

Prognostic significance of early lactate clearance in patients with suspected infection admitted to the intensive care unit from the emergency department

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Cite this article: Taştumur Ş, Demir E. Prognostic significance of early lactate clearance in patients with suspected infection admitted to the intensive care unit from the emergency department. *Intercont J Emerg Med.* 2026;4(1):13-17.

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Received: 04/02/2026

Accepted: 04/03/2026

Published: 07/03/2026

ABSTRACT

Aims: To evaluate the association between early lactate clearance and short-term outcomes in patients admitted to the intensive care unit (ICU) from the emergency department with suspected infection.

Methods: This single-center, retrospective observational study included adult patients admitted to the internal medicine ICU between January 1, 2023 and June 30, 2025. Serum lactate levels measured at admission and approximately 6 hours later were used to calculate lactate clearance. Patients were stratified into two groups based on lactate clearance: inadequate (<20%) and adequate (≥20%). The primary outcome was 28-day all-cause mortality.

Results: Among the 117 patients analyzed, those with inadequate lactate clearance had significantly higher 28-day mortality than those with adequate clearance (p=0.025). Inadequate lactate clearance was also associated with older age, whereas APACHE II scores, routine biochemical parameters and arterial blood gas values did not differ significantly between groups.

Conclusion: Early lactate clearance was associated with short-term mortality in critically ill patients admitted from the emergency department with suspected infection. Serial lactate assessment may provide complementary prognostic information beyond baseline severity scores and routine laboratory findings.

Keywords: Lactate clearance, intensive care unit, suspected infection, mortality, emergency department

INTRODUCTION

Patients admitted to the intensive care unit (ICU) from the emergency department with suspected infection represent a clinically heterogeneous population characterized by variable disease severity and a substantial risk of adverse outcomes. Early identification of individuals at increased risk is a key challenge in critical care, especially during the initial phase of ICU admission when resuscitation and management strategies are being implemented.¹

Serum lactate serves as a marker of tissue hypoperfusion and metabolic stress in critically ill patients. Elevated lactate concentrations are associated with increased mortality; however, a single measurement offers limited insight into the dynamic response to initial treatment.²

Changes in lactate levels, known as lactate kinetics or clearance, reflect the physiologic response to illness. Evidence suggests that lactate clearance during the initial hours of illness has greater prognostic value than baseline lactate measurements, supporting its use in early risk assessment.³

Most research on lactate kinetics has focused on patients with sepsis or septic shock. In contrast, limited data exist on the prognostic significance of lactate clearance in ICU patients with suspected infection, particularly in clinical practice.⁴

This study considers the relationship between lactate clearance within the first 6 hours and clinical outcomes in ICU patients admitted from the emergency department with suspected infection.

METHODS

This study was conducted with the approval of the Ethics Committee of the Health Sciences Researches Center at Sivas Cumhuriyet University (Date: 08.01.2026, 2026-01/57). All procedures were carried out in accordance with the ethical rules and the principles of the Declaration of Helsinki.

This study was designed as a single-center, retrospective, observational cohort study. Data were obtained from the electronic medical records of patients admitted to the

Emergency Department of Sivas Cumhuriyet University Faculty of Medicine Hospital and subsequently transferred to the Internal Medicine ICU.

The study population included adults admitted between January 1, 2023 and June 30, 2025, with suspected infection. Suspected infection was defined as a clinical presentation, such as respiratory symptoms with imaging infiltrates or urinary symptoms with pyuria, that prompted the attending emergency physician to initiate empirical antibiotic therapy. To ensure a standardized and objective triage process, the final decision on ICU admission was made by the investigating Internal Medicine specialist in accordance with established institutional protocols. These protocols prioritize patients presenting with acute organ dysfunction or those requiring advanced monitoring and life-sustaining interventions, such as vasopressor support or mechanical ventilation, regardless of the specific pathogen. This recruitment strategy intentionally prioritized a pragmatic, real-world triage model over formal sepsis-3 criteria, recognizing that intensive care management often commences before definitive microbiological confirmation is available.

To be included, patients had to meet all of the following criteria: I) Admission to the internal medicine ICU from the emergency department with suspected infection or sepsis. II) An initial serum lactate measured before or immediately after ICU admission. III) At least one more measurement, about 6 hours (± 2 hours) after the first. Patients were excluded if: I) their ICU stay was less than 6 hours. II) Serial lactate measurements were missing. III) Baseline clinical or laboratory data were incomplete. Additionally, to ensure that lactate kinetics primarily reflected the response to infection rather than alternative pathologies, patients with non-infectious conditions known to cause significant hyperlactatemia, such as major trauma, acute mesenteric ischemia or primary metabolic disorders, were excluded during the initial specialist-led triage. This rigorous selection process was maintained to minimize diagnostic uncertainty regarding the etiology of elevated lactate levels at presentation. The detailed process of patient screening, including specific reasons for exclusion and the subsequent stratification into study groups, is illustrated in the patient flow chart (Figure).

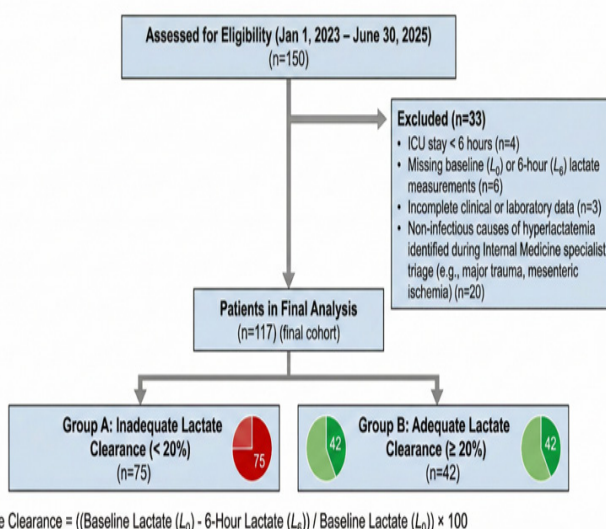


Figure. Patient enrollment and study flow chart. The diagram illustrates the standardized triage and selection process for patients admitted with suspected infection, including the systematic exclusion of non-infectious causes of hyperlactatemia

Serum lactate was first measured at emergency department presentation or ICU admission. A repeat measurement was taken about 6 hours later, allowing a ± 2 -hour tolerance window. If multiple lactate values were within the time window, the value closest to the target time was used in the analysis.

Lactate clearance (%) was calculated according to the formula previously described in the literature:

$$\text{"Lactate clearance"} = (L_0 - L_6) / L_0 \times 100$$

where L_0 represents the baseline serum lactate level and L_6 represents the serum lactate level measured approximately 6 hours later.⁵

Patients were grouped by lactate clearance, using cutoffs from previous studies on critically ill patients. Lactate clearance of less than 20% was considered inadequate. Clearance of 20% or higher was considered adequate.^{5,6}

Patients in whom the 6-hour lactate level exceeded the baseline value ($L_6 > L_0$) were considered to have negative lactate clearance and were included in the inadequate lactate clearance group, consistent with prior methodological strategies.⁷

Demographic data (age, gender), clinical characteristics and ICU treatment variables were pulled from medical records. Indicators of disease severity included the need for vasopressors within the first 6 hours (yes/no) and the APACHE II score. Source of infection, comorbidities and 28-day mortality were also recorded.

Baseline laboratory parameters were defined as the first available tests collected within 24 hours after ICU admission. These included: serum albumin, electrolytes (sodium, potassium, chloride, magnesium, calcium), blood urea nitrogen, creatinine, hemoglobin, white cell and platelet counts, CRP and arterial blood gas values (pH, $p\text{CO}_2$, bicarbonate, base excess [BE] and lactate).

Comorbidities were classified based on the presence of coronary artery disease, chronic kidney disease, chronic heart failure, active malignancy or liver cirrhosis and were summarized as major comorbidity (yes/no).

The primary outcome was 28-day all-cause mortality, defined as death occurring within 28 days following ICU admission.

Statistical Analysis

The data analyses were performed using IBM SPSS Statistics version 27.0 (IBM Corp., Armonk, NY, USA). Continuous variables were assessed for normality and are presented as mean \pm standard deviation or median (interquartile range), as appropriate. Categorical variables are expressed as counts and percentages. Between-group comparisons were conducted using the independent sample t-test or Mann-Whitney U test for continuous variables and the Chi-square test for categorical variables. Associations with secondary outcomes were analyzed using appropriate parametric or non-parametric methods. A two-sided p-value < 0.05 was considered statistically significant.

RESULTS

A total of 117 patients admitted to the ICU from the emergency department with suspected infection were

included in the final analysis. The study cohort was evaluated for lactate clearance status and categorized into inadequate (<20%) and adequate (\geq 20%) groups. Demographic characteristics, laboratory parameters and clinical outcomes were compared between these groups.

The most common suspected source of infection was the respiratory tract (88,9%). Procedure-related (4.3%), urinary tract (3.4%), bloodstream (1.7%) and unknown origin infections (1.7%) were less frequent.

Baseline serum lactate levels at admission (lactate₀), serum lactate levels measured at approximately 6 hours (lactate₆) and calculated lactate clearance values for the overall study population are summarized in **Table 1**. Descriptive statistics include measures of central tendency and distribution for each parameter. Baseline lactate levels showed a wide range (0.6–12.9 mmol/L), with a right-skewed distribution. The mean baseline lactate level was 2.63 mmol/L, while the mean 6-hour lactate level was 2.25 mmol/L. Similar distributional characteristics, including right skewness and increased kurtosis, were observed for 6-hour lactate values.

Lactate clearance values showed substantial variability, ranging from –252.00% to 84.85%, with a heterogeneous, negatively skewed distribution. Measures of central tendency and dispersion indicated considerable inter-individual variation in lactate clearance within the study population.

Baseline hematological and biochemical parameters were compared between patients with inadequate and adequate lactate clearance (**Table 2**). Patients with inadequate lactate clearance had a significantly higher median age than those in the adequate clearance group ($p=0.034$). No significant differences were observed between groups in APACHE II score, serum albumin levels, electrolyte parameters or renal function markers ($p>0.05$ for all).

White blood cell counts were significantly lower in the inadequate lactate clearance group ($p=0.018$), whereas CRP levels were significantly higher in the adequate lactate clearance group ($p=0.035$). No statistically significant differences were identified between groups in arterial blood gas parameters, including the pH, bicarbonate, pCO₂ or BE ($p>0.05$ for all).

The association between lactate clearance status and 28-day mortality is presented in **Table 3**. A statistically significant difference in 28-day mortality was observed between patients with inadequate and adequate lactate clearance ($p=0.025$), with a higher proportion of deaths in the inadequate lactate clearance group. No statistically significant differences were observed between groups for gender, comorbidity or vasopressor use within the first 6 hours after ICU admission ($p>0.05$ for all).

Table 2. Baseline characteristics according to lactate clearance status

Variable	Inadequate lactate clearance (n=75)	Adequate lactate clearance (n=42)	p value
Age, years	79 (66-84)	72.50 (52.52-80.25)	.034*
APACHE II score	25.88±8.87	25.62±8.34	.876
Albumin, g/L	23.96±4.68	24.01±4.70	.957
Chloride, mmol/L	104 (100-108)	103 (99.75-108.50)	.733
Sodium, mmol/L	143 (139-147)	141 (138.75-146.50)	.477
Potassium, mmol/L	3.90 (3.43-4.30)	3.88 (3.51-4.35)	.495
Calcium, mg/dl	7.92±0.82	7.99±0.79	.617
Magnesium, mg/dl	1.87 (1.65-2.10)	1.89 (1.6 8-2.07)	.814
BUN, mg/dl	35.90 (23.50-53.30)	33.45 (22.60-55.30)	.765
Creatinine, mg/dl	0.77 (0.52-1.04)	0.36 (0.53-1.77)	.619
WBC, ×10 ³ /μL	10.28 (7.98-14.49)	13.8 (9.09-18.57)	.018*
Hgb, g/dl	11.83±2.40	11.38±2.70	.347
PLT, ×10 ³ /μL	254.05±119.14	292.57±118.62	.096
CRP, mg/L	45.5 (15.2-100.3)	81.90 (27.52-199.52)	.035*
pH	7.41 (7.31-7.44)	7.39 (7.32-7.43)	.552
Bicarbonate, mmol/L	24.81±7.18	23.46±4.77	.276
pCO ₂ , mmHg	41.3 (33.2-49.0)	38.25 (34.00-48.32)	.845
BE, mmol/L	-0.50 (-3.8-4.1)	-1.70 (-5.45-2.10)	.085

Data are presented as mean±standard deviation for normally distributed variables and as median (interquartile range) for non-normally distributed variables. Between-group comparisons were performed using the independent-samples t-test or the Mann-Whitney U test for continuous variables and the Chi-square test for categorical variables, as appropriate. p-values <0.05 were considered statistically significant and are indicated with an asterisk. APACHE II indicates Acute Physiology and Chronic Health Evaluation II, BUN: Blood urea nitrogen, WBC: White blood cell count, Hgb: Hemoglobin, PLT: Platelet count, CRP: C-reactive protein, pCO₂: Partial pressure of carbon dioxide

Table 3. Clinical characteristics and 28-day mortality according to lactate clearance status

Variable	Inadequate lactate clearance (n=75)	Adequate lactate clearance (n=42)	p value	
28-day mortality	Yes	66 (68.8%)	30 (31.3%)	.025*
	No	9 (42.9%)	12 (57.1%)	
Gender	Female	36 (64.3%)	20 (35.7%)	.968
	Male	39 (63.9%)	22 (36.1%)	
Comorbidity	Absent	9 (56.3%)	7 (43.8%)	.481
	Present	66 (65.3%)	35 (34.7%)	
Vasopressor use	Yes	51 (63%)	30 (37%)	.700
	No	24 (66.7%)	12 (33.3%)	

Comparisons between groups were performed using the Chi-square test as appropriate. A p-value <0.05 was considered statistically significant and is indicated with an asterisk. Vasopressor use refers to the requirement for vasopressor support within the first 6 hours following ICU admission

DISCUSSION

In this study of patients admitted to the ICU from the emergency department with suspected infection, early lactate clearance within the first 6 hours was associated with short-term mortality. This finding supports the growing body of

Table 1. Descriptive statistics of baseline lactate, 6-hour lactate and lactate clearance values

	Min	Max	\bar{X}	SD	Median	Skewness	Kurtosis
Lactate ₀	0.6	12.9	2.63	2.27	2.00	2.42	6.45
Lactate ₆	0.5	12.7	2.25	1.94	1.70	2.77	9.39
Lactate clearance	-252	84.85	-0.49	52.32	5.26	-1.56	4.88

Min: Minimum, Max: Maximum, SD: Standard deviation

evidence suggesting that dynamic changes in lactate levels provide more clinically meaningful prognostic information than a single static admission measurement. Recent studies have emphasized that early lactate trajectories reflect the balance between ongoing tissue hypoperfusion, metabolic stress and the physiologic response to initial resuscitative interventions, thereby giving insight into early disease evolution in critically ill patients.^{8,9}

Importantly, the association between impaired lactate clearance and mortality observed in the present cohort was identified in a population defined by suspected infection, rather than by strict sepsis or septic shock criteria. This distinction is clinically relevant, as many patients admitted to the ICU from the emergency department fall into this intermediate diagnostic category during the early phase of illness. Emerging literature indicates that lactate kinetics may retain prognostic value across a broad spectrum of critical illness severity, including varied populations encountered in routine clinical practice.¹⁰ In this context, early lactate clearance may serve as a practical adjunct for early risk stratification during the transition from emergency care to intensive care management.

Although patients with inadequate lactate clearance were older, no significant differences were observed between clearance groups in APACHE II scores, serum albumin levels, electrolyte profiles or renal function markers. This result suggests that impaired lactate clearance may not be adequately accounted for by conventional severity scoring systems or static biochemical measurements obtained at admission. Global scores such as APACHE II primarily summarize physiological derangement at a single time point, whereas lactate clearance reflects an evolving process that integrates tissue perfusion, metabolic adaptation and early response to treatment.¹¹

Current international guidelines emphasize that early assessment of patients with suspected infection should incorporate dynamic indicators of tissue perfusion rather than depending solely on static severity scores or single laboratory measurements.¹² In this context, serial lactate measurements are recommended to monitor changes in global perfusion and metabolic stress during early resuscitation. From this perspective, lactate clearance may serve as a complementary indicator of evolving physiologic responses not fully captured by routine laboratory values or composite severity scores.

Previous studies have shown that a substantial proportion of critically ill patients may exhibit impaired lactate clearance despite similar baseline severity scores, indicating that dynamic metabolic markers can provide prognostic information beyond classic static indices.^{13,14} In this context, lactate clearance may capture early physiological trajectories that are not fully reflected by composite severity scores or routine laboratory measurements, supporting its function as a complementary tool in early risk assessment.

In this study, differences in inflammatory markers between lactate clearance groups should be interpreted with caution. Patients with inadequate lactate clearance had lower white blood cell counts, whereas higher C-reactive protein levels were observed in patients with adequate clearance.

This pattern may reflect differences in the timing and heterogeneity of the inflammatory response rather than absolute differences in inflammatory burden. As previously highlighted, traditional inflammatory markers, such as leukocyte count and CRP, may exhibit discordant behavior during early infection and critical illness, depending on the phase and regulation of the host response.¹⁵

Furthermore, growing evidence suggests that lactate is not simply a marker of tissue hypoperfusion but may actively interact with immune cells, influencing cytokine production and immune cell function. Such metabolic-immune interactions may contribute to early biological phenotypes in which inflammatory markers and metabolic recovery do not evolve in parallel.¹⁶ From this perspective, the observed dissociation between WBC, CRP and lactate clearance may indicate heterogeneous immune-metabolic responses during the early course of critical illness.

In addition to inflammatory and immune responses, recent observational studies have shown that integrating lactate dynamics with conventional severity scores improves prognostic value. A large retrospective cohort study demonstrated that the combination of lactate levels, lactate clearance and APACHE II scores predicted short-term outcomes more reliably than any single indicator, suggesting that dynamic metabolic changes capture prognostic information not fully reflected by static assessments.¹⁷

Similarly, a pilot study in patients with cardiogenic shock found that lower lactate clearance was significantly associated with worse outcomes and correlated negatively with both fluid balance and APACHE II scores, supporting the relevance of early lactate kinetics for risk stratification across several critical care settings.¹⁸

Together, these outcomes support the notion that lactate clearance, particularly when considered alongside other clinical indicators, may help identify patients with a distinct metabolic and inflammatory phenotype in the early phases of critical illness. This integrated perspective may guide clinicians toward more customized monitoring and clinical strategies to modify both perfusion and immune-metabolic responses.

Clinically, these data indicate that early lactate clearance may enhance risk stratification for patients admitted to the ICU from the emergency department with suspected infection. Given that serum lactate is routinely measured and readily available, serial evaluation of lactate dynamics during the initial hours of admission may help clinicians distinguish patients with different physiological trajectories, even when clinical presentations appear similar. Variability in lactate clearance may reveal underlying heterogeneity in metabolic stress and recovery that is not fully reflected in baseline severity scores or single laboratory values. Lactate clearance should be interpreted as a complementary marker, integrated with clinical assessment and additional physiological parameters, rather than as a standalone indicator. This approach is consistent with recent observational studies and current clinical guidelines, which underline the importance of serial lactate monitoring for early risk assessment in patients with suspected infection.^{19,20}

Limitations

There are various limitations on this study. The results may not be generalizable to other ICU settings due to the retrospective, single-center design and small sample size. Although multivariable analyses were performed, residual confounding cannot be excluded, as treatment-related factors such as timing of resuscitation, fluid management and antibiotic strategies were not fully captured. In addition, lactate clearance was categorized using a 20% cutoff, consistent with prior studies; different thresholds or alternative modeling approaches may yield different prognostic performance. Finally, inclusion was based on suspected infection rather than strict sepsis definitions, reflecting real-world ICU admission practices but potentially introducing clinical heterogeneity. Further prospective, multicenter studies are needed to validate these findings.

CONCLUSION

Early lactate clearance was significantly associated with short-term mortality in critically ill patients admitted to the ICU from the emergency department with suspected infection. Serial assessment of lactate dynamics may offer clinically relevant prognostic information beyond baseline severity scores and routine laboratory parameters, supporting early risk stratification during the initial phase of critical illness. Although the results should be interpreted in light of the retrospective design, they suggest a potential role for lactate clearance as a practical adjunct to early intensive care assessment and warrant confirmation in prospective studies.

ETHICAL DECLARATIONS

Ethics Committee Approval

This study was conducted with the approval of the Ethics Committee of the Health Sciences Researches Center at Sivas Cumhuriyet University (Date: 08.01.2026, 2026-01/57).

Informed Consent

As this was a retrospective study, formal written informed consent was not required and was therefore not obtained.

Peer Review Process

This manuscript was subject to external peer review.

Conflict of Interest

The authors declare no conflicts of interest related to this study.

Financial Disclosure

The authors received no financial support for the conduct or publication of this research.

Author Contributions

Conceptualization: ST; Design: ST; Project Control and Supervision: ST, ED; Resources: ST; Materials: ST; Data Collection and/or Processing: ST, ED; Analysis and/or Interpretation: ED; Literature Review: ST; Writing the Article: ST; Critical Review: ST, ED.

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