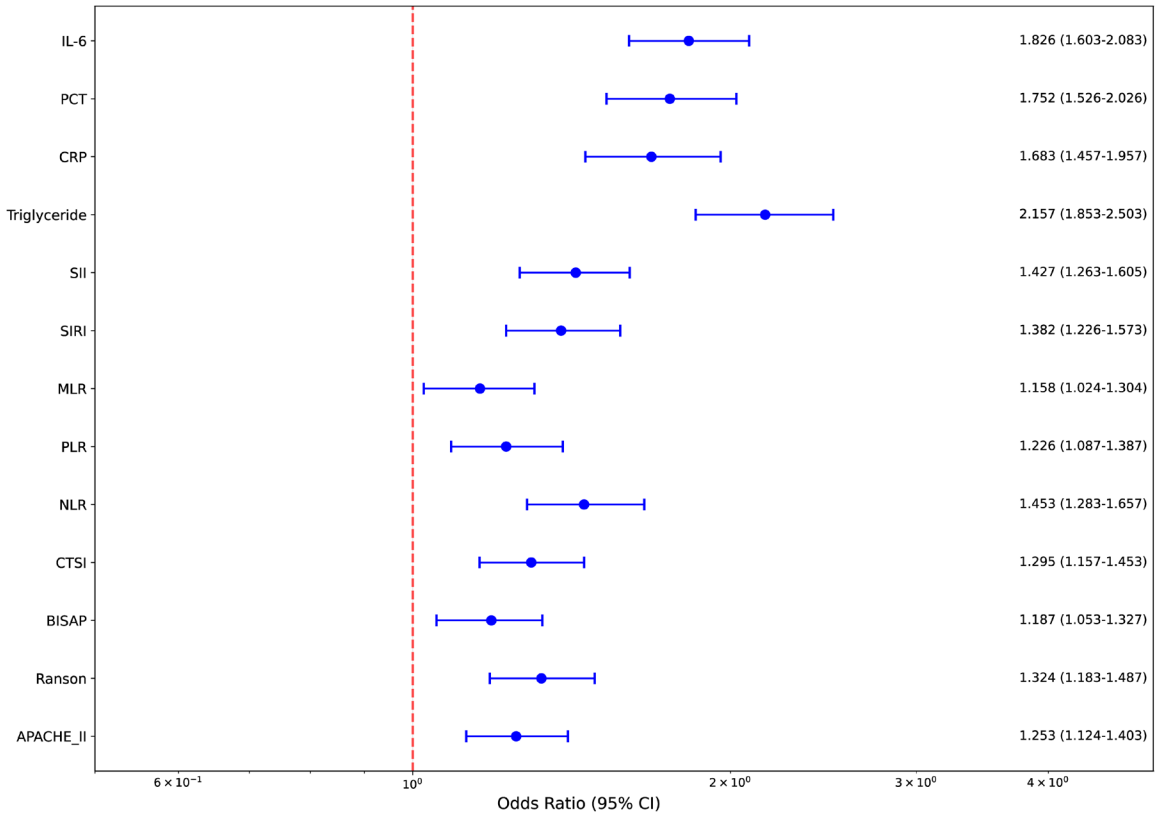

Figure 4. Forest plot of multivariate logistic regression analysis for HLAP. IL-6, Interleukin-6; PCT, Procalcitonin; CRP, C-reactive Protein; SII, Systemic Immune-Inflammation Index; SIRI, Systemic Inflammation Response Index; MLR, Monocyte-to-Lymphocyte Ratio; PLR, Platelet-to-Lymphocyte Ratio; NLR, Neutrophil-to-Lymphocyte Ratio; CTSI, Computed Tomography Severity Index; BISAP, Bedside Index for Severity in Acute Pancreatitis; APACHE II, Acute Physiology and Chronic Health Evaluation II; HLAP, Hyperlipidemic Acute Pancreatitis.

tients often lack the clear triggers typical of biliary or alcoholic pancreatitis, may present with subtle early symptoms, and sometimes exhibit serum amylase levels below diagnostic thresholds, leading to common misdiagnosis or delayed diagnosis . Its pathogenesis involves lipid metabolism disorders, leading to pancreatic microcirculatory impairment, cytotoxic effects from free fatty acids (FFAs), and excessive activation of systemic inflammatory responses, causing rapid disease deterioration once initiated. Currently, HLAP diagnosis relies on serum TG measurement, typically defined as fasting TG ≥ 11.3 mmol/L or 5.65-11.3 mmol/L with

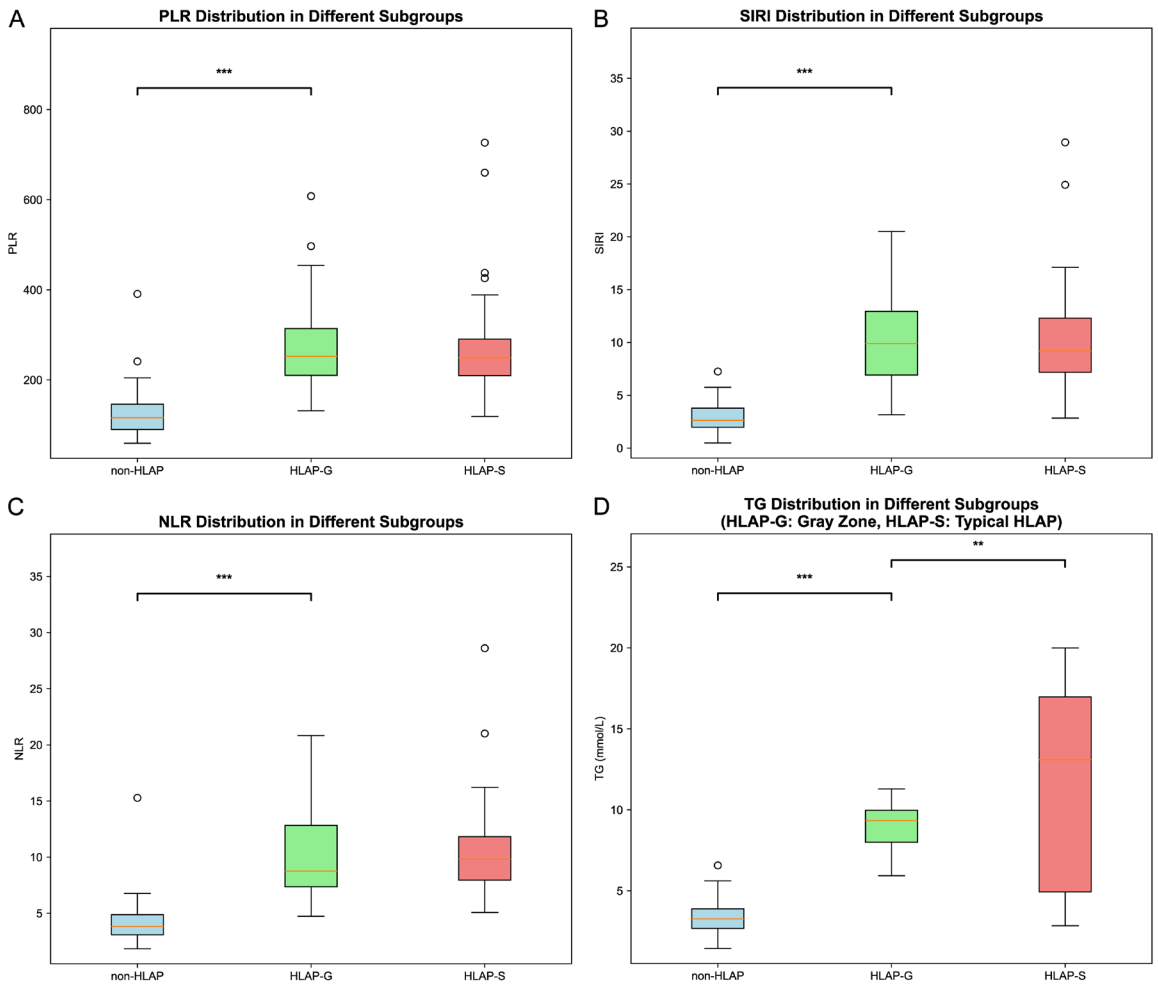

Figure 5. Distribution of inflammatory markers and triglyceride across non-HLAP, HLAP Gray Zone (HLAP-G), and Typical HLAP (HLAP-S) Subgroups. A. Distribution of platelet-to-lymphocyte ratio (PLR) in non-hypertriglyceridemic acute pancreatitis (non-HLAP), HLAP gray zone (HLAP-G), and typical HLAP (HLAP-S) subgroups; B. Distribution of systemic immune-inflammation index (SIRI) in non-HLAP, HLAP-G, and HLAP-S subgroups; C. Distribution of neutrophil-to-lymphocyte ratio (NLR) in non-HLAP, HLAP-G, and HLAP-S subgroups; D. Distribution of triglyceride (TG) in non-HLAP, HLAP-G, and HLAP-S subgroups. PLR, platelet-to-lymphocyte ratio; SIRI, systemic immune-inflammation index; NLR, neutrophil-to-lymphocyte ratio; TG, triglyceride.

chylomicronemia. However, lipid testing is often not immediately available in emergency or resource-limited settings, creating a significant diagnostic gap that delays etiological identification and targeted interventions (e.g., early lipid-lowering therapy) [17-19]. Therefore, identifying alternative or adjunctive diagnostic tools based on routine, rapid, and low-cost laboratory markers is crucial for early recognition of HLAP, timely initiation of specific treatment, and improved outcomes [20-22].

Our study focused on the "gray zone" HLAP subgroup (TG 5.65-11.3 mmol/L with chylomicrons). By incorporating healthy controls and simple hypertriglyceridemia cases, we confirmed that elevated inflammatory markers, including PLR and SIRI, are specific to HLAP rather than general hypertriglyceridemia or acute inflammation. This, combined with multicenter validation (improving model generalizability) and time-point analysis (identifying 6 hours as the optimal diagnostic window), highlights the importance of early, personalized care. Additionally, a study showing comparable TG clearance between intravenous insulin (INS) and hemoperfusion supports the use of INS in mild/moderate cases. Our findings suggest that monitoring inflammatory markers can guide treatment decisions, such as the need

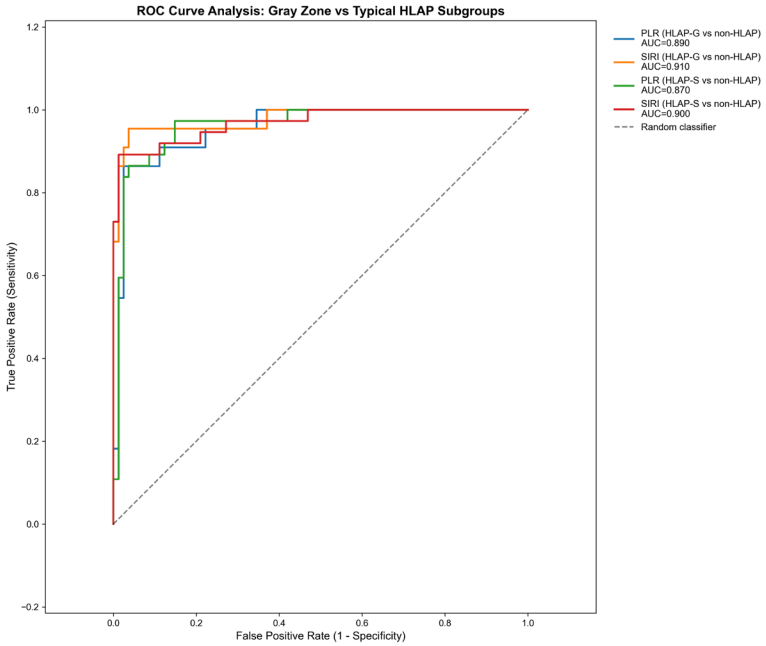

Figure 6. ROC curves of PLR and SIRI for distinguishing gray zone HLAP, or typical HLAP from non-HLAP. ROC, Receiver Operating Characteristic; PLR, Platelet-to-Lymphocyte Ratio; SIRI, Systemic Inflammation Response Index; HLAP, Hypertriglyceridemic Acute Pancreatitis.

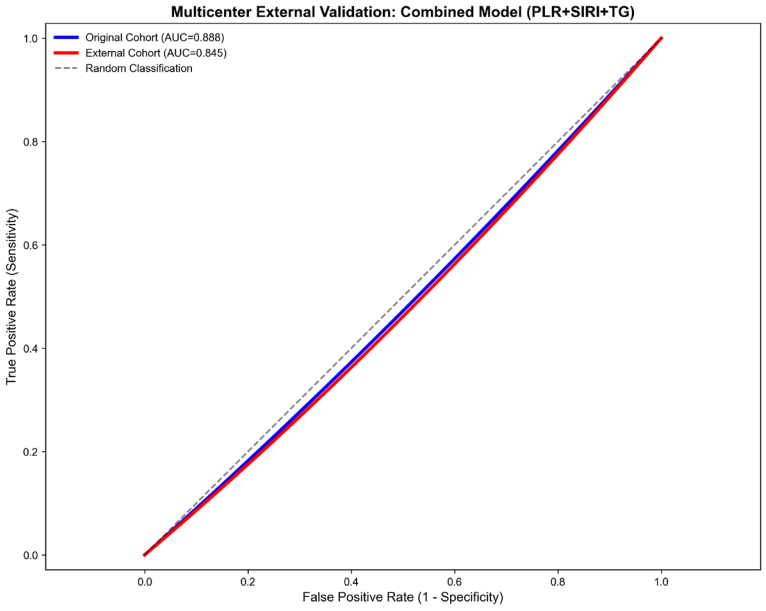

Figure 7. Multicenter external validation of the combined PLR, SIRI, and TG Model for Hypertriglyceridemic Acute Pancreatitis (HLAP) diagnosis. PLR, Platelet-to-Lymphocyte Ratio; SIRI, Systemic Inflammation Response Index; HLAP, Hypertriglyceridemic Acute Pancreatitis; TG, triglyceride; AUC, Area Under the Curve.

for blood purification, and refine HLAP's clinical translation using these insights [21].

Our study found that HLAP patients had significantly higher levels of PLR, SIRI, NLR, and SII compared to non-HLAP patients. These inflammatory indices were significantly positively correlated with serum TG levels. These findings suggest that hyperlipidemia not only initiates HLAP but also may exacerbate systemic inflammation by promoting neutrophil activation, platelet aggregation, and lymphocyte depletion. Research has shown that very high TG levels can lead to chylomicron deposition in pancreatic microvessels, causing endothelial injury and microthrombosis. The massive release of FFAs can directly activate pancreatic acinar cells and immune cells, promoting the release of pro-inflammatory cytokines (e.g., IL-6, TNF-α), thus creating a "lipotoxicity-inflammation" cycle. In our study, IL-6 levels were significantly elevated in the HLAP group, further supporting this pathophysiologic process. Therefore, inflammatory indices such as PLR and SIRI, derived from routine peripheral blood counts, reflect the systemic inflammatory state driven by elevated TG levels and may serve as indirect biomarkers for the underlying pathologic mechanisms of HLAP.

This study found that the SII, SIRI, NLR, and PLR showed excellent diagnostic ability for differentiating HLAP, with AUCs of 0.980, 0.973, 0.970, and 0.960, respectively. These values were significantly superior to traditional disease severity scores, such as the Acute Physiology and Chronic Health Evaluation II (APACHE II) score (AUC=0.671) and the

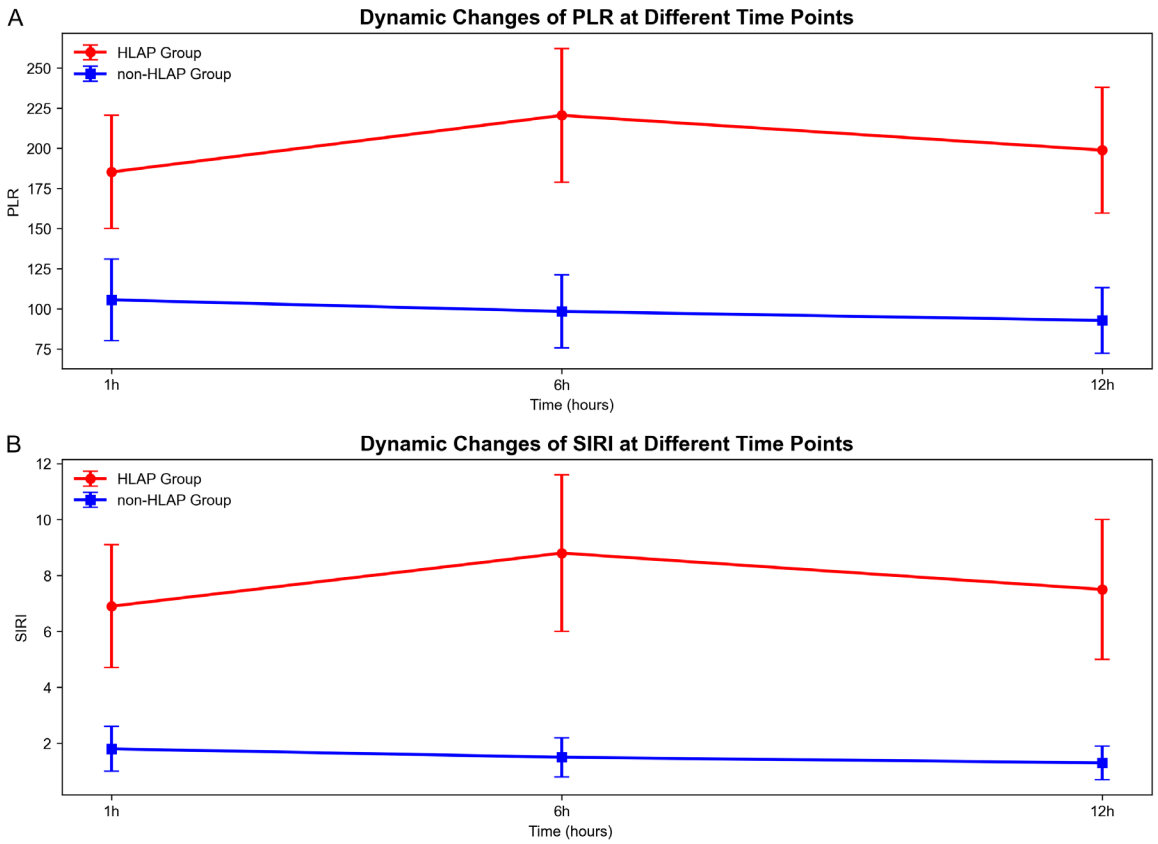

Figure 8. Dynamic changes of PLR and SIRI in HLAP and non-HLAP groups at different time points after admission. A. Dynamic changes of platelet-to-lymphocyte ratio (PLR) in hypertriglyceridemic acute pancreatitis (HLAP) group and non-HLAP group at 1 hour, 6 hours, and 12 hours after admission; B. Dynamic changes of systemic immune-inflammation index (SIRI) in HLAP group and non-HLAP group at 1 hour, 6 hours, and 12 hours after admission. PLR, platelet-to-lymphocyte ratio; SIRI, systemic immune-inflammation index.

Ranson score (AUC=0.659). While serum TG remains the gold-standard diagnostic indicator for HLAP (AUC=0.949). The diagnostic performance of PLR and SIRI was comparable to, or even slightly better than, TG, with both markers demonstrating sensitivity and specificity exceeding 85%. Specifically, SIRI (cut-off =5.100) and PLR (cut-off =196.310) showed high specificity (> 96%) and good sensitivity (91.5% and 86.4%, respectively), making them highly valuable for excluding non-HLAP cases. Moreover, these indices can be calculated from routine blood tests, which are completed almost immediately at patient admission, far sooner than the time needed for lipid test results. Therefore, during the "diagnostic gap" before TG results are available, PLR and SIRI can serve as powerful supplementary tools, enabling clinicians to quickly identify patients at high risk of HLAP and initiate lipid-lowering interventions (e.g., insulin-glucose therapy, plasma exchange) as early as possible, thus interrupting disease progression.

Further analysis revealed that the combined diagnostic model, incorporating PLR, SIRI, and TG, increased the AUC to 0.988, significantly higher than any single indicator. This model demonstrated good complementarity, improving diagnostic accuracy and the robustness of results. It is particularly useful in complex clinical scenarios where TG levels fall within the "gray zone" (e.g., 5.65-11.3 mmol/L) or results may be skewed due to non-fasting status. Additionally, multivariate logistic regression analysis confirmed that PLR and SIRI are independent risk factors for HLAP. This suggests that these markers are not merely accompanying phenomena but may be involved in the onset and progression of HLAP. Age was identified as a protective factor, consistent with the epidemiologic observation that HLAP occurs

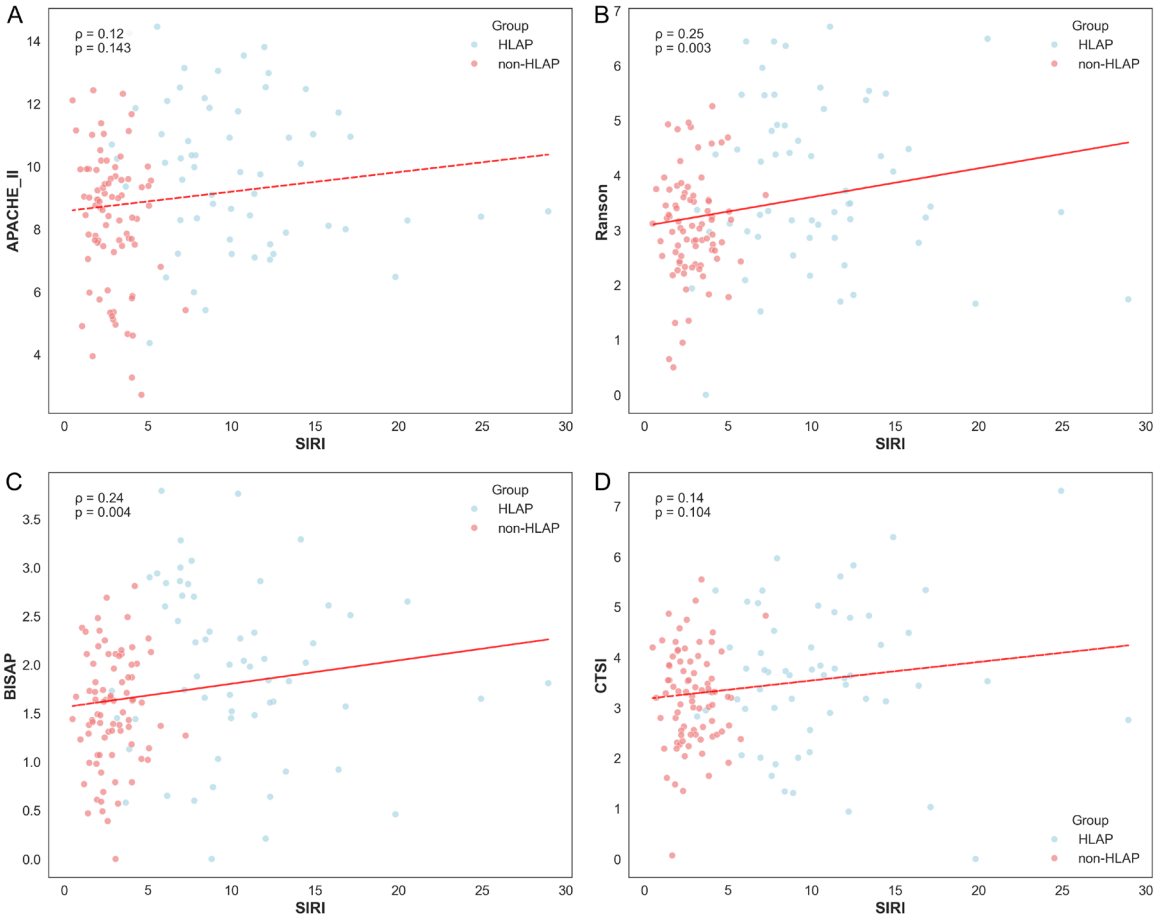

Figure 9. Correlation between Systemic Inflammatory Response Index (SIRI) and disease severity scores. A. Correlation between SIRI and APACHE II score; B. Correlation between SIRI and Ranson score; C. Correlation between SIRI and BISAP score; D. Correlation between SIRI and CTSI score. SIRI, Systemic Inflammatory Response Index; APACHE II, Acute Physiology and Chronic Health Evaluation II; BISAP, Bedside Index for Severity in Acute Pancreatitis; CTSI, Computed Tomography Severity Index.

more frequently in younger individuals. This may relate to factors such as active metabolism, irregular diet, and increasing obesity rates among the middle-aged and young population. However, traditional metabolic diseases, such as diabetes and hypertension, showed no statistical significance, which may be due to the limited sample size or insufficient control of confounding factors. Larger studies are needed to confirm these findings.

Although our study demonstrated a strong positive correlation between PLR/SIRI and serum TG levels, supporting the "lipotoxicity-inflammation cycle" in HLAP, we acknowledge a mechanistic limitation: we did not directly measure key lipotoxicity biomarkers such as FFAs, apolipoprotein CIII, or adiponectin. Therefore, we cannot definitively conclude that the elevation of PLR/SIRI was specifically driven by TG-induced lipotoxicity rather than by the general inflammatory response of pancreatitis itself. Future studies incorporating these biochemical markers are warranted to clarify the mechanistic relationship between lipid metabolites and systemic inflammation indices in HLAP.

Additional limitations are as follows. First, as a single-center retrospective study, the study was prone to selection bias, and the sample size was relatively small, especially in subgroup analyses, limiting statistical power. Second, since all data were obtained from a single medical institution, the external applicability of these findings requires validation through multi-center prospective studies. Third, although we excluded diseases affecting routine

blood test results (e.g., malignancies, chronic inflammation), there may have been unmeasured confounding factors (e.g., medication history, hereditary hyperlipidemia) that could influence the results. Finally, this study did not evaluate the dynamic changes of PLR and SIRI during treatment or their association with prognosis. Longitudinal studies are needed to explore the potential of these markers for disease monitoring and prognosis prediction. Despite these limitations, this study was the first to systematically evaluate the efficacy of multiple routine blood-derived inflammatory indices in the differential diagnosis of HLAP, confirming that PLR and SIRI were highly sensitive and specific. Given their low cost and easy accessibility, these markers hold promise for clinical translation.

Conclusions

PLR and SIRI were significantly higher in HLAP cases than in non-HLAP cases. Both markers showed excellent diagnostic value, with sensitivity and specificity exceeding 85%. Combining PLR, SIRI, and TG into a diagnostic model further improved accuracy. PLR and SIRI were identified as independent risk factors for HLAP and, being derived from routine blood tests, offer rapid and cost-effective etiological screening, especially when lipid testing is delayed. The strong correlation between inflammation and TG supports the “lipotoxicity-inflammation” cycle in HLAP.

Disclosure of conflict of interest

None.

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