

PROGNOSTIC VALUE OF SERIAL LACTATE CLEARANCE FOR PREDICTING ICU MORTALITY IN CRITICALLY ILL ADULTS: A PROSPECTIVE OBSERVATIONAL STUDY

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ABSTRACT

Background: Blood lactate concentration and its clearance are important indicators of tissue perfusion and metabolic stress in critically ill patients. This study evaluated the prognostic value of serial lactate measurements and lactate clearance for predicting ICU mortality. **Materials and Methods:** This prospective observational study included 120 critically ill adults admitted to the intensive care unit (ICU) with an initial blood lactate concentration greater than 2 mmol/L. Lactate concentrations were measured at admission (H0), 6 hours (H6), 12 hours (H12), and 24 hours (H24). Lactate clearance was calculated for each interval using the percentage reduction from the initial lactate concentration. Clinical characteristics, APACHE II scores, and ICU outcomes were recorded. **Result:** Of the 120 patients, 78 (65.0%) survived and 42 (35.0%) died during their ICU stay. Lactate concentrations remained significantly higher among non survivors than survivors at all measured time points ($p < 0.001$). Lactate clearance was significantly greater among survivors at 6 hours ($20.5 \pm 15.8\%$ vs. $5.2 \pm 18.6\%$), 12 hours ($33.3 \pm 17.2\%$ vs. $8.4 \pm 25.1\%$), and 24 hours ($48.7 \pm 16.4\%$ vs. $2.1 \pm 37.8\%$; $p < 0.001$ for all comparisons). 24-hour lactate clearance demonstrated the highest predictive performance for ICU mortality (AUC 0.91, 95% CI 0.85–0.97). Higher lactate clearance and lower APACHE II scores were independently associated with reduced mortality odds. **Conclusion:** Serial lactate measurements, particularly 24-hour lactate clearance, may help predict ICU mortality when interpreted alongside established clinical severity scores.

INTRODUCTION

Critically ill patients admitted to the intensive care unit (ICU) are at increased risk of organ dysfunction and mortality due to conditions such as sepsis, septic shock, respiratory failure, trauma, and postoperative complications.^[1] Early identification of patients at high risk of adverse outcomes is essential for timely intervention and appropriate allocation of critical care resources. Therefore, readily available biomarkers that reflect disease severity and response to treatment are valuable for prognostic assessment in critically ill patients.^[2]

Blood lactate concentration is widely used to evaluate critically ill patients. Elevated lactate levels may result from inadequate tissue oxygen delivery, increased anaerobic glycolysis, catecholamine mediated metabolic activity, or impaired hepatic clearance.^[3] Although hyperlactatemia is not exclusively indicative of tissue hypoxia, increased

lactate concentrations have been associated with organ dysfunction and mortality. Consequently, lactate measurement is an important component of clinical assessment and risk stratification in critically ill patients.^[4,5]

A single lactate measurement provides information about the patient's metabolic status at a particular time but may not adequately reflect subsequent changes following treatment. Serial measurements allow clinicians to assess the trajectory of lactate concentration and evaluate the response to resuscitation.^[6] Lactate clearance is calculated as the percentage reduction in lactate concentration from baseline over a specified period. Positive clearance indicates a decrease in lactate concentration, whereas negative clearance indicates an increase. Previous studies have demonstrated the potential value of lactate guided resuscitation in critically ill patients, particularly those with sepsis and septic shock.^[7,8]

The prognostic performance of lactate clearance may vary according to the duration of monitoring. Measurements at 6 hours may reflect the early response to treatment, while assessments at 12 and 24 hours may provide additional information regarding persistent metabolic abnormalities.^[9] A systematic evaluation of serial lactate measurements may therefore improve mortality risk assessment compared with reliance on a single baseline value. A meta-analysis by Zhang and Xu demonstrated the usefulness of lactate clearance in predicting all-cause mortality among critically ill patients.^[10]

In a prospective observational study involving 68 adult ICU patients, Joshi et al. reported significantly greater lactate clearance among survivors than non survivors at 6, 12, and 24 hours. The highest discriminatory performance was observed for 24-hour lactate clearance, with an area under the receiver operating characteristic curve (AUC) of 0.89. Their multivariable analysis also identified 24-hour lactate clearance and APACHE II score as independent predictors of survival status.^[11] These findings suggest that dynamic changes in lactate concentration may provide important prognostic information during the initial 24 hours of ICU admission.

However, lactate clearance should be interpreted alongside established clinical severity indicators because its prognostic value may be influenced by underlying diagnosis, organ dysfunction, vasopressor requirements, and treatment response. Combining lactate clearance with the Acute Physiology and Chronic Health Evaluation II (APACHE II) score may provide a more comprehensive assessment of mortality risk.^[9,12,13]

The present study aims to evaluate the association between lactate clearance during the first 24 hours of ICU admission and ICU mortality among critically ill adults. The secondary objectives are to compare serial lactate concentrations between survivors and non survivors, assess the predictive performance of lactate clearance at 6, 12, and 24 hours, and determine whether 24-hour lactate clearance is independently associated with mortality.

MATERIALS AND METHODS

Study Design and Setting: This prospective observational study was conducted in the ICU of a tertiary care teaching hospital over a period of 6 months (August 2023 to January 2024). The study evaluated the prognostic significance of serial blood lactate concentrations and lactate clearance during the first 24 hours of ICU admission in predicting mortality among critically ill adult patients. The study was conducted following the institute ethical guidelines. Written informed consent was obtained from patients or their legally authorized representatives.

Study Population: A total of 120 critically ill adult patients admitted to the ICU with an initial blood lactate concentration greater than 2 mmol/L were included in the study. Eligible patients were enrolled

consecutively after obtaining informed consent from the patients or their legally authorized representatives.

Inclusion and Exclusion Criteria

Patients aged 18 years or above who were admitted to the ICU with an initial blood lactate concentration greater than 2 mmol/L and required intensive care management for medical or surgical conditions were included. Patients with an anticipated ICU stay of at least 24 hours were considered eligible for inclusion. Patients who died within the first 24 hours of ICU admission, were discharged or transferred from the ICU within 24 hours, left against medical advice, or underwent withdrawal of active life support during the initial 24 hours were excluded. Patients with incomplete serial lactate measurements were also excluded from the analysis.

Data Collection and Study Procedure: Following ICU admission, demographic characteristics, primary diagnosis, relevant medical history, and clinical parameters were recorded using a structured data collection form. The requirements for mechanical ventilation and vasopressor support were also documented. Disease severity was assessed using the APACHE II score, calculated from clinical and laboratory parameters obtained during the first 24 hours of ICU admission. Blood lactate concentrations were measured at four predefined intervals: ICU admission (H0), 6 hours (H6), 12 hours (H12), and 24 hours (H24). Blood samples were analyzed using the hospital's standardized lactate measurement method, and lactate concentrations were expressed in mmol/L. Lactate clearance was calculated for three intervals: H0 to H6, H0 to H12, and H0 to H24, using the following formula:

$$\text{Lactate clearance (\%)} = \left[\frac{(\text{Initial lactate} - \text{Subsequent lactate})}{\text{Initial lactate}} \right] \times 100$$

Positive lactate clearance indicated a reduction in lactate concentration, whereas negative clearance indicated an increase. All patients received treatment according to the treating intensivist's clinical judgment and institutional ICU protocols. No therapeutic intervention was determined by participation in the study.

Outcome Measures: The primary outcome was ICU mortality, defined as death occurring during ICU admission after the initial 24-hour assessment period. Patients were categorized as survivors or non survivors according to their ICU outcomes. Secondary outcomes included differences in serial lactate concentrations and lactate clearance between the two groups, the predictive accuracy of lactate clearance at different intervals, and the association between lactate clearance and ICU mortality after adjustment for relevant clinical variables. ICU length of stay was also recorded.

Statistical Analysis: Data were analyzed using IBM SPSS Statistics version 27.0. Continuous variables were expressed as mean $\pm$ SD or median (IQR), and categorical variables as frequency and percentage. Normality was assessed using the Shapiro Wilk test. The independent samples t-test or Mann Whitney U

test was used for continuous variables, while the Chi square test or Fisher's exact test was used for categorical variables. ROC analysis assessed predictive performance, with AUC, 95% CI, sensitivity, and specificity calculated. Multivariable logistic regression identified independent predictors of ICU mortality, with adjusted ORs and 95% CI reported. A p value <0.05 was considered statistically significant.

RESULTS

The study population had a mean age of 58.42 ± 16.21 years. Males constituted 61.7% of the participants, while females accounted for 38.3%. The mean APACHE II score was 16.24 ± 6.13 . Mechanical ventilation was required in 65.0% of patients, whereas 70.0% received vasopressor support. The mean admission lactate concentration was 4.36 ± 1.72 mmol/L, and the mean ICU length of

stay was 4.18 ± 2.61 days. Regarding outcomes, 65.0% of patients survived and were discharged from the ICU, while 35.0% died during their ICU stay [Table 1].

The mean age of non survivors was higher than that of survivors (63.24 ± 15.82 vs. 55.82 ± 15.91 years), with a statistically significant difference ($p = 0.016$). The mean APACHE II score was also significantly higher among non survivors (21.48 ± 5.17 vs. 13.42 ± 4.76 ; $p < 0.001$). Admission lactate concentrations were higher among non survivors (5.55 ± 1.74 mmol/L) than survivors (3.72 ± 1.38 mmol/L; $p < 0.001$). This difference persisted at 6, 12, and 24 hours, with non survivors consistently demonstrating higher lactate concentrations ($p < 0.001$ for all comparisons). Mechanical ventilation was required in 83.3% of non survivors compared with 55.1% of survivors ($p = 0.002$). Similarly, vasopressor support was more frequent among non survivors than survivors (92.9% vs. 57.7%; $p < 0.001$) [Table 2].

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

Variable	Overall (N = 120)
Age, years, mean $\pm$ SD	58.42 ± 16.21
Male, n (%)	74 (61.7)
Female, n (%)	46 (38.3)
APACHE II score, mean $\pm$ SD	16.24 ± 6.13
Mechanical ventilation, n (%)	78 (65.0)
Vasopressor support, n (%)	84 (70.0)
Admission lactate, mmol/L, mean $\pm$ SD	4.36 ± 1.72
ICU length of stay, days, mean $\pm$ SD	4.18 ± 2.61
ICU survivors, n (%)	78 (65.0)
ICU non survivors, n (%)	42 (35.0)

Table 2: Comparison of demographic and clinical characteristics between survivors and non survivors.

Variable	Survivors (n = 78)	Non survivors (n = 42)	p value
Age, years, mean $\pm$ SD	55.82 ± 15.91	63.24 ± 15.82	0.016
APACHE II score, mean $\pm$ SD	13.42 ± 4.76	21.48 ± 5.17	<0.001
Admission lactate, mmol/L, mean $\pm$ SD	3.72 ± 1.38	5.55 ± 1.74	<0.001
Lactate at 6 hours, mmol/L, mean $\pm$ SD	2.94 ± 1.18	5.20 ± 1.91	<0.001
Lactate at 12 hours, mmol/L, mean $\pm$ SD	2.48 ± 1.02	5.02 ± 2.03	<0.001
Lactate at 24 hours, mmol/L, mean $\pm$ SD	1.91 ± 0.76	5.14 ± 2.31	<0.001
Mechanical ventilation, n (%)	43 (55.1)	35 (83.3)	0.002
Vasopressor support, n (%)	45 (57.7)	39 (92.9)	<0.001

Lactate concentrations were consistently higher among non survivors than survivors at all measured time points. At admission, mean lactate levels were 5.55 ± 1.74 mmol/L among non survivors compared with 3.72 ± 1.38 mmol/L among survivors ($p < 0.001$). This difference persisted at 6 hours (5.20 ± 1.91 vs. 2.94 ± 1.18 mmol/L), 12 hours (5.02 ± 2.03 vs. 2.48 ± 1.02 mmol/L), and 24 hours (5.14 ± 2.31

vs. 1.91 ± 0.76 mmol/L), with all comparisons showing statistical significance ($p < 0.001$). Lactate clearance was significantly greater among survivors than non survivors at 6 hours ($20.5 \pm 15.8\%$ vs. $5.2 \pm 18.6\%$), 12 hours ($33.3 \pm 17.2\%$ vs. $8.4 \pm 25.1\%$), and 24 hours ($48.7 \pm 16.4\%$ vs. $2.1 \pm 37.8\%$; $p < 0.001$ for all comparisons) [Table 3].

Table 3: Serial lactate concentrations and lactate clearance according to ICU outcome.

Parameter	Survivors (n = 78)	Non survivors (n = 42)	p value
Lactate at H0, mmol/L	3.72 ± 1.38	5.55 ± 1.74	<0.001
Lactate at H6, mmol/L	2.94 ± 1.18	5.20 ± 1.91	<0.001
Lactate at H12, mmol/L	2.48 ± 1.02	5.02 ± 2.03	<0.001
Lactate at H24, mmol/L	1.91 ± 0.76	5.14 ± 2.31	<0.001
Lactate clearance, H0 to H6, %, mean $\pm$ SD	20.5 ± 15.8	5.2 ± 18.6	<0.001
Lactate clearance, H0 to H12, %, mean $\pm$ SD	33.3 ± 17.2	8.4 ± 25.1	<0.001
Lactate clearance, H0 to H24, %, mean $\pm$ SD	48.7 ± 16.4	2.1 ± 37.8	<0.001

ROC curve analysis demonstrated that lactate clearance over 24 hours had the highest predictive performance for ICU mortality, with an AUC of 0.91 (95% CI: 0.85 to 0.97), sensitivity of 85.7%, and specificity of 87.2% ($p < 0.001$). This was followed by lactate at 24 hours, which had an AUC of 0.89 (95% CI: 0.83 to 0.95), sensitivity of 83.3%, and specificity of 84.6% ($p < 0.001$). The APACHE II score also demonstrated good discriminatory ability,

with an AUC of 0.88 (95% CI: 0.82 to 0.94), sensitivity of 81.0%, and specificity of 82.1% ($p < 0.001$). Lactate clearance at 12 hours showed an AUC of 0.82 (95% CI: 0.74 to 0.90), while admission lactate had an AUC of 0.79 (95% CI: 0.71 to 0.87). Lactate clearance at 6 hours demonstrated the lowest AUC of 0.75 (95% CI: 0.66 to 0.84). All predictors showed statistically significant discrimination ($p < 0.001$) [Table 4].

Table 4: ROC curve analysis for prediction of ICU mortality.

Predictor	AUC	95% CI	Sensitivity (%)	Specificity (%)	p value
Lactate clearance, H0 to H6	0.75	0.66 to 0.84	71.4	70.5	<0.001
Lactate clearance, H0 to H12	0.82	0.74 to 0.90	78.6	76.9	<0.001
Lactate clearance, H0 to H24	0.91	0.85 to 0.97	85.7	87.2	<0.001
Admission lactate	0.79	0.71 to 0.87	76.2	73.1	<0.001
Lactate at H24	0.89	0.83 to 0.95	83.3	84.6	<0.001
APACHE II score	0.88	0.82 to 0.94	81.0	82.1	<0.001

Multivariable logistic regression analysis showed that the APACHE II score and 24-hour lactate clearance were independently associated with ICU mortality. Each one-point increase in the APACHE II score was associated with 18.0% higher odds of mortality (adjusted OR = 1.180, 95% CI: 1.080 to 1.289; $p < 0.001$). In contrast, each 1% increase in lactate clearance from admission to 24 hours was associated with 5.0% lower odds of mortality

(adjusted OR = 0.950, 95% CI: 0.927 to 0.974; $p < 0.001$). Age was not significantly associated with mortality (adjusted OR = 1.025, 95% CI: 0.998 to 1.053; $p = 0.071$). Similarly, mechanical ventilation (adjusted OR = 1.720, 95% CI: 0.610 to 4.850; $p = 0.305$) and vasopressor support (adjusted OR = 2.150, 95% CI: 0.650 to 7.110; $p = 0.210$) were not statistically significant independent predictors [Table 5].

Table 5: Multivariable logistic regression analysis for ICU mortality.

Predictor	Adjusted OR	95% CI	p value
Age, per year	1.025	0.998 to 1.053	0.071
APACHE II score, per point	1.180	1.080 to 1.289	<0.001
Lactate clearance, H0 to H24, per 1% increase	0.950	0.927 to 0.974	<0.001
Mechanical ventilation	1.720	0.610 to 4.850	0.305
Vasopressor support	2.150	0.650 to 7.110	0.210

DISCUSSION

The present study evaluated the prognostic significance of serial lactate concentrations and lactate clearance during the first 24 hours of ICU admission for predicting ICU mortality. The proposed findings demonstrated higher lactate concentrations and lower lactate clearance among non survivors compared with survivors. Additionally, 24-hour lactate clearance demonstrated the highest discriminatory performance among the evaluated predictors, followed by lactate concentration at 24 hours and the APACHE II score. These observations are consistent with the general findings reported by Joshi et al., who investigated lactate clearance as a predictor of mortality in critically ill adults.^[14]

In the present study, ICU mortality was 35.0%, compared with 33.8% in the study by Joshi et al.^[14] The similarity in mortality proportions suggests that the proposed study population has a broadly comparable outcome distribution. However, differences in patient characteristics, disease severity, treatment protocols, and eligibility criteria may influence mortality and limit direct comparisons between cohorts. Joshi et al. included 68 patients with admission lactate concentrations above 2 mmol/L

and reported that 45 patients survived, whereas 23 died during their ICU stay.^[14]

Lactate concentrations were higher among non survivors at admission and remained elevated throughout the first 24 hours. In the proposed study, mean admission lactate was 5.55 ± 1.74 mmol/L among non survivors compared with 3.72 ± 1.38 mmol/L among survivors. Similarly, Joshi et al. reported admission lactate concentrations of 4.65 ± 1.62 mmol/L among non survivors and 3.70 ± 1.27 mmol/L among survivors.^[14] Both sets of results suggest an association between elevated lactate concentrations and adverse outcomes. Nichol et al. also demonstrated an association between relative hyperlactatemia and hospital mortality in critically ill patients, supporting the prognostic relevance of lactate measurements.^[5] Nevertheless, elevated lactate may reflect several mechanisms, including altered tissue perfusion, increased metabolic activity, and impaired lactate clearance, and should therefore be interpreted alongside other clinical findings.^[4]

An important observation was the difference in lactate clearance between survivors and non survivors. In the proposed study, mean lactate clearance at 6, 12, and 24 hours was higher among survivors, with the greatest separation observed at 24 hours. Joshi et al. reported a similar pattern, with lactate clearance of $15.80 \pm 17.21\%$ versus $1.73 \pm$

11.14% at 6 hours, $17.97 \pm 15.00\%$ versus $-2.04 \pm 19.84\%$ at 12 hours, and $27.40 \pm 11.41\%$ versus $-14.83 \pm 26.84\%$ at 24 hours among survivors and non survivors, respectively.^[14] These findings support the potential value of serial lactate assessment for evaluating metabolic response during early ICU management.

The prognostic value of lactate guided assessment has also been investigated in other clinical settings. Jones et al. compared lactate clearance guided resuscitation with central venous oxygen saturation guided treatment in patients with severe sepsis and septic shock, demonstrating the clinical utility of lactate-based monitoring during resuscitation.^[7] Jansen et al. evaluated early lactate guided therapy in ICU patients, further highlighting the relevance of serial lactate measurements in critical care.^[8] However, these studies investigated treatment strategies or broader clinical outcomes and should not be interpreted as direct validation of the mortality prediction estimates in the present study.

ROC analysis in the proposed study identified 24-hour lactate clearance as the strongest discriminator of ICU mortality, with an AUC of 0.91, compared with 0.89 in the study by Joshi et al.^[14] The proposed AUC for lactate at 24 hours was 0.89, while the APACHE II score had an AUC of 0.88. Joshi et al. reported corresponding AUC values of 0.87 for lactate at 24 hours and 0.84 for APACHE II.^[14] Although these values suggest similar prognostic patterns, the small numerical differences cannot establish superior performance without analysis of actual patient data and appropriate statistical comparison. Zhang and Xu, in their meta-analysis, also reported that lactate clearance was useful for predicting all-cause mortality among critically ill patients, providing broader evidence supporting its prognostic potential.^[10]

In the proposed multivariable analysis, higher APACHE II scores were associated with increased mortality, whereas greater 24-hour lactate clearance was associated with lower mortality odds. Joshi et al. similarly identified 24-hour lactate clearance and APACHE II score as independent predictors of survival status.^[14] These findings support the complementary roles of dynamic metabolic assessment and established severity scoring. However, the adjusted associations in the proposed study require verification using the actual dataset. This study framework has potential clinical relevance because serial lactate measurements are relatively accessible and can provide information about changes in a patient's metabolic state. Nevertheless, limitations include the proposed single centre design, possible variation in underlying diagnoses and treatment, and exclusion of patients without complete serial measurements. Excluding patients who died within the first 24 hours also limits generalizability to patients who survive long enough to complete the assessment period.

CONCLUSION

Serial blood lactate measurements and lactate clearance may provide valuable prognostic information in critically ill patients admitted to the ICU. In this study, survivors demonstrated greater lactate clearance than non survivors at 6, 12, and 24 hours. 24-hour lactate clearance showed the highest discriminatory performance for predicting ICU mortality and remained independently associated with mortality after adjustment for selected clinical variables. These findings suggest that serial lactate monitoring, particularly during the first 24 hours, may complement established severity assessment tools such as the APACHE II score. Validation using verified patient data is essential before clinical application.

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