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RESEARCH

Prognostic significance of lactate clearance in severe acute pancreatitis

Şiddetli akut pankreatitte laktat klirensinin prognostik önemi

Betül Çiğdem Yortanlı[1], Korhan Kollu[1], Burcu Kuş[1], Ekrem Taha Sert[2], Mehmet Yortanlı[3]

[1]University of Health Sciences, Konya, Türkiye
[2]Aksaray University, Aksaray, Türkiye
[3]Konya Numune Hospital, Konya, Türkiye

Abstract

Purpose: This study aimed to evaluate the prognostic value of lactate clearance in predicting severe acute pancreatitis (SAP) in patients with acute pancreatitis (AP). Identifying early biomarkers for SAP can help in risk stratification and guide clinical management.

Materials and Methods: This retrospective, single-center observational study included 183 patients diagnosed with AP between January 2022 and January 2023. Patients were classified as SAP or non-SAP based on the 2012 Atlanta Classification. Demographic data, laboratory parameters, and clinical outcomes were analyzed. Lactate clearance was calculated as [(initial lactate – 24-hour lactate)/initial lactate] × 100..

Results: Among 183 patients, 105 (57.4%) had SAP. SAP patients had significantly longer hospital stays, higher intensive care unit admissions, and increased mortality rates). SAP patients had significantly higher initial and 24-hour lactate levels but lower lactate clearance. Lower lactate clearance was an independent predictor of SAP (OR: 3.051, 95% CI: 2.030–5.072, p<0.001). ROC analysis revealed that lactate clearance had an AUC of 0.835 (95% CI: 0.776–0.894), with 81.9% sensitivity and 76.9% specificity at a cutoff value of 40.9%.

Conclusion: Low lactate clearance is strongly associated with SAP development, longer hospitalization, ICU need, and increased mortality. Lactate clearance may serve as a valuable early prognostic marker. Future studies should explore integrating lactate clearance with markers such as SII, SII/albumin ratio, and RDW to enhance risk stratification and clinical decision-making in AP.

Keywords:. Acute pancreatitis, lactate clearance, prognostic biomarker

Öz

Amaç: Bu çalışma, akut pankreatit (AP) hastalarında laktat klirensinin şiddetli akut pankreatit (SAP) gelişimini öngörmedeki prognostik değerini değerlendirmeyi amaçlamaktadır. SAP için erken dönemde belirteçlerin tanımlanması, risk sınıflandırmasını kolaylaştırarak klinik yönetimi yönlendirebilir.

Gereç ve Yöntem: Bu retrospektif, tek merkezli gözlemsel çalışma, Ocak 2022 ile Ocak 2023 tarihleri arasında AP tanısı alan 183 hastayı içermektedir. Hastalar, 2012 Atlanta Klasifikasyonu'na göre SAP ve non-SAP gruplarına ayrıldı. Demografik veriler, laboratuvar parametreleri ve klinik sonuçlar analiz edildi. Laktat klirensi [(ilk laktat – 24. saat laktat) / ilk laktat] × 100 formülü ile hesaplandı.

Bulgular: Toplam 183 hastanın 105'i (%57.4) SAP grubundaydı. SAP hastalarında hastane yatış süresi, yoğun bakım gereksinimi ve mortalite oranları anlamlı olarak daha yüksekti. SAP hastalarında başlangıç ve 24. saat laktat seviyeleri daha yüksekti, ancak laktat klirensi anlamlı şekilde daha düşüktü. Laktat klirensi, SAP için bağımsız bir belirleyici olarak bulundu (OO = 3.051, %95 CI: 2.030-5.072, p<0.001). ROC analizi, laktat klirensinin %40,9'luk bir kesme değerinde %81,9 duyarlılık ve %76,9 özgüllük ile 0,835'lik (%95 GA: 0,776-0,894) bir AUC sahip olduğunu ortaya koymuştur.

Sonuç: Düşük laktat klirensi SAP gelişimi, daha uzun süre hastanede kalma, YBÜ ihtiyacı ve artmış mortalite ile güçlü bir şekilde ilişkilidir. Laktat klirensi değerli bir erken prognostik belirteç olarak hizmet edebilir. Gelecekteki çalışmalar, AP'de risk sınıflandırmasını ve klinik karar verme sürecini geliştirmek için laktat klirensini SII, SII/albümin oranı ve RDW gibi belirteçlerle entegre etmeyi araştırmalıdır.

Anahtar kelimeler: Akut pankreatit, laktat klirensi, prognostik biyobelirteç

Address for Correspondence: Betül Çiğdem Yortanlı, University of Health Sciences Turkey, Konya City Hospital, Department of Internal Medicine, Konya, Türkiye E-mail: drbetul85@gmail.com
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INTRODUCTION

Acute pancreatitis (AP) is one of the most common gastrointestinal diseases leading to hospital admissions worldwide, with an incidence that has continued to rise over recent decades. The clinical course of the disease varies widely, ranging from mild cases to multiple organ failure and mortality. AP is an inflammatory process characterized by abnormal enzyme activation in pancreatic acinar cells, triggering an auto-digestion mechanism. The most common causes of AP are gallstones and alcohol consumption, although hypertriglyceridemia, hypercalcemia, medications, and genetic factors also contribute to its etiology[1,2]. Recent data indicate that approximately 15–20% of AP cases progress to moderately severe or severe forms, with mortality rates reaching up to 30% in these patients[3]. This clinical burden underscores the importance of early and accurate severity assessment to guide monitoring and therapeutic decision-making.

A wide array of scoring systems including APACHE II, Ranson, BISAP, and MCTSI have been developed for severity stratification in AP. However, the complexity, delayed applicability, or limited sensitivity of these tools in the early phase often restrict their routine use in urgent care settings. For instance, both APACHE II and Ranson scores require time-dependent parameters that are not always available at admission. Consequently, early-stage multi-indicator models have been proposed as more dynamic, cost-effective, and feasible alternatives for clinical use[3-5].

Lactate levels and lactate clearance have emerged as significant prognostic markers in patients with acute pancreatitis (AP), reflecting tissue hypoxia and systemic inflammation. Traditionally considered a metabolic waste product, lactate is now recognized as a crucial energy source and cellular signaling molecule. Elevated lactate levels under conditions of hypoxia and inflammation have been associated with increased disease severity and mortality in AP patients[6,7]. Beyond its metabolic functions, lactate plays important regulatory roles in immune response and redox homeostasis, influencing inflammatory pathways and cellular survival mechanisms. Lactate clearance, defined as the reduction in blood lactate concentration over time, serves as an indirect marker of tissue oxygenation and perfusion. Impaired lactate clearance has been linked to adverse outcomes in sepsis, trauma, and cardiovascular diseases. Although its prognostic value has been well-established in these conditions, its utility in predicting outcomes in AP remains relatively underexplored[1,6]. Nevertheless, accumulating evidence suggests that impaired lactate clearance may similarly reflect a poor prognosis in AP[8-10]. Moreover, recent mechanistic studies have shown that lactate may exacerbate pancreatic inflammation by activating hypoxia-inducible factor 1-alpha (HIF1A), which promotes ferroptosis through the ACSL4/LPCAT3/ALOX15 signaling pathway, ultimately aggravating tissue injury in severe acute pancreatitis (SAP)[11].

We hypothesized that lower lactate clearance at 24 hours would serve as an independent predictor of SAP. The novelty of this study lies in demonstrating the clinical utility of 24-hour lactate clearance as an independent predictor of SAP and comparing it against alternative inflammatory biomarkers.

MATERIALS AND METHODS

Study design and sample

This retrospective, single-center observational study was conducted in the internal medicine ward and intensive care unit (ICU) of a tertiary hospital. Patients admitted between January 1, 2022, and January 31, 2023, with a diagnosis of AP were included. Patients were excluded if they had incomplete medical records, were under 18 years old, had autoimmune diseases, cardiopulmonary disease, end-stage renal failure, active tuberculosis, cirrhosis, or cancer, had a diagnosis of chronic pancreatitis, were pregnant, or were transferred to another hospital during follow-up.

The study was conducted at the University of Health Sciences Turkey, Konya City Hospital, a tertiary academic and referral center. All data were retrieved from the hospital's electronic medical record system, which records clinical and laboratory parameters in a standardized and time-stamped manner. Data reliability was ensured through institutional documentation protocols and regular quality control audits. All diagnostic evaluations, laboratory investigations, imaging procedures, and clinical follow-up were performed by healthcare professionals involved in the routine care of patients, following institutional standards and clinical guidelines.

A total of 218 patients were retrospectively screened. Thirty-five patients were excluded due to the following reasons: incomplete medical records (n=12), end-stage renal failure (n=8), malignancy (n=6), active tuberculosis (n=5), and cirrhosis (n=4). After applying these exclusion criteria, 183 patients were included in the final analysis. The patient selection process is summarized in Figure 1.

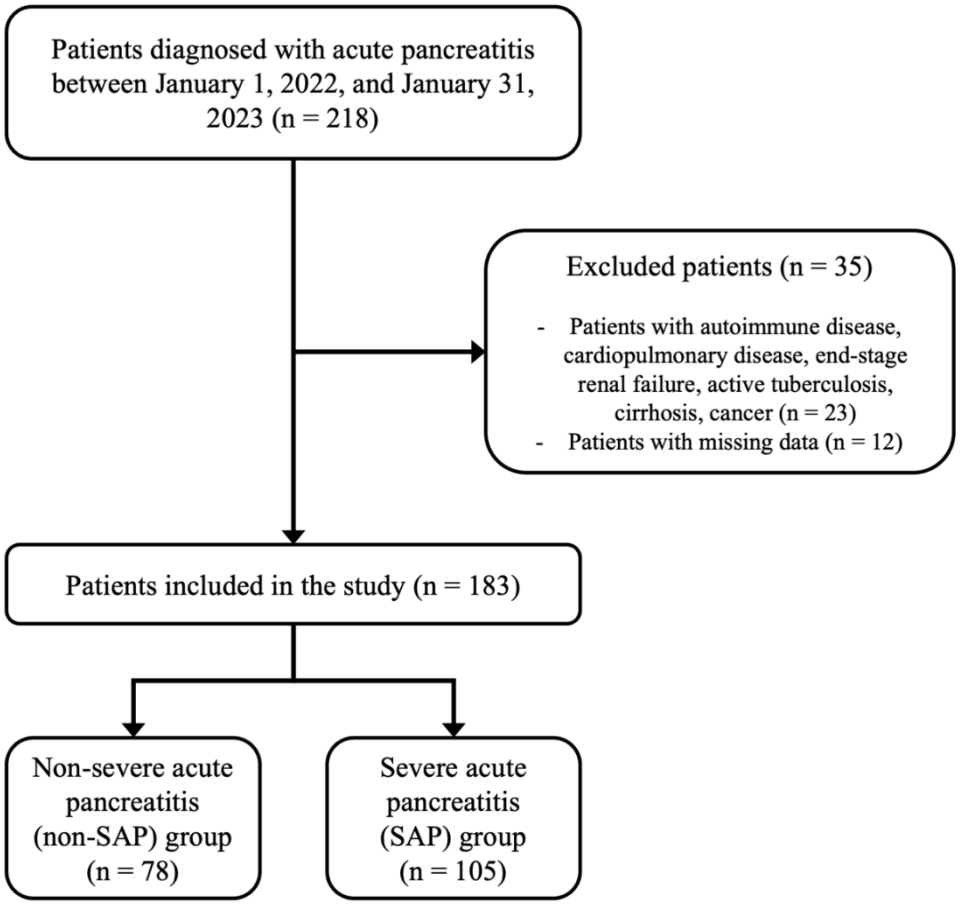


Figure 1. Flowchart of patient selection for the study.

The sample size was determined based on prior studies on lactate clearance[12,13]. A clinically significant difference of at least 20% between the two groups (60% vs. 40%) was assumed. Accordingly, a minimum of 178 patients was required for the study to achieve 85% power with a 0.05 alpha error[14]. To account for potential data loss, the sample size was increased by 10%, and 195 patients were initially included. Following data collection, 12 patients with missing data were excluded, and the final study population comprised 183 patients. This sample size was considered adequate to perform ROC analysis with sufficient statistical power, based on detecting clinically meaningful differences in lactate clearance between groups.

Procedure

Ethical approval for this study was obtained from the Ethics Committee of Karatay University Faculty of Medicine on September 21, 2023 (Decision No: 2023/027). The research was conducted in compliance with the principles of the Declaration of Helsinki. As the study was based on retrospective data collection, the requirement for informed consent was waived.

Demographic data, etiological factors, laboratory parameters, and clinical outcomes were obtained from hospital records. Patients were categorized into two groups based on AP severity: those with moderately severe AP (MSAP) and severe AP (SAP) were classified as SAP, while those with mild AP (MAP) were included in the non-SAP group. Lactate measurements were obtained from venous blood samples using the GEM Premier 3500 blood gas analyzer (Instrumentation Laboratory, USA). Lactate clearance was calculated using the formula: [(initial lactate – 24-hour lactate) / initial lactate] × 100. The neutrophil-to-lymphocyte ratio (NLR), platelet-to-lymphocyte ratio (PLR), and systemic immune-inflammation index (SII) were also calculated. SII was determined using the formula: (neutrophil × platelet) / lymphocyte. ICU admission data were collected only for patients classified as SAP, as none of the non-SAP patients required ICU care.

Patients were diagnosed with AP and classified according to the 2012 Atlanta Classification15. The diagnosis of AP was determined by the presence of at least two of the following criteria: sudden onset of severe epigastric pain, often radiating to the back; serum lipase or amylase levels exceeding three times the upper normal limit; or imaging findings indicative of AP on contrast-enhanced CT, with MRI or abdominal ultrasound used less frequently. Mortality was defined as in-hospital mortality, occurring during the index hospitalization for AP.

According to the 2012 revised Atlanta Classification, MAP is characterized by the absence of organ failure or complications, MSAP includes organ failure that resolves within 48 hours and/or the presence of local or systemic complications, and SAP is defined as persistent organ failure lasting longer than 48 hours. In our study, MSAP and SAP patients were initially classified separately; however, due to the lack of statistically significant differences between these groups, they were combined into a single group (SAP group) for statistical analysis.

Statistical analysis

Data were analyzed using SPSS version 27 (Statistical Package for the Social Sciences). The normality of continuous variables was evaluated using the Kolmogorov-Smirnov test. Normally distributed variables (e.g., age, hemoglobin) were reported as mean ± standard deviation (SD), while non-normally distributed variables (e.g., lactate levels, lactate clearance, SII, NLR, PLR) were presented as median (1st quartile - 3rd quartile). Categorical variables were reported as numbers (percentages, %). To compare SAP and non-SAP groups, the independent samples t-test was used for normally distributed variables, the Mann–Whitney U test for non-normally distributed variables, and the Chi-square test or Fisher's exact test for categorical variables. The association between clinical variables (including age, gender, initial and 24-hour lactate levels, lactate clearance, NLR, PLR, SII, RDW, AST/ALT ratio, and SII/albumin ratio) and SAP was first evaluated using univariate logistic regression. Variables with a p-value <0.05 in univariate analysis were included in the multivariate logistic regression model using a stepwise backward elimination method to identify independent predictors of SAP. Odds ratios (ORs) and 95% confidence intervals (CIs) were reported. To assess the diagnostic performance of lactate clearance and other inflammatory markers (SII, NLR, PLR, RDW, AST/ALT, and SII/albumin ratio) in predicting SAP, Receiver Operating Characteristic (ROC) curve analysis was performed. Area under the curve (AUC) values were calculated, and comparisons between AUCs were performed using the DeLong test. A p-value <0.05 was considered statistically significant.

RESULTS

A total of 183 AP patients were included in the study, with 78 patients in the non-SAP group and 105 patients in the SAP group. There was no significant difference in demographic characteristics between the groups. However, hospital length of stay was significantly longer in the SAP group ($p < 0.001$). The ICU stay was evaluated only for SAP patients, with a median duration of 8 (4–18) days. The mortality rate was 28.6% in the SAP group ($p < 0.001$).

The SAP group exhibited significantly higher levels of neutrophils, red cell distribution width (RDW), NLR, PLR, SII, SII/Albumin (ALB), and AST/ALT ratios compared to the non-SAP group ($p < 0.001$). In contrast, albumin, calcium, and lymphocyte levels

were markedly reduced in the SAP group ($p < 0.001$). Both initial lactate and 24-hour lactate levels were significantly higher in SAP patients ($p < 0.001$), while lactate clearance was significantly lower in the SAP group ($p < 0.001$) (Table 1). Patients with lower lactate clearance values had longer hospital stays and higher mortality rates, as illustrated by the scatter plot (Figure 2).

Table 1. Comparison of demographic data and laboratory findings of SAP and non-SAP patients

	Total (n = 183)	**Non-SAP (n = 78)**	**SAP (n = 105)**	**p**
Age, years	59 (42 – 76)	59 (44 – 77)	63 (41 – 76)	.783
Sex, n (%)				
Male	60 (32.8)	24 (40.0)	36 (60.0)	.616
Female	123 (67.2)	54 (43.9)	69 (56.1)	
Etiology, n (%)				
Gallstones	99 (54.1)	45 (45.5)	54 (54.5)	.270
Alcohol	15 (8.2)	3 (20.0)	12 (80.0)	
Hypertriglyceridemia	9 (4.9)	3 (33.3)	6 (66.7)	
Other	60 (32.8)	27 (45.0)	33 (55.0)	
ICU length of stay, day	8 (4 – 18)	-	8 (4 – 18)	
Length of hospital stay, day	7 (5 – 11)	5 (4 – 7)	9 (6 – 12)	<.001
In-hospital mortality, n (%)	30 (16.4)	0 (0.0)	30 (100.0)	<.001
Laboratory test				
Neutrophil, $10^3/\mu L$	7.1 (5.8 – 9.1)	6.3 (4.5 – 7.4)	8.0 (6.7 – 10.4)	<.001
Lymphocyte, $10^3/\mu L$	1.5 (1.1 – 2.2)	1.9 (1.3 – 2.6)	1.4 (1.1 – 1.9)	<.001
Platelet, $10^3/\mu L$	263 ± 69	252 ± 58	272 ± 75	.042
RDW, %	13.7 (12.8 – 14.5)	13.1 (12.3 – 14.0)	14.1 (13.3 – 14.7)	<.001
ALB, mg/dL	38 ± 9	41 ± 7	35 ± 10	<.001
Calcium, mg/dL	8.7 (7.8 – 9.3)	9.2 (8.6 – 9.6)	8.2 (7.3 – 8.9)	<.001
Initial lactate	1.6 (0.9 – 2.4)	1.3 (0.8 – 1.8)	2.1 (1.2 – 3.3)	<.001
24th hour lactate	0.8 (0.3 – 1.8)	0.4 (0.2 – 0.8)	1.3 (0.6 – 2.6)	<.001
Lactate clearance	36 (25 – 64)	61 (42 – 77)	27 (15 – 38)	<.001
NLR	4.6 (2.9 – 7.4)	3.1 (2.1 – 4.8)	5.7 (4.1 – 8.7)	<.001
PLR	167.3 (105.3 – 244.4)	134.9 (89.4 – 187.9)	199.2 (119.1 – 290.7)	<.001
SII	1133.2 (675.9 – 2072.6)	766.5 (525.9 – 1245.4)	1537.7 (925.8 – 2609.7)	<.001
SII/ALB ratio	30.0 (17.2 – 57.8)	20.6 (13.0 – 31.1)	43.8 (24.5 – 93.0)	<.001
AST/ALT ratio	1.06 (0.84 – 1.54)	0.96 (0.79 – 1.22)	1.23 (0.98 – 1.70)	<.001

Data are presented as mean ± standard deviation, median and 25th-75th percentiles or number (percentage).
ICU: intensive care unit; SAP: severe acute pancreatitis; WBC: white blood cell; RDW: red cell distribution width; ALB: albumin; AST: aspartate aminotransferase; ALT: alanine aminotransferase; CRP: C-reactive protein; NLR: neutrophil-lymphocyte ratio; PLR: platelet-lymphocyte ratio; SII: systemic immune-inflammation index.

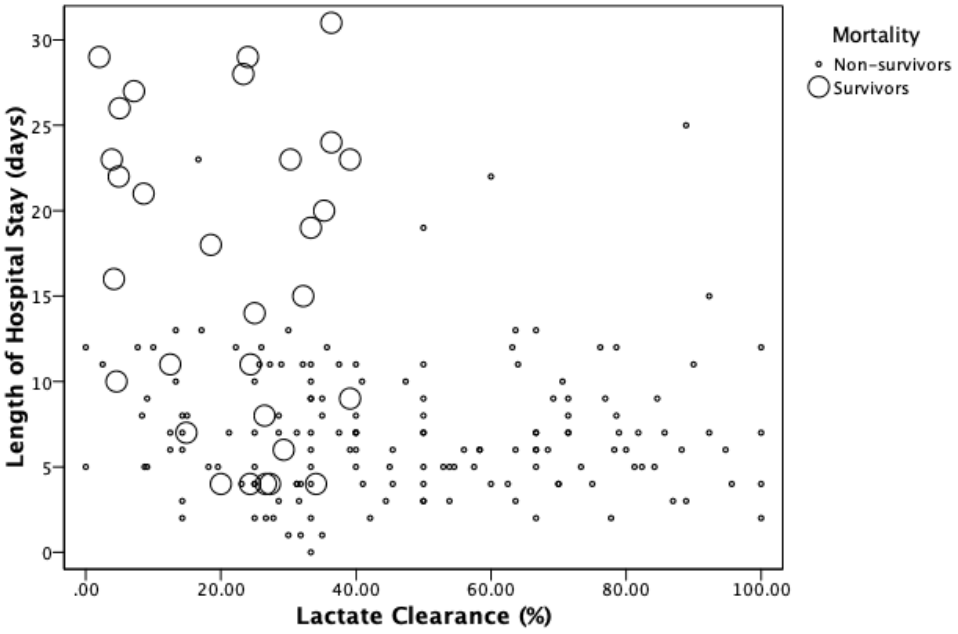


Figure 2. Scatter plot of lactate clearance and length of hospital stay according to mortality status.

Logistic regression analysis identified lactate clearance as one of the strongest independent predictors of SAP development. A decrease in lactate clearance increased the risk of SAP by 3-fold ($p < 0.001$). Additionally, SII/ALB ratio (OR = 1.1, $p = 0.004$) and AST/ALT ratio (OR = 2.0, $p = 0.047$) were determined as independent risk factors for SAP. RDW was also significantly associated with SAP development (Table 2). In predicting SAP, lactate clearance had the highest diagnostic value with an AUC of 0.835. Using a cutoff value of 40.9%, lactate clearance demonstrated 81.9% sensitivity and 76.9% specificity. The AUC values for SII/ALB and NLR were 0.782 and 0.771, respectively (Table 3, Figure 3).

Table 2. Logistic Regression Analysis of Predictors for SAP

Variables	Univariate logistic regression		Multivariate logistic regression	
	OR (95% Cl)	p	OR (95% Cl)	p
Lactate clearance	4.058 (2.040 – 7.076)	<.001	3.051 (2.030 – 5.072)	<.001
NLR	1.398 (1.221 – 1.600)	<.001	0.837 (0.545 – 1.285)	.416
PLR	1.006 (1.003 – 1.010)	<.001	0.991 (0.981 – 1.000)	.052
SII	1.001 (1.001 – 1.002)	<.001	1.000 (0.997 – 1.002)	.735
SII/ALB ratio	1.046 (1.027 – 1.065)	<.001	1.107 (1.034 – 1.186)	.004
AST/ALT ratio	2.520 (1.418 – 4.477)	.002	2.134 (1.011 – 4.505)	.047
RDW	2.337 (1.700 – 3.215)	<.001	1.757 (1.163 – 2.654)	.007

SAP: severe acute pancreatitis; OR: odds ratio; CI: confidence interval; NLR: neutrophil-lymphocyte ratio; PLR: platelet-lymphocyte ratio; SII: systemic immune-inflammation index; ALB: albumin; AST: aspartate aminotransferase; ALT: alanine aminotransferase; RDW: red cell distribution width.

Table 3. Comparison of ROC curves for predicting SAP

	AUC (%95 Cl)	p	Cut-off	Sensitivity	Specificity	PPV	NPP
PLR	0.659 (0.581 – 0.738)	<.001	> 191.4	52.4	75.6	74.3	54.1
AST/ALT ratio	0.676 (0.598 – 0.754)	<.001	> 1.04	61.9	61.5	68.4	54.5
RDW	0.739 (0.668 – 0.809)	<.001	> 13.6	64.8	61.5	69.4	56.5
SII	0.757 (0.688 – 0.826)	<.001	> 1290.1	59.0	78.2	78.5	58.7
NLR	0.771 (0.701 – 0.841)	<.001	> 3.9	81.0	61.5	73.9	70.6
SII/ALB ratio	0.782 (0.716 – 0.847)	<.001	> 26.7	73.3	71.8	77.8	66.7
Lactate clearance	0.835 (0.776 – 0.894)	<.001	< 40.9	81.9	76.9	82.7	75.9

ROC: receiver operating characteristic; SAP: severe acute pancreatitis; AUC: area under the curve; PPV: positive predictive value; NPV: negative predictive value; PLR: platelet-lymphocyte ratio; ALB: albumin; AST: aspartate aminotransferase; ALT: alanine aminotransferase; RDW: red cell distribution width; SII: systemic immune-inflammation index; NLR: neutrophil-lymphocyte ratio.

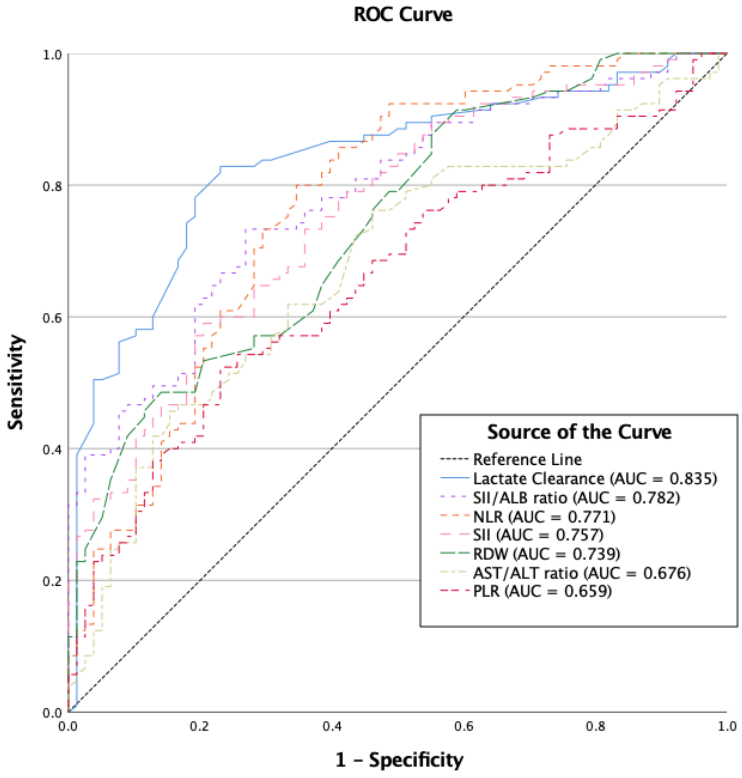


Figure 3. ROC curve shows the predictive performance of various biomarkers for SAP.

ROC: receiver operating characteristic; SAP: severe acute pancreatitis; PLR: platelet-lymphocyte ratio; AST: aspartate aminotransferase; ALT: alanine aminotransferase; RDW: red cell distribution width; SII: systemic immune-inflammation index; NLR: neutrophil-lymphocyte ratio; ALB: albumin.

DISCUSSION

In this study, the prognostic value of lactate clearance in predicting SAP development was evaluated. Our findings indicate that low lactate clearance is strongly associated with SAP development, suggesting that early assessment of lactate clearance may play a crucial role in predicting disease progression.

Lactate is considered a marker of anaerobic metabolism resulting from hypoperfusion and hypoxia. In critically ill patients, low lactate clearance is an important indicator of systemic inflammation, organ failure, and increased mortality risk. In our study, lactate clearance was significantly lower in SAP patients, and early low lactate clearance was identified as a strong independent predictor of SAP development. Previous studies have shown that low lactate clearance is associated with in-hospital mortality, multiple organ failure, and poor clinical outcomes in critically ill patients[12,13,16,17]. These findings suggest that low lactate clearance may also be related to disease severity and poor clinical outcomes in SAP patients.

The AST/ALT ratio is an important indicator of hepatic dysfunction and systemic inflammation. In a study by Mühling et al., an elevated AST/ALT ratio was found to reflect the severity of acute hepatic inflammation and liver injury[18]. Similarly, in our study, SAP patients had significantly higher AST/ALT ratios, which were associated with severe disease progression. Another study also demonstrated that the AST/ALT ratio is significantly associated with SAP severity, and higher levels of this ratio correlate with more severe disease progression[19]. These findings suggest that early assessment of the AST/ALT ratio in SAP patients may be necessary, and patients with elevated AST/ALT ratios should be monitored more closely. However, our study demonstrated that lactate clearance was a superior predictor of SAP severity compared to the AST/ALT ratio.

Systemic inflammation plays a crucial role in determining AP severity. In our study, SII, SII/ALB ratio, NLR, PLR, and RDW levels were significantly higher in SAP patients ($p < 0.001$). Previous studies have reported that NLR and PLR are important predictors of SAP diagnosis, while RDW has been identified as a prognostic marker for disease severity[19-24]. Additionally, elevated SII and SII/ALB ratios have been associated with poor prognosis, with certain cutoff values demonstrating high sensitivity and specificity in predicting SAP. The prognostic relevance of the SII/ALB ratio may be attributed to its ability to simultaneously capture systemic inflammation, indicated by neutrophil and platelet counts, and impaired nutritional status, reflected by low albumin levels. Together, these pathophysiological mechanisms contribute to adverse clinical outcomes in patients with severe inflammatory diseases, including SAP[25-27]. However, our study found that lactate clearance was a stronger prognostic indicator for SAP than other inflammatory markers. Notably, although some inflammatory markers such as NLR and PLR demonstrated significant associations with SAP in univariate analysis, they did not retain significance in multivariate analysis. This may be attributed to the overlapping inflammatory pathways reflected by these markers and their strong correlation with lactate clearance, which emerged as a more robust independent predictor.

Moreover, patients with SAP demonstrated significantly higher in-hospital mortality compared to non-SAP patients, highlighting the critical need for early identification of high-risk cases. In this context, early assessment of lactate clearance may not only predict SAP development but also help guide timely clinical decisions, such as prioritizing ICU admission for patients at elevated risk. Incorporating lactate clearance into early management strategies could potentially improve patient outcomes by enabling prompt intensive monitoring and intervention.

Although multifactorial scoring systems such as BISAP and APACHE II are widely used for early risk stratification in acute pancreatitis, they have certain limitations. APACHE II, while highly sensitive, is complex and primarily designed for ICU patients, limiting its routine use in emergency settings[28]. BISAP offers a simpler alternative with high specificity but moderate sensitivity[29,30]. In contrast, lactate clearance provides a dynamic and readily available biomarker that reflects early tissue hypoperfusion and systemic inflammatory changes, offering potential advantages in rapid clinical decision-making.

However, it should be acknowledged that some studies have reported inconsistent findings regarding the prognostic value of lactate clearance. Zhou et al. indicated that while lactate levels were consistently associated with neurological outcomes after cardiac arrest, lactate clearance was less reliable[31]. Similarly, During et al. found that although admission and 12-

hour lactate levels predicted 30-day mortality, 12-hour lactate clearance did not show a significant prognostic value[32]. Furthermore, Emhoff and Messonnier emphasized that lactate clearance rates are highly dependent on multiple physiological and metabolic factors, potentially limiting their clinical applicability across different patient populations[33]. These discrepancies highlight the need for standardized protocols and multicenter validation studies before lactate clearance can be fully integrated into routine prognostic assessments for acute pancreatitis.

This study suggests that lactate clearance is a reliable biomarker for predicting SAP development, yet it should be evaluated alongside other inflammatory and metabolic markers in clinical decision-making. In clinical practice, serial lactate monitoring may be particularly useful for patients presenting with elevated initial lactate levels, early signs of systemic inflammation, or organ dysfunction at admission. Regular assessment of lactate clearance within the first 24 to 48 hours could help identify patients at higher risk of SAP progression who may benefit from closer monitoring, aggressive fluid resuscitation, and early ICU admission. The combination of lactate clearance with NLR, PLR, SII, SII/ALB, RDW, and AST/ALT ratios may enhance prognostic accuracy in patient management. Based on our findings, a composite scoring system incorporating lactate clearance, SII/ALB ratio, and RDW values could potentially improve early identification of high-risk SAP patients. Combining these parameters, which reflect tissue hypoxia, systemic inflammation, and hematological abnormalities respectively, may provide a more comprehensive assessment of disease severity and guide clinical decision-making more effectively. Prospective studies are needed to validate such an integrated risk model.

This study has some limitations. Primarily, its retrospective design restricts the ability to determine causal associations. Additionally, as the data were collected from a single center, the generalizability of the results may be limited. The assessment of lactate clearance was based on venous blood sampling, which might introduce slight variations compared to arterial measurements. Furthermore, although we considered key inflammatory and metabolic markers while evaluating the prognostic value of lactate clearance, other potential prognostic factors, such as genetic predispositions and advanced imaging findings, were not assessed. These limitations highlight the need for larger, prospective, multicenter studies to more comprehensively investigate these relationships and validate our findings.

In conclusion, our study demonstrates that reduced lactate clearance within the first 24 hours of admission is a strong independent predictor of SAP development. With a threshold of <40.9%, lactate clearance accurately predicted SAP with 81.9% sensitivity and 76.9% specificity. These findings suggest that early assessment of lactate clearance, particularly when combined with other inflammatory markers such as the SII/ALB ratio and RDW, may enhance early risk stratification and clinical decision-making in AP patients. Furthermore, a lactate clearance value of less than 40.9% within the first 24 hours may warrant early ICU admission considerations. Prospective, multicenter studies are warranted to validate these results and to develop integrated prognostic models incorporating lactate clearance into routine clinical practice.

Author Contributions: Concept/Design : BÇY, KK, BK, ETS, MY; Data acquisition: BÇY, KK, BK; Data analysis and interpretation: MY, BÇY, KK; Drafting manuscript: MY, BÇY, ETS, KK; Critical revision of manuscript: NÖM; Final approval and accountability: ETS, BÇY, KK, BK, MY; Technical or material support: BÇY, KK, BK, MY; Supervision: ETS, BÇY, MY; Securing funding (if available): n/a.
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