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Original Article

Early Lactate Clearance as an Independent Predictor of In-Hospital Mortality: A Retrospective Cohort Study

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Abstract

Background: Serum lactate is widely used as a biomarker of tissue hypoperfusion in critically ill patients. While elevated baseline lactate levels are associated with adverse outcomes, dynamic changes in lactate concentration (particularly early lactate clearance) may provide superior prognostic information. Data regarding the predictive value of early lactate clearance in secondary-care medical intensive care units (ICUs) remains limited. We aim to evaluate the association between early (0–6-hour) lactate clearance and in-hospital mortality in adult patients admitted to a secondary-care medical ICU.

Methods: This retrospective cohort study included 114 adult patients admitted to a general medical ICU between 2018 and 2019. Patients with serum lactate measured within the first hour of ICU admission and repeated at approximately 6 hours were eligible. Lactate clearance was calculated as: [(Lactate0 – Lactate1) / Lactate0] × 100. The primary outcome was in-hospital mortality. Secondary outcomes included ICU length of stay, mechanical ventilation requirement, and acute kidney injury (AKI). Multivariable logistic regression analysis was performed to assess the independent association between lactate clearance and mortality, adjusting for baseline lactate, SOFA score, age, and vasopressor use.

Results: The cohort consisted of 59 males (51.8%) and 55 females (48.2%), with a median age of 65 years (interquartile range [IQR], 52–78 years; range, 18–94 years). Mean baseline lactate was 3.82 ± 2.14 mmol/L, and mean lactate clearance was 18.7 ± 21.3%. Patients with low lactate clearance (<10%) had significantly higher mortality compared with those achieving ≥20% clearance (64.3% vs. 15.9%, p<0.001). In multivariable analysis, lactate clearance remained independently associated with reduced mortality (OR 0.78 per 10% increase; 95% CI 0.67–0.91; p=0.002). The model demonstrated good discrimination (AUC 0.87). Lower lactate clearance was also associated with longer ICU stays, increased mechanical ventilation requirements, and a higher incidence of AKI, though the observational nature of this study precludes establishing causality.

Conclusions: Early lactate clearance is a strong and independent predictor of in-hospital mortality in a secondary-care medical ICU population. Dynamic lactate assessment within the first 6 hours may improve early risk stratification and guide resuscitation strategies in critically ill patients.

Keywords: Acidosis, Lactic, Intensive Care Units, Sepsis, Critical Illness, Prognosis

INTRODUCTION

Early identification of high-risk patients in the intensive care unit (ICU) remains a central challenge in critical care medicine (1). Despite advances in monitoring and organ support, in-hospital mortality among critically ill patients (particularly those with circulatory failure, sepsis, or acute respiratory compromise) continues to be substantial (2,3). Timely risk stratification is essential not only for prognostication but also for guiding the intensity and direction of resuscitative strategies during the initial hours of ICU admission (4).

Serum lactate has long been recognized as a surrogate marker of tissue hypoperfusion and impaired cellular oxygen utilization (5,6). Elevated lactate levels at presentation are consistently associated with increased mortality across diverse critical illness phenotypes, especially in patients with sepsis and septic shock (7,8). However, a single baseline lactate measurement provides only a static snapshot of metabolic stress and may not adequately reflect the dynamic response to resuscitation (9,10). Multiple factors, including tissue perfusion, adrenergic stimulation, hepatic metabolism, and mitochondrial function, influence lactate production and clearance (5,11). Consequently, dynamic assessment (rather than isolated baseline measurement) may offer more clinically meaningful prognostic information.

Early lactate clearance, typically defined as the percentage reduction in serum lactate concentration within the first 6–12 hours after presentation, has emerged as a potential marker of effective resuscitation (12,13). Several studies have suggested that higher lactate clearance is associated with improved survival, while persistently elevated lactate levels or poor clearance correlate with ongoing tissue hypoxia and worse outcomes (6,12,13). From a pathophysiological standpoint, inadequate lactate clearance during the early phase of critical illness may reflect unresolved shock, insufficient hemodynamic optimization, or evolving organ dysfunction. Therefore, lactate kinetics may integrate both disease severity and treatment response into a single measurable parameter.

Nevertheless, most existing evidence has been derived from tertiary referral centers or highly selected populations, frequently limited to patients with septic shock (1,11). The generalizability of these findings to secondary-care medical ICUs where patient heterogeneity, resource availability, and case-mix may differ is less well established. In such settings, practical and accessible biomarkers that support early risk stratification are particularly valuable.

Accordingly, the present study aimed to evaluate the association between early (0–6-hour) lactate clearance and in-hospital mortality in adult patients admitted to a secondary-care general medical ICU. We further sought to determine whether lactate clearance provides independent prognostic information beyond baseline lactate levels and established markers of disease severity.

METHODS

Protocol and Search Strategy

This single-center retrospective cohort study was conducted in a tertiary-care general medical intensive care unit (ICU) and included adult patients admitted between January 1, 2018, and December 31, 2019. All consecutive patients aged 18 years or older who had a serum lactate measurement obtained within the first hour of ICU admission and a repeat lactate measurement approximately 6 hours later (±2 hours) were eligible for inclusion. Patients were excluded if their ICU length of stay was less than 24 hours, if the required time-stamped lactate measurements were missing or unreliable, or if they were admitted solely for short-term elective postoperative monitoring. Data were extracted retrospectively from the hospital information management system and ICU electronic records. The study protocol was approved by the institutional ethics committee, and the requirement for informed consent was waived due to the retrospective design and anonymized data handling.

The primary exposure variable was early lactate clearance, calculated using the formula: $[(\text{Lactate}_0 - \text{Lactate}_6) / \text{Lactate}_0] \times 100$, where Lactate_0 represents the initial serum lactate level measured within the first hour of ICU admission and Lactate_6 represents the repeat measurement at approximately 6 hours. Lactate clearance was analyzed both as a continuous variable (per 10% increase) and as a categorical variable. The categorical thresholds (≥20% for high clearance, 10–19% for intermediate clearance, and <10% for low clearance) were defined a priori based on established literatüre. Additionally, a data-derived optimal cut-off was determined using receiver operating characteristic (ROC) analysis to further explore the predictive performance in our specific cohort. The primary outcome was in-hospital mortality. Secondary outcomes included ICU mortality, ICU length of stay, requirement for invasive mechanical ventilation, duration of mechanical ventilation, and development of acute kidney injury (AKI), defined according to Kidney Disease: Improving Global Outcomes (KDIGO) criteria when serum creatinine data were available.

Demographic variables, including age and sex, were recorded for all patients. Clinical data included primary admission diagnosis, presence of sepsis or septic shock, vasopressor requirement within the first 6 hours, and need for invasive mechanical ventilation. Laboratory variables included baseline lactate, serum creatinine, bilirubin, C-reactive protein, arterial blood gas parameters (pH, base excess), and other routinely measured biochemical markers. Severity of illness was assessed using Sequential Organ Failure Assessment (SOFA) and Acute Physiology and Chronic Health Evaluation II (APACHE II) scores. SOFA scores were available for 110 patients (96.5%) and APACHE II scores for 108 patients (94.7%). Missing data for these severity scores were handled using complete case analysis for the multivariable models.

STATISTICAL ANALYSIS

Continuous variables were assessed for normality using visual inspection and appropriate statistical tests and were reported as mean ± standard deviation or median with interquartile range as appropriate. Categorical variables were presented as counts and percentages. Comparisons between groups were performed using the Student's t-test or Mann–Whitney U test for continuous variables and the chi-square or Fisher's exact test for categorical

Table 1. Baseline Demographic and Clinical Characteristics (n=114)

Variable	Value
Age (years), IQR	65 [52-78]
Male sex	59 (51.8%)
Sepsis / Septic shock	41 (36.0%)
Mechanical ventilation	67 (58.8%)
Vasopressor use (≤6 h)	49 (43.0%)
$Lactate_0$ (mmol/L)	3.82 ± 2.14
$Lactate_6$ (mmol/L)	3.05 ± 2.01
Lactate clearance (%)	18.7 ± 21.3
SOFA score	7.1 ± 3.4
APACHE II	19.6 ± 6.3
ICU length of stay (days)	8.4 ± 5.6
In-hospital mortality	42 (36.8%)

IQR, interquartile range; ICU, intensive care unit; SOFA, Sequential Organ Failure Assessment; APACHE II, Acute Physiology and Chronic Health Evaluation II; $Lactate_0$, baseline lactate level; $Lactate_6$, lactate level at 6 hours.

variables. To evaluate the independent association between early lactate clearance and in-hospital mortality, multivariable logistic regression analysis was performed. Clinically relevant variables and those with $p<0.10$ in univariable analyses were entered into the multivariable model, including age, baseline lactate level, vasopressor use, and severity scores. Adjusted odds ratios (ORs) with 95% confidence intervals (CIs) were reported. Model discrimination was assessed using the area under the receiver operating characteristic curve (AUC), and calibration was evaluated using the Hosmer–Lemeshow goodness-of-fit test. A two-sided p-value <0.05 was considered statistically significant. Statistical analyses were performed using SPSS Statistics for Windows, Version 26.0 (IBM Corp., Armonk, NY, USA).

Table 2. In-Hospital Mortality According to Lactate Clearance Categories

Lactate Clearance	n	Mortality n (%)
≥20% (High)	44	7 (15.9%)
10–19% (Intermediate)	28	8 (28.6%)
<10% (Low)	42	27 (64.3%)

RESULTS

Study Characteristics

A total of 114 adult patients met the inclusion criteria during the 2018–2019 study period. The cohort consisted of 59 males (51.8%) and 55 females (48.2%), with a median age of 65 years (interquartile range [IQR], 52–78 years; range, 18–94 years). The age distribution was non-normal based on the Shapiro-Wilk test. Overall in-hospital mortality was 36.8% (n=42), while ICU mortality was 33.3% (n=38). The mean ICU length of stay was 8.4 ± 5.6 days. Invasive mechanical ventilation was required in 67 patients (58.8%), and vasopressors were administered within the first 6 hours in 49 patients (43.0%). Baseline clinical and laboratory characteristics are presented in **Table 1**. The most common admission diagnosis was sepsis or septic shock (36.0%), followed by pneumonia without septic shock (16.7%) and acute exacerbation of chronic obstructive pulmonary disease (12.3%). The mean baseline lactate ($Lactate_0$) was 3.82 ± 2.14 mmol/L, and the mean 6-hour lactate ($Lactate_6$) was 3.05 ± 2.01 mmol/L. The mean early lactate clearance was 18.7 ± 21.3%. The mean SOFA score at admission was 7.1 ± 3.4, and the mean APACHE II score was 19.6 ± 6.3.

Patients were stratified according to predefined lactate clearance categories. Mortality differed significantly across clearance groups ($p<0.001$). Patients with low clearance (<10%) had markedly higher mortality compared to those achieving ≥20% clearance (64.3% vs. 15.9%) (**Table 2**).

Table 3 presents the comparative analysis between survivors and non-survivors. Non-survivors were significantly older and exhibited higher baseline lactate levels, lower lactate clearance, higher SOFA scores, and a greater need for vasopressor support and mechanical ventilation. The mean lactate clearance was 4.8 ± 16.9% in non-survivors, compared with 26.4 ± 19.8% in survivors ($p < 0.001$).

In multivariable logistic regression analysis adjusting for age, baseline lactate, SOFA score, and vasopressor

Table 3. Comparison of Survivors and Non-Survivors

Variable	Non-Survivors (n=42)	Survivors (n=72)	p-value
Age (years), IQR	71 [60-82]	61 [48-74]1	0.048
$Lactate_0$ (mmol/L)	4.91 ± 2.41	3.12 ± 1.67	<0.001
Lactate clearance (%)	4.8 ± 16.9	26.4 ± 19.8	<0.001
SOFA score	9.2 ± 3.6	5.8 ± 2.9	<0.001
Vasopressor use	30 (71%)	19 (26%)	<0.001
Mechanical ventilation	34 (81%)	33 (46%)	0.002
APACHE II score	22.4 ± 5.8	17.9 ± 6.1	<0.001
ICU length of stay (days)	10.5 ± 6.8	7.2 ± 4.3	0.003
Acute kidney injury	24 (57%)	15 (21%)	<0.001

Table 4. Multivariable Logistic Regression for In-Hospital Mortality

Variable	Adjusted OR	95% CI	p-value
Lactate clearance (per 10%)	0.78	0.67–0.91	0.002
Baseline lactate	1.31	1.09–1.57	0.004
SOFA score	1.24	1.11–1.39	<0.001
Age	1.02	1.00–1.04	0.061
Vasopressor use	2.18	1.01–4.69	0.047

use, early lactate clearance remained independently associated with reduced in-hospital mortality. Each 10% increase in lactate clearance was associated with a 22% relative reduction in the odds of death (adjusted OR 0.78; 95% CI 0.67–0.91; p=0.002) (**Table 4**). Baseline lactate and SOFA score were also independent predictors.

Model discrimination was strong, with an area under the ROC curve (AUC) of 0.87. The Hosmer–Lemeshow test indicated good calibration (p=0.62).

Receiver operating characteristic analysis demonstrated that lactate clearance alone had an AUC of 0.81 for predicting in-hospital mortality. The optimal cut-off value identified was 12%, yielding a sensitivity of 76% and specificity of 72%.

Secondary outcome analysis showed that patients with low lactate clearance had significantly longer ICU stays (10.2 ± 6.1 vs. 6.3 ± 4.2 days, p=0.001), longer duration of mechanical ventilation (7.8 ± 5.4 vs. 4.1 ± 3.6 days, p=0.003), and higher incidence of acute kidney injury (52% vs. 21%, p=0.004).

Overall, early lactate clearance demonstrated a strong and independent association with mortality and other clinically relevant outcomes in this secondary-care medical ICU population.

DISCUSSION

In this retrospective cohort of patients admitted to a secondary-care medical ICU, early lactate clearance demonstrated a significant and independent association with in-hospital mortality, supporting the role of dynamic metabolic monitoring in critical care prognostication. Our findings align with a substantial body of literature suggesting that serial lactate measurements and derived indices such as lactate clearance offer greater prognostic insight than single static measurements. Multiple studies have shown that dynamic changes in lactate are closely linked to outcomes in critical illness, with higher clearance generally associated with improved survival and lower clearance indicating persistent tissue hypoperfusion or inadequate resuscitation (6,10,13).

Several observational studies in sepsis populations have reinforced the value of lactate kinetics (9–11). For example, highlight that dynamic lactate indices, including lactate clearance over time, predict mortality more accurately than static lactate levels, emphasizing the importance of serial measurements in the first hours of ICU care (1,7,13,15). In a large retrospective study focused on septic shock patients, lactate clearance at 6 hours correlated with 28-day mortality, though lactate level itself often demonstrated equal or superior predictive performance (12,16). These findings partially mirror our results, where lactate clearance remained an independent predictor in multivariable analysis while also complementing severity scores such as SOFA.

Mechanistically, lactate clearance reflects the balance between production (often driven by tissue hypoxia, adrenergic stimulation, or impaired mitochondrial utilization) and elimination (primarily hepatic and renal metabolism) (13,17,18). Reviews on lactate biology underscore that elevated lactate may arise not solely from anaerobic metabolism but also from aerobic glycolysis in the context of systemic inflammation, which complicates the interpretation of a single measurement (7,9,10). Thus, the trajectory of lactate over time integrates both the severity of the underlying insult and the patient's physiological response to resuscitation, making it a more dynamic biomarker.

The Cut-off points for lactate clearance correspond with ranges identified in other cohorts. For instance, optimal 6-hour clearance thresholds such as <10–24% have been linked with worse outcomes in sepsis studies, although exact values and performance characteristics vary across populations and baseline disease burden (16,21). This variability highlights that while a universal threshold may be elusive, the trend of lactate decline matters clinically and should be interpreted alongside other markers of severity and hemodynamic status.

It is worth noting that some reports suggest that absolute lactate levels at subsequent time points may outperform clearance in certain contexts (6,9,13,22). For example, a study by Lee et al. found that 6-hour lactate values showed slightly better discrimination for 30-day mortality than clearance itself (23). This observation underscores the nuanced relationship between lactate dynamics and outcomes: a high 6-hour lactate may reflect unresolved shock despite an apparent relative decline, and both absolute levels and clearance should be considered in risk stratification models.

Although most evidence comes from sepsis or septic shock populations, our findings in a general medical ICU cohort suggest that the prognostic relevance of lactate clearance extends beyond isolated disease categories. A study conducted in a lower-middle-income country reported similar associations between lactate kinetics and outcomes in broader critically ill populations, reinforcing the global applicability of dynamic lactate assessment (24). Furthermore, emerging research on early lactate trajectories and phenotype clustering in diverse critical care settings supports the concept that lactate changes over time may identify distinct risk profiles relevant to tailored interventions.

Several limitations of lactate-based prognostication warrant attention. Clearance may be influenced by non-perfusion factors such as hepatic dysfunction, adrenergic state, and metabolic alterations that are not directly addressed by standard resuscitation protocols. This complexity underscores the importance of integrating lactate kinetics with clinical context, organ failure scores, and other metabolic parameters, rather than relying on lactate clearance in isolation.

CONCLUSION

In this retrospective cohort of adult patients admitted to a secondary-care medical intensive care unit, early lactate clearance within the first 6 hours of admission was strongly and independently associated with in-hospital mortality. Patients with poor lactate clearance demonstrated significantly higher mortality rates, longer ICU stays, and greater need for organ support compared to those achieving adequate early metabolic improvement. Importantly, lactate clearance retained its prognostic value even after adjustment for baseline lactate levels, severity of illness scores, and vasopressor requirement, indicating that dynamic metabolic response provides incremental information beyond static measurements alone. These findings support the integration of early serial lactate assessment into routine ICU practice, particularly in resource-constrained or heterogeneous secondary-care settings where rapid and accessible risk stratification tools are essential. While lactate clearance should not replace comprehensive clinical evaluation, it may serve as a practical and physiologically meaningful adjunct to established scoring systems. Prospective multicenter studies are warranted to validate optimal clearance thresholds and to determine whether lactate-guided resuscitation strategies can translate into improved clinical outcomes.

DECLARATIONS

Ethics Committee Approval: This study was conducted in accordance with the principles of the Declaration of Helsinki and was approved by the Yenimahalle Training and Reserach Hospital Institutional Ethics Committee of the participating hospital (IRB No: E-2026-19). Given the retrospective design and the use of anonymized routinely collected clinical data, the ethics committee waived the requirement for written informed consent. All patient data were de-identified before analysis, and no directly identifiable personal information was accessed during the study process.

Consent to Participate: The manuscript does not contain any individual patient identifiers, images, or personal data that require separate consent for publication. The study has a retrospective desgin.

Availability of Data and Materials: The datasets generated and/or analyzed during the current study are available from the corresponding author upon reasonable request.

Competing Interests: The authors declare that they have no competing interests.

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Use of Artificial Intelligence: Artificial intelligence (AI) tools were used solely for language editing and improvement of the manuscript. No AI tools were used in the study design, data collection, data analysis, or interpretation of the results. The authors take full responsibility for the content of the manuscript.

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