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Prognostic value of lactate, lactate clearance, CRP, procalcitonin, and clinical scoring systems in sepsis patients: A retrospective observational study

Sepsisli hastalarda laktat, laktat klirensi, CRP, prokalsitonin ve klinik puanlama sistemlerinin prognostik değeri: Retrospektif gözlemsel bir çalışma

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ABSTRACT

Sepsis is a critical health issue worldwide, associated with high mortality rates and significant healthcare burdens. Early identification and prognosis assessment of sepsis patients are essential for optimal management. Various biomarkers, including lactate, procalcitonin (PCT), and C-reactive protein (CRP), as well as clinical scoring systems such as the Acute Physiology and Chronic Health Evaluation II (APACHE II) and Sequential Organ Failure Assessment (SOFA), have been used to predict outcomes in sepsis patients. This study aimed to evaluate the prognostic effectiveness of lactate, lactate clearance, CRP, PCT, APACHE II, and SOFA scores in predicting mortality in sepsis patients.

A retrospective observational study was conducted on 118 adult patients diagnosed with sepsis and admitted to the intensive care unit (ICU) between January 2016 and January 2019. Patient demographics, comorbidities, admission lactate, CRP, and PCT levels, serial lactate measurements at 6, 12, and 24 hours, and corresponding lactate clearances were recorded. APACHE II and SOFA scores were calculated at admission. Statistical analyses, including ROC curve analysis and logistic regression, were performed to determine the prognostic significance of these variables in predicting 28-day mortality.

The overall 28-day mortality rate was 48.3%. Higher initial lactate levels were significantly associated with mortality ($p<0.001$), with an optimal cut-off value of ≥2.2 mmol/L, yielding a sensitivity of 82.5% and specificity of 85.2%. The 6-hour lactate level was also a strong predictor of mortality (AUC 0.839, $p<0.001$). Lactate clearance at 6, 12, and 24 hours demonstrated weaker prognostic value compared to initial lactate. Higher APACHE II (≥22) and SOFA (≥8) scores were significantly correlated with mortality ($p<0.001$). Logistic regression analysis revealed that male gender (OR: 6.53, $p=0.018$), hypotension at admission (OR: 29.78, $p=0.011$), initial lactate (OR: 11.95, $p=0.004$), and vasopressor requirement (OR: 114.98, $p=0.007$) were independent predictors of mortality.

In conclusion; lactate and its serial measurements were found to be the most reliable biomarkers for predicting mortality in sepsis patients, with superior sensitivity and specificity compared to lactate clearance, CRP, and PCT. APACHE II and SOFA scores were also significant prognostic indicators. A comprehensive approach integrating multiple biomarkers and clinical scoring systems is recommended for optimal risk stratification in sepsis management.

Keywords: Sepsis; Lactate; Biomarkers; APACHE II; SOFA

ÖZET

Sepsis, yüksek ölüm oranları ve önemli sağlık yükleriyle ilişkili, dünya çapında kritik bir sağlık sorunudur. Sepsis hastalarının erken teşhisi ve prognoz değerlendirmesi, optimum yönetim için esastır. Laktat, prokalsitonin (PCT) ve C-reaktif protein (CRP) dahil olmak üzere çeşitli biyobelirteçler ve Akut Fizyoloji ve Kronik Sağlık Değerlendirmesi II (APACHE II) ve Sıralı Organ Yetmezliği Değerlendirmesi (SOFA) gibi klinik puanlama sistemleri, sepsis hastalarında sonuçları tahmin etmek için kullanılmıştır. Bu çalışma, laktat, laktat klirensi, CRP, PCT, APACHE II ve SOFA puanlarının sepsis hastalarında mortaliteyi tahmin etmedeki prognostik etkinliğini değerlendirmeyi amaçlamıştır.

Ocak 2016 ile Ocak 2019 arasında sepsis tanısı konulan ve yoğun bakım ünitesine (YBÜ) yatırılan 118 yetişkin hasta üzerinde retrospektif bir gözlemsel çalışma yürütüldü. Hasta demografisi, eşlik eden hastalıklar, yatış laktat, CRP ve PCT düzeyleri, 6, 12 ve 24. saatlerde seri laktat ölçümleri ve karşılık gelen laktat klirensleri kaydedildi. APACHE II ve SOFA skorları yatışta hesaplandı. Bu değişkenlerin 28 günlük mortaliteyi tahmin etmedeki prognostik önemini belirlemek için ROC eğrisi analizi ve lojistik regresyon dahil istatistiksel analizler yapıldı.

Genel 28 günlük mortalite oranı %48,3 idi. Daha yüksek başlangıç laktat düzeyleri mortalite ile önemli ölçüde ilişkiliydi ($p<0,001$), optimum kesme değeri ≥2,2 mmol/L idi ve %82,5 duyarlılık ve %85,2 özgüllük sağladı. 6 saatlik laktat seviyesi de mortalitenin güçlü bir öngörücüsüydü (AUC 0,839, $p<0,001$). 6, 12 ve 24. saatlerdeki laktat klirensi, başlangıç laktatına kıyasla daha zayıf prognostik değer gösterdi. Daha yüksek APACHE II (≥22) ve SOFA (≥8) skorları mortalite ile önemli ölçüde ilişkiliydi ($p<0,001$). Lojistik regresyon analizi, erkek cinsiyetinin (OR: 6,53, $p=0,018$), kabul sırasında hipotansiyonun (OR: 29,78, $p=0,011$), başlangıç laktatının (OR: 11,95, $p=0,004$) ve vazopressör gereksiniminin (OR: 114,98, $p=0,007$) mortalitenin bağımsız öngörücüleri olduğunu ortaya koydu.

Laktat ve seri ölçümlerinin sepsis hastalarında mortaliteyi tahmin etmede en güvenilir biyobelirteçler olduğu, laktat klirensi, CRP ve PCT ile karşılaştırıldığında üstün duyarlılık ve özgüllüğe sahip olduğu bulundu. APACHE II ve SOFA skorları da önemli prognostik göstergelerdi. Sepsis yönetiminde optimum risk sınıflandırması için birden fazla biyobelirteç ve klinik puanlama sistemini entegre eden kapsamlı bir yaklaşım önerilir.

Anahtar kelimeler: Sepsis; Lactat; Biyomarker; APACHE II; SOFA

INTRODUCTION

Sepsis is a life-threatening syndrome characterized by a dysregulated immune response to infection, leading to multi-organ failure and high mortality rates (1). It remains a global health challenge, with an increasing incidence despite advances in intensive care medicine. According to recent estimates, sepsis affects approximately 31.5 million people annually, resulting in nearly 5.3 million deaths worldwide (2). The incidence of sepsis continues to rise due to an aging population, increased use of immunosuppressive therapies, and the widespread application of invasive medical procedures (3). Despite improvements in supportive care, mortality rates remain unacceptably high, ranging between 30% and 50% in ICU settings (1,4). Given the complexity of sepsis pathophysiology, early identification of high-risk patients and precise prognostication are essential for timely therapeutic interventions and improved patient outcomes.

Biomarkers play a critical role in sepsis diagnosis, severity assessment, and prognostication. Lactate, a byproduct of anaerobic metabolism, is widely recognized as an indicator of tissue hypoxia and impaired perfusion (5). Several studies have demonstrated that elevated lactate levels are associated with increased mortality in sepsis patients, making lactate an important prognostic biomarker (6–8). Additionally, lactate clearance, defined as the rate of lactate reduction over time, has been proposed as a surrogate marker for treatment response and organ function recovery (9). However, the prognostic significance of lactate clearance compared to initial lactate levels remains controversial, necessitating further research (6).

Alongside lactate, other inflammatory biomarkers such as C-reactive protein (CRP) and procalcitonin (PCT) have been widely investigated for their roles in sepsis management. CRP, an acute-phase protein synthesized by the liver in response to infection and inflammation, has been used as a diagnostic and prognostic marker, though its specificity for sepsis remains debated (10,11). PCT, a precursor of calcitonin, is considered more specific for bacterial infections and has been shown to correlate with disease severity and mortality risk (12,13). However,

the relative prognostic value of CRP and PCT compared to lactate and lactate clearance remains uncertain. In addition to biomarkers, clinical scoring systems such as the Acute Physiology and Chronic Health Evaluation II (APACHE II) and Sequential Organ Failure Assessment (SOFA) scores have been utilized to assess disease severity and predict mortality in sepsis patients (14,15). These scoring systems provide objective measures of organ dysfunction, but their predictive accuracy varies based on patient populations and healthcare settings (16,17). While previous studies have established the prognostic utility of APACHE II and SOFA scores, their comparative effectiveness alongside biomarkers such as lactate, CRP, and PCT requires further validation.

This study aimed to evaluate the prognostic effectiveness of lactate, lactate clearance, CRP, and PCT levels in predicting 28-day mortality in ICU patients diagnosed with sepsis. Additionally, the study sought to compare the predictive performance of these biomarkers with established clinical scoring systems (APACHE II and SOFA). The primary hypothesis was that elevated lactate and reduced lactate clearance are stronger predictors of mortality than CRP and PCT levels. A secondary hypothesis was that APACHE II and SOFA scores provide valuable prognostic information, but their predictive accuracy may be enhanced when combined with lactate-based parameters. By investigating these associations, the study aims to contribute to the ongoing effort to refine risk stratification and guide clinical decision-making in sepsis management.

MATERIAL and METHOD

Study Design

This study was designed as a retrospective observational cohort study evaluating the prognostic value of lactate, lactate clearance, CRP, PCT, and clinical scoring systems (APACHE II and SOFA) in predicting mortality among adult patients diagnosed with sepsis and admitted to the intensive care unit (ICU). The study followed the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) guidelines for observational studies to ensure methodological rigor and transparency (Supp. S1). Given the retrospective nature of the study, no interventions or randomization were performed.

Setting and Participants

The study was conducted at the Anesthesiology and Reanimation Intensive Care Unit of Izmir Katip Çelebi University Atatürk Training and Research Hospital. Data were collected from January 1, 2016, to December 31, 2018, using electronic health records, archive files, and ICU patient charts. This ICU is a tertiary referral center, providing care to critically ill patients, including those admitted from the emergency department, internal medicine wards, and surgical units. The ICU is equipped with advanced hemodynamic monitoring, mechanical ventilation, and continuous renal replacement therapy (CRRT) capabilities, ensuring comprehensive critical care support.

Inclusion and Exclusion Criteria

Patients were retrospectively identified through the hospital information management system using the Sepsis-3 diagnostic criteria (1). Sepsis was defined as a life-threatening organ dysfunction caused by a dysregulated host response to infection, with organ dysfunction identified by an increase of ≥2 points in the SOFA score.

Inclusion Criteria: Patients aged ≥18 years; Diagnosed with sepsis based on Sepsis-3 criteria; Admitted to the ICU between January 2016 and December 2018; Availability of laboratory and clinical data required for the study.

Exclusion Criteria: Patients aged <18 years; Pregnant women; Patients with advanced malignancies receiving only palliative care; Patients with terminal-stage organ failure (end-stage liver disease, end-stage renal disease requiring dialysis prior to ICU admission); Do-not-resuscitate (DNR) orders prior to ICU admission; Patients with incomplete or missing laboratory data.

Variables, Potential Confounders and Effect Modifiers

The study aimed to evaluate lactate, lactate clearance, CRP, PCT, and clinical scoring systems (APACHE II and SOFA) as predictors of 28-day mortality in sepsis patients. Primary Outcome: 28-day mortality, defined as all-cause mortality occurring within 28 days of ICU admission.

Independent Variables (Predictors): Lactate levels at ICU admission and serial measurements at 6, 12, and 24 hours; CRP and PCT levels at ICU admission; APACHE II and SOFA scores, calculated within the first 24 hours of ICU admission; Demographic variables: age, gender, and presence of comorbidities; Clinical parameters: presence of hypotension, vasopressor requirement, renal function (creatinine, blood urea nitrogen), and hematologic parameters; Lactate clearance, calculated at 6, 12, and 24 hours using the formula:

Lactate Clearance = (Initial Lactate − Lactate at Timepoint) /Initial Lactate × 100

The following factors were considered as potential confounders: Comorbid conditions: Diabetes mellitus (DM), hypertension (HT), coronary artery disease (CAD), chronic obstructive pulmonary disease (COPD), chronic renal failure (CRF), and malignancy; Severity of sepsis: Based on APACHE II and SOFA scores; Hemodynamic instability: Defined by the need for vasopressors.

Data Sources and Measurement

All data were extracted from electronic medical records and archived ICU patient files. Laboratory data (lactate, CRP, PCT, creatinine, bilirubin, sodium, potassium, hemoglobin, platelet count, and white blood cell count) were collected from hospital laboratory information systems. Vital signs, use of vasopressors, and mechanical ventilation status were retrieved from ICU charts. APACHE II and SOFA scores were calculated manually using standard scoring guidelines. Data extraction was performed by two independent critical care physicians, and discrepancies were resolved by a third investigator to ensure accuracy.

To minimize selection bias, the study included all eligible sepsis patients admitted during the study period. Information bias was addressed by ensuring that all laboratory measurements followed standardized hospital protocols. Observer bias in scoring systems (APACHE II, SOFA) was mitigated by having two independent physicians verify scores.

Study Size

The sample size (n=118) was determined based on available ICU admissions meeting the inclusion criteria during the study period. As a retrospective study, no prior sample size calculation was performed. However, post-hoc power analysis indicated that the study had adequate statistical power (≥80%) to detect significant differences in mortality outcomes based on lactate levels and APACHE II scores.

Statistical Analyses

The data obtained in the study were analyzed using Rstudio version 2024.09.0+375 (Posit Software, Boston, USA) and Stata 15 software (StataCorp, Texas, USA). Continuous variables (lactate levels, CRP, PCT, APACHE II, and SOFA scores) were summarized using mean ± standard deviation (SD) or median with interquartile range (IQR) based on normality distribution (assessed using the Shapiro-Wilk test). Categorical variables (e.g., mortality, gender, comorbidities) were reported as frequencies and percentages.

Kruskal-Wallis test was used to compare numerical variables across different groups. Chi-square (χ^2) test was used for categorical variables. Receiver operating characteristic (ROC) curve analysis was performed to determine the predictive accuracy of lactate, lactate clearance, CRP, PCT, APACHE II, and SOFA scores for mortality. Optimal cut-off values were determined using Youden's index. Logistic regression analysis was conducted to identify independent predictors of mortality, adjusting for potential confounders. Results were reported as odds ratios (OR) with 95% confidence intervals (CI). A p-value <0.05 was considered statistically significant. Patients with missing lactate, CRP, or PCT values were excluded from the study to ensure data integrity. Sensitivity analyses were conducted by imputing missing values using multiple imputation techniques, but no significant impact on the primary outcomes was observed.

Subgroup analysis was performed based on lactate levels (<2.2 mmol/L vs. ≥2.2 mmol/L), SOFA scores (<8 vs. ≥8), and APACHE II scores (<22 vs. ≥22). Sensitivity analysis was conducted by excluding outliers in lactate and PCT values to assess robustness.

RESULTS

Study Flow and Participants

Between January 1, 2016, and December 31, 2018, a total of 118 patients diagnosed with sepsis based on Sepsis-3 criteria were included in this retrospective cohort study at Izmir Katip Çelebi University Atatürk Training and Research Hospital's ICU. Of these, 59 (50.0%) were male and 59 (50.0%) were female. The mean age was 69.05 ± 14.72 years (range: 18–94 years).

Descriptive Characteristics of Study Population

Among the 118 patients, 91.5% (n=108) had comorbid conditions, with hypertension 42.4% being the most common. Other prevalent comorbidities included diabetes mellitus (34.7%), coronary artery disease (30.5%), chronic renal failure (16.9%), chronic obstructive pulmonary disease (17.8%), and malignancy (22.9%). The 28-day mortality rate was 48.3% (n=57). There was no significant difference in mortality based on gender or age (p>0.05). No significant relationship was observed between comorbidities and mortality (p>0.05) (Table 1).

Upon examining the hematological parameters of the patients, no statistically significant difference was observed in terms of hemoglobin, hematocrit, WBC, or platelet values between the mortality and survival groups. However, when analyzing the biochemical parameters (Na, K, creatinine, bilirubin) and pH values, notable differences were identified. In patients who did not survive, the initial CRP and PCT values were found to be significantly higher compared to those who survived (p < 0.01). Higher lactate levels at ICU admission and over 24 hours were significantly associated with increased mortality (p<0.001) (Table 2).

Table 1: Demographic and clinical characteristics of the study population.

Characteristic	All Patients (n=118)	Survived (n=61)	Deceased (n=57)	p-value
Age (years)	70 [62-80]	71 [62-80]	68 [60-77]	0.359
Male	59 (50.0)	28 (45.9)	31 (54.4)	0.357
No Comorbidities	10 (8.5)	7 (11.5)	3 (5.3)	0.278
DM	41 (34.7)	24 (39.3)	17 (29.8)	0.278
HT	50 (42.4)	25 (41.0)	25 (43.9)	0.752
CRF	20 (16.9)	8 (13.1)	12 (21.1)	0.251
CAD	36 (30.5)	21 (34.4)	15 (26.3)	0.339
COPD	21 (17.8)	12 (19.7)	9 (15.8)	0.582
Cancer	27 (22.9)	10 (16.4)	17 (29.8)	0.083
Other Comorbidities	49 (41.5)	28 (45.9)	21 (36.8)	0.318

CAD: Coronary Artery Disease; COPD: Chronic Obstructive Pulmonary Disease; CRF: Chronic Renal Failure; DM: Diabetes Mellitus; HT: Hypertension.
* Variables conforming to numeric presented as median [25-75 IQR], and categorical variables presented as number (%).
** Mann Whitney U test employed for analysis of variables not conforming to normal distribution, and chi-square test or Fisher's exact test used to determine differences between groups for categorical variables.

Table 2: Laboratory parameter, score and mortality comparison.

Laboratory Parameter	Survived (n=61)	Deceased (n=57)	p-value
pH	7.40 ± 0.08	7.34 ± 0.10	< 0.001
CRP	12.0 [7.9-20.3]	18.7 [12.8-24.7]	0.040
PCT	1.29 [0.42-12.1]	9.81 [2.90-28.2]	0.001
WBC (x10³/µL)	14.8 ± 6.9	15.5 ± 9.8	0.897
Hemoglobin (g/dL)	10.5 ± 1.9	10.2 ± 1.8	0.475
Hematocrit (%)	33.2 ± 5.5	32.1 ± 5.6	0.371
Platelet (x10³/µL)	258 ± 141	228 ± 149	0.147
Creatinine (mg/dL)	1.08 [0.72-2.38]	2.17 [1.16-3.47]	0.019
Bilirubin (mg/dL)	0.68 [0.49-1.45]	0.96 [0.52-2.78]	0.110
Sodium (mmol/L)	138.5 ± 6.3	139.3 ± 8.1	0.779
Potassium (mmol/L)	3.97 ± 0.70	4.30 ± 0.90	0.017
Lactate Levels			
Admission (mmol/L)	1.3 [0.9-1.9]	3.0 [2.3-4.3]	<0.001
6-hour	1.3 [1.0-1.8]	2.5 [2.0-3.6]	<0.001
12-hour	1.6 [1.0-1.9]	2.3 [1.7-3.8]	<0.001
24-hour	1.2 [1.0-1.5]	2.1 [1.5-4.1]	<0.001
Score			
APACHE II	17 [15-19]	25 [21-28]	<0.001
SOFA	5 [4-6]	9 [7-12]	<0.001

APACHE II: Acute Physiology and Chronic Health Evaluation II; CRP: C-reactive Protein; PCT: Procalcitonin; SOFA: Sequential Organ Failure Assessment; WBC: White Blood Cell.
* Variables conforming to normal distribution presented as mean ± standard deviation, and variables not conforming to normal distribution presented as median [interquartile range].
** Independent samples t-test employed for analysis of variables conforming to normal distribution, and Mann-Whitney U test for variables not conforming to normal distribution.

Receiver Operating Characteristic (ROC) analysis identified admission lactate (AUC = 0.867, sensitivity 82.5%, specificity 85.2%) as the strongest predictor of mortality, followed by 6-hour lactate (AUC = 0.839, sensitivity 77.2%, specificity 85.7%). Following the ROC analysis, the optimal cut-off point for initial lactate was determined to be ≥2.2 mmol/L. When patients were categorized based on an initial lactate level of ≥2.2 mmol/L, a statistically significant difference in mortality was observed between the groups. Among clinical scoring systems, SOFA (AUC = 0.806) and APACHE II (AUC = 0.784) demonstrated strong discriminatory power, with sensitivities of 70.2% and 68.4%, respectively. The statistical analysis identified a significant difference between the two groups based on the optimal cut-off value of SOFA ≥ 8 ($p < 0.001$), and optimal cut-off value of the APACHE II score ≥ 22 ($p<0.001$) (Table 3).

Inflammatory biomarkers procalcitonin (PCT ≥3 ng/mL, AUC = 0.697, $p<0.001$) and C-reactive protein (CRP ≥12.58 mg/dL, AUC = 0.610, $p=0.041$) were also associated with mortality, though their predictive value was lower. Lactate clearance at 6, 12, and 24 hours showed limited predictive ability (AUC <0.64, $p>0.01$), suggesting that static lactate values are more reliable for mortality prediction than clearance trends (Table 3).

Multivariate logistic regression showed male gender, hypotension, vasopressor requirement, higher admission lactate, and APACHE II scores were independent predictors of mortality. Lactate clearance at 6, 12, and 24 hours was not statistically significant in predicting mortality ($p>0.05$) (Table 4).

Table 3: ROC analysis results.

Parameter	AUC	95% CI	Sensitivity	Specificity	p-value
Admission Lactate	0.867	0.799 - 0.935	82.5%	85.2%	<0.001
SOFA Score	0.806	0.728 - 0.885	70.2%	83.6%	<0.001
APACHE II Score	0.784	0.699 - 0.869	68.4%	82.0%	<0.001
WBC	0.493	0.387 - 0.599	84.2%	6.6%	0.899
CRP	0.610	0.507 - 0.713	77.2%	49,2%	0.041
PCT	0.697	0.592 - 0.803	76.2%	66,7%	<0.001
6-hour Lactate	0.839	0.762 - 0.915	77.2%	85.7%	<0.001
12-hour Lactate	0.796	0.715 - 0.878	60.7%	82.8%	<0.001
24-hour Lactate	0.798	0.714 - 0.881	74.1%	75.4%	<0.001
6-hour Lactate Clerens	0.633	0.535 - 0.731	54.4%	21.4%	0.010
12-hour Lactate Clerens	0.623	0.526 - 0.719	53.6%	22.4%	0.013
24-hour Lactate Clerens	0.614	0.515 - 0.714	42.6%	34.4%	0.023

APACHE II: Acute Physiology and Chronic Health Evaluation II; CRP: C-reactive Protein; PCT: Procalcitonin; SOFA: Sequential Organ Failure Assessment; WBC: White Blood Cell.

Table 4: Logistic regression model.

Variable	OR	95% CI	p-value
Male Gender	6.53	1.38 – 30.75	0.018
Hypotension	29.78	2.14 – 412.97	0.011
Vasopressor Requirement	114.98	3.55 – 3718.23	0.007
Admission Lactate	11.95	2.19 – 65.17	0.004
APACHE II Score	1.29	1.10 – 1.53	0.002

APACHE II: Acute Physiology and Chronic Health Evaluation II

DISCUSSION

Sepsis remains a major global health challenge, with high mortality rates despite advances in intensive care management. This study aimed to evaluate the prognostic value of admission lactate, serial lactate measurements, lactate clearance at different time points, CRP, PCT, SOFA, and APACHE II scores in sepsis patients admitted to the ICU. The 28-day mortality rate in this study was 48.3%, consistent with findings from previous studies reporting mortality rates between 30–50% in septic patients (1,4). Additionally, a significant association was found

between higher admission lactate levels and increased mortality. The optimal cut-off for admission lactate (≥2.2 mmol/L) demonstrated high sensitivity (82.5%) and specificity (85.2%) in predicting mortality. This result aligns with prior research indicating that elevated lactate levels at admission are strongly associated with sepsis severity and adverse outcomes (6–8,18). Furthermore, 6-hour lactate levels also exhibited a strong predictive value (AUC = 0.839), showing the importance of serial lactate monitoring in early risk stratification. In contrast, lactate clearance at 6, 12, and 24 hours was not found to be a statistically significant predictor of mortality. While prior studies have suggested that lactate clearance is an important parameter for guiding resuscitation and predicting outcomes (3,19–21), our findings indicate that single lactate measurements, particularly at admission and 6 hours, are stronger predictors of mortality than clearance-based measures. Both SOFA and APACHE II scores were significantly higher in patients who did not survive, with cut-off values of ≥8 for SOFA (AUC = 0.806) and ≥22 for APACHE II (AUC = 0.784). These findings confirm the clinical utility of these scoring systems in sepsis prognosis. The observed higher mortality risk among male patients (OR = 6.53, p=0.018) is consistent with prior studies reporting worse sepsis outcomes in men compared to women (22,23). Among inflammatory biomarkers, PCT levels were significantly higher in non-survivors, with an optimal cut-off of ≥3 ng/mL (sensitivity: 76.1%, specificity: 66.7%), supporting the role of PCT as a prognostic marker in sepsis. However, CRP levels were only weakly predictive of mortality (AUC = 0.610), suggesting limited utility in prognostication when used alone. The results of this study support the clinical utility of admission lactate and 6-hour lactate levels as strong predictors of mortality in sepsis patients. Higher APACHE II and SOFA scores were also strongly associated with increased mortality risk, reinforcing their continued role in ICU prognostic assessment.

Lactate has been extensively studied as a marker of tissue hypoxia and anaerobic metabolism in sepsis, and elevated levels have been associated with increased mortality (6–8). Our findings are consistent with existing literature, showing that higher admission lactate levels were significantly associated with mortality (p<0.001). Patients who did not survive had a mean admission lactate of 3.896 mmol/L, whereas survivors had a significantly lower mean of 1.544 mmol/L. This supports prior studies where lactate levels above 4 mmol/L were strongly predictive of poor outcomes (18,24). Additionally, serial lactate measurements at 6, 12, and 24 hours remained significantly higher in non-survivors, reinforcing its role as a dynamic prognostic tool. Prior studies have indicated that persistent hyperlactatemia and failure to clear lactate correlate with poor prognosis (19,20). Our findings align with these observations, indicating that higher 6-hour lactate levels (AUC = 0.839) were the second strongest predictor of mortality after admission lactate.

Although lactate clearance has been proposed as a better prognostic indicator than static lactate levels, our study found that 6-hour, 12-hour, and 24-hour lactate clearance values were not statistically significant in predicting mortality (p>0.05) (9,21,25). This contrasts with findings from Nguyen et al., who reported that lactate clearance >10% within the first 6 hours was associated with improved survival (9,25). One possible explanation for this discrepancy is variability in resuscitation strategies, treatment protocols, and patient heterogeneity, as well as differences in sepsis severity and ICU treatment protocols across studies. Additionally, our study was retrospective and single-centered, which may have introduced selection biases affecting lactate clearance outcomes. Despite the limited predictive value of lactate clearance, our study showed that patients with lower clearance values had poorer outcomes, similar to prior research suggesting that lactate clearance below 20% within 6–12 hours is associated with increased mortality (21,26). However, with these findings, due to its low specificity and sensitivity, lactate clearance should not be used in isolation but rather in combination with other markers. Our study also highlights the need for careful interpretation of lactate trends. Although lactate clearance has been widely studied, our findings suggest that clinicians should prioritize absolute lactate levels over clearance rates when assessing mortality risk. This is particularly relevant in settings where aggressive resuscitation protocols are not consistently applied, as lactate clearance may be affected by multiple confounding factors, including renal and hepatic dysfunction (19,20,26).

Clinical scoring systems remain valuable tools for mortality prediction in critically ill patients. Among them, the SOFA and APACHE II scores are widely used to evaluate organ dysfunction and disease severity. Our study demonstrated that higher SOFA and APACHE II scores at ICU admission were significantly associated with mortality (p<0.001), in line with previous research (16,17,27). These findings align with prior studies where APACHE II scores >27 were linked to significantly higher mortality rates (17). Similarly, the SOFA score has been consistently associated with mortality risk, reinforcing its utility in early risk stratification (28–30). However, serial SOFA score assessments may provide more precise prognostic value than a single ICU admission score with future studies. Inflammatory biomarkers such as PCT and CRP have been extensively studied in sepsis but remain controversial in their prognostic utility. Our study found that PCT levels at ICU admission were significantly higher in non-survivors compared to survivors (p<0.001). This supports previous findings that elevated PCT levels (>10 ng/mL) are associated with

organ failure and increased short-term mortality (31,32). However, PCT alone is not a definitive predictor and should be interpreted in conjunction with clinical findings and other biomarkers. Similarly, CRP levels were higher in non-survivors, but its predictive value was lower than lactate or scoring systems (AUC = 0.61, p=0.040). Prior studies have suggested that serial CRP measurements may be more valuable than single measurements in tracking sepsis progression and treatment response (33,34). CRP had limited clinical utility, suggesting that PCT should be preferred over CRP for sepsis prognosis when available (31,32,35). Our findings align with these observations, indicating that while CRP can provide some prognostic insight, it lacks the sensitivity and specificity required for robust mortality prediction.

This study has several limitations that must be considered when interpreting the findings. Firstly, this study was conducted in a single ICU, which may limit the generalizability of the results to other populations with different sepsis management protocols. Also, the retrospective nature may introduce selection bias and incomplete data capture for some variables. The study included 118 patients as small sample size, which, while sufficient for detecting significant trends, may be underpowered for certain subgroup analyses. A larger, multi-center study would provide more robust conclusions regarding the predictive accuracy of the evaluated biomarkers. Additionally, patients were admitted from different clinical settings, including emergency departments and hospital wards, which may have led to variations in initial resuscitation strategies. Standardized sepsis management protocols may not have been implemeted uniformly applied across all cases, potentially affecting the lactate clearance results. The study focused on 28-day mortality as limited folllow-up period, which captures short-term outcomes but does not account for long-term survival and functional recovery. Future studies should include longer follow-up periods to assess post-sepsis complications and quality of life. While lactate, CRP, and PCT were measured at admission, serial PCT and CRP measurements were not consistently available, limiting the ability to assess their dynamic changes over time. Despite these limitations, this study has several notable strengths. It utilizes a rigorous statistical approach, including ROC analysis and logistic regression, to validate the predictive performance of multiple biomarkers and clinical scores. The comprehensive evaluation of lactate dynamics, inflammatory markers, and established ICU severity scores provides clinically relevant insights into sepsis prognosis. Additionally, the findings contribute to evidence-based decision-making in ICU settings, supporting the integration of admission lactate, serial lactate levels, and severity scoring systems into routine risk stratification protocols for sepsis patients.

Conclusion

This study confirms the strong prognostic value of admission lactate, 6-hour lactate levels, and ICU severity scores (SOFA and APACHE II) in predicting sepsis-related mortality. While lactate clearance was not found to be a significant predictor, absolute lactate levels at ICU admission and early post-admission periods were highly predictive of poor outcomes. Among inflammatory markers, PCT was moderately predictive of mortality, whereas CRP showed limited prognostic utility. These findings underscore the importance of integrating multiple clinical parameters (including lactate, SOFA, APACHE II, and PCT) for optimal sepsis risk stratification.

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Contributorship statement

M.A.C. contributed to the study conception and design, data collection, analysis, and manuscript drafting. E.N.G. contributed to data collection, interpretation, critical revision of the manuscript. Both authors read and approved the final version of the manuscript.

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Competing interests

None declared.

Ethics approval and consent to participate

Approval was obtained from the Non-Interventional Ethics Committee of Izmir Katip Celebi University Faculty of Medicine. Informed consent was obtained from the first-degree relatives of the patients.

Consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests.

Data availability statement

All data necessary to support the protocol are available upon reasonable request.

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