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Original Research Article

Evaluation of Arterial Lactate as a Predictive Marker in Severe Septic Shock: A Prospective Clinical Study

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Abstract

Aim: To evaluate the prognostic significance of arterial lactate levels and lactate clearance as independent predictive markers for in-hospital mortality and clinical outcomes in patients with severe septic shock.

Materials and Methods: This prospective observational study was conducted over 18 months in the medical intensive care unit of a tertiary care hospital. A total of 150 patients with severe septic shock (SEPSIS-3 criteria) were enrolled. Arterial blood samples were collected at admission (H0), 6 hours (H6), and 24 hours (H24) post-admission. Arterial lactate levels, lactate clearance, and clinical parameters including APACHE II scores, SOFA scores, vasopressor requirements, and mechanical ventilation needs were recorded. Lactate clearance was calculated as [(L0 − Lx) / L0 × 100%]. Statistical analysis was performed using SPSS version 26.0, with multivariate logistic regression analysis to identify independent predictors of mortality.

Results: Among 150 patients with severe septic shock, 104 (69.3%) were survivors and 46 (30.7%) were non-survivors. Mean arterial lactate at admission was significantly higher in non-survivors (7.2 ± 2.4 mmol/L) compared to survivors (3.1 ± 1.5 mmol/L, $p < 0.001$). At 24 hours, non-survivors demonstrated significantly lower lactate clearance (−12 ± 15%) compared to survivors (58 ± 22%, $p < 0.001$). Arterial lactate ≥4 mmol/L at admission (OR 8.2, 95% CI 3.6–18.5) and lactate clearance <10% at 24 hours (OR 6.4, 95% CI 2.8–14.7) were independent predictors of mortality. ROC analysis revealed an AUC of 0.812 for admission lactate and 0.845 for 24-hour lactate clearance in predicting mortality.

Conclusion: Arterial lactate levels and lactate clearance are powerful independent predictors of in-hospital mortality in severe septic shock. Serial measurements of arterial lactate at 6 and 24 hours provide superior prognostic value compared to admission lactate alone. Implementation of lactate-guided resuscitation protocols may improve clinical outcomes and guide therapeutic decisions in septic shock management.

Keywords: Arterial lactate; Septic shock; Lactate clearance; Prognostic marker; Mortality prediction; Tissue hypoperfusion.

Introduction

Sepsis and septic shock remain leading causes of morbidity and mortality in intensive care units worldwide, with an estimated global burden exceeding 11 million deaths annually. Early recognition and risk stratification of septic shock patients are crucial for initiating timely, goal-directed therapy and improving clinical outcomes.

Arterial lactate accumulation indicates inadequate tissue oxygenation and anaerobic metabolism, directly reflecting the severity of shock and organ perfusion status.

Multiple landmark studies have demonstrated that elevated arterial lactate levels at presentation and persistent elevation during resuscitation are independently associated with poor prognosis in septic shock. This study aims to prospectively evaluate arterial lactate as an independent predictive marker for mortality and clinical outcomes in severe septic shock, compare its prognostic performance with established severity scores (APACHE II, SOFA), and establish evidence-based lactate thresholds for guiding clinical decision-making and resuscitation strategies.

Materials and Methods

Study Design and Setting: This was a prospective observational cohort study conducted at the Medical Intensive Care Unit of a tertiary care teaching hospital over an 18-month period (January 2024 – June 2025). The study was approved by the Institutional Ethics Committee, and written informed consent was obtained from all patients or their legal representatives.

Patient Selection

Inclusion Criteria:

- Age ≥18 years
- Septic shock diagnosed within 4 hours of hospital presentation
- Septic shock meeting SEPSIS-3 criteria (infection with hypotension requiring vasopressors and elevated lactate ≥2 mmol/L despite adequate fluid resuscitation)
- Arterial line in place for continuous hemodynamic monitoring
- Expected ICU stay >48 hours

Exclusion Criteria:

- Cardiogenic shock or hypovolemic shock from non-infectious sources
- Chronic liver disease (Child-Pugh grade C) affecting lactate metabolism
- Malignancy or active chemotherapy
- Immunosuppression (HIV/AIDS with CD4 <200 cells/mm³)

Data Collection: Demographic data, clinical characteristics, comorbidities, and infection source were recorded at enrollment.

Arterial blood samples were collected at three time points: admission (H0), 6 hours post-admission (H6), and 24 hours post-admission (H24).

Samples were analyzed for lactate concentration (mmol/L), pH, bicarbonate, base excess, and arterial blood gases using a point-of-care blood gas analyzer (ABL90 FLEX, Radiometer, Copenhagen).

Clinical Parameters

- **APACHE II Score:** Calculated at ICU admission
- **SOFA Score:** Calculated at admission, 24 hours, and 48 hours
- **Organ Support Requirements:** Mechanical ventilation, vasopressor use (noradrenaline, dopamine, dobutamine), renal replacement therapy
- **Clinical Outcomes:** ICU length of stay, hospital length of stay, 28-day mortality, 90-day mortality

Observation Tables

Table 1: Demographic, Clinical Characteristics, And Severity Scores in Study Population

Demographic and Clinical Characteristics	Survivors (n=104)	Non-Survivors (n=46)	p-value
Age (years, mean ± SD)	52.4 ± 16.2	58.7 ± 14.9	0.018
Male gender (n, %)	62 (59.6%)	28 (60.9%)	0.872
Comorbidities			
Diabetes mellitus	34 (32.7%)	19 (41.3%)	0.258
Hypertension	41 (39.4%)	22 (47.8%)	0.308
Chronic kidney disease	12 (11.5%)	18 (39.1%)	<0.001
Chronic liver disease	6 (5.8%)	8 (17.4%)	0.022
APACHE II score (mean ± SD)	18.2 ± 7.4	28.6 ± 8.9	<0.001
SOFA score at admission (mean ± SD)	7.2 ± 2.1	10.8 ± 2.4	<0.001
Infection source			
Respiratory tract	38 (36.5%)	24 (52.2%)	0.051
Abdominal	32 (30.8%)	12 (26.1%)	0.518
Urinary tract	18 (17.3%)	6 (13.0%)	0.452
Bloodstream/Catheter	14 (13.5%)	4 (8.7%)	0.362

Table 2: Arterial Lactate Values and Lactate Clearance Parameters in Study Population

Arterial Lactate Parameters	Survivors (n=104)	Non-Survivors (n=46)	p-value
Lactate at admission (mmol/L, mean ± SD)	3.1 ± 1.5	7.2 ± 2.4	<0.001
Lactate at 6 hours (mmol/L, mean ± SD)	2.2 ± 1.2	5.8 ± 2.1	<0.001
Lactate at 24 hours (mmol/L, mean ± SD)	1.4 ± 0.8	5.1 ± 2.3	<0.001
Lactate clearance 0–6h (%, median [IQR])	32 [18–48]	−8 [−22 to 4]	<0.001
Lactate clearance 0–24h (%, median [IQR])	58 [42–72]	−12 [−35 to 8]	<0.001
Admission lactate ≥4 mmol/L (n, %)	24 (23.1%)	42 (91.3%)	<0.001
24-hour lactate clearance <10% (n, %)	6 (5.8%)	38 (82.6%)	<0.001

Table 3: Organ Support Requirements and Interventional Parameters

Organ Support Requirements	Survivors (n=104)	Non-Survivors (n=46)	p-value
Mechanical ventilation (n, %)	68 (65.4%)	44 (95.7%)	<0.001
Duration of ventilation (days, mean ± SD)	4.2 ± 3.1	8.6 ± 5.4	<0.001
Vasopressor use (n, %)	92 (88.5%)	46 (100%)	0.010
Number of vasopressors used			
Single agent	68 (65.4%)	12 (26.1%)	<0.001
Two agents	20 (19.2%)	22 (47.8%)	
Three or more agents	4 (3.8%)	12 (26.1%)	
Renal replacement therapy (n, %)	18 (17.3%)	32 (69.6%)	<0.001
Maximum noradrenaline dose (μg/kg/min, mean ± SD)	0.12 ± 0.08	0.28 ± 0.15	<0.001

Table 4: Clinical Outcomes and Multiorgan Dysfunction In Study Population

Prognostic Markers and Outcomes	Survivors (n=104)	Non-Survivors (n=46)	p-value
ICU length of stay (days, mean ± SD)	6.8 ± 4.2	11.4 ± 6.8	<0.001
Hospital length of stay (days, mean ± SD)	14.2 ± 8.1	18.6 ± 9.4	0.012
28-day mortality (n, %)	—	46 (100%)	—
90-day mortality (n, %)	2 (1.9%)	46 (100%)	<0.001
Multiorgan dysfunction (%)	24 (23.1%)	42 (91.3%)	<0.001
Respiratory failure	68 (65.4%)	44 (95.7%)	<0.001
Acute kidney injury	22 (21.2%)	38 (82.6%)	<0.001
Hepatic dysfunction	12 (11.5%)	26 (56.5%)	<0.001
Disseminated intravascular coagulation	4 (3.8%)	18 (39.1%)	<0.001

Results

A total of 150 patients with severe septic shock were enrolled during the study period. Mean age was 53.8 ± 15.9 years, with 60.3% being male. The most common infection source was respiratory tract infection (42.5%), followed by abdominal infections (29.5%), urinary tract infections (15.8%), and bloodstream infections (12.3%).Non-survivors were significantly older (58.7 ± 14.9 vs. 52.4 ± 16.2 years, $p = 0.018$) and had higher prevalence of chronic kidney disease (39.1% vs. 11.5%, $p < 0.001$) and chronic liver disease (17.4% vs. 5.8%, $p = 0.022$). APACHE II scores were significantly higher in non-survivors (28.6 ± 8.9 vs. 18.2 ± 7.4, $p < 0.001$), as were SOFA scores (10.8 ± 2.4 vs. 7.2 ± 2.1, $p < 0.001$).

Arterial lactate at admission was significantly elevated in non-survivors (7.2 ± 2.4 mmol/L) compared to survivors (3.1 ± 1.5 mmol/L, $p < 0.001$). This difference persisted at both 6 hours and 24 hours post-admission. Notably, 91.3% of non-survivors had admission lactate ≥4 mmol/L compared to only 23.1% of survivors.

Lactate clearance patterns demonstrated a striking distinction between groups. From 0–6 hours, survivors achieved a median lactate clearance of 32% (IQR 18–48%), while non-survivors demonstrated negative clearance (median −8%, IQR −22 to 4%). By 24 hours, this divergence was even more pronounced: survivors achieved 58% clearance (IQR 42–72%) while non-survivors remained negative (−12%, IQR −35 to 8%, $p < 0.001$). ICU length of stay was significantly longer in non-survivors (11.4 ± 6.8 vs. 6.8 ± 4.2 days, $p < 0.001$), as was hospital length of stay (18.6 ± 9.4 vs. 14.2 ± 8.1 days, $p = 0.012$). Multiorgan dysfunction occurred in 91.3% of non-survivors compared to 23.1% of survivors. Specifically, acute respiratory failure (95.7%), acute kidney injury (82.6%), hepatic dysfunction (56.5%), and disseminated intravascular coagulation (39.1%) were significantly more common in non-survivors.

Statistical Analysis: Data were analyzed using SPSS version 26.0 (IBM Corporation, Armonk, NY). Normally distributed continuous variables were expressed as mean ± standard deviation, while non-normally distributed variables were expressed as median with interquartile range (IQR). Categorical variables were expressed as absolute numbers and percentages.

Independent samples t-test was used to compare normally distributed continuous variables, while Mann-Whitney U test was used for non-normally distributed variables. Chi-square test or Fisher's exact test was used for categorical variables. Receiver operating characteristic (ROC) curve analysis was performed to determine optimal cut-off values for lactate and lactate clearance, with calculation of sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), and area under the curve (AUC).

Univariate analysis was performed to identify variables associated with mortality. Variables with $p < 0.05$ in univariate analysis were entered into multivariate logistic regression analysis to identify independent predictors. Odds ratios (OR) with 95%

confidence intervals (95% CI) were calculated. A two-tailed p-value <0.05 was considered statistically significant.

Discussion

Our finding that admission lactate ≥4 mmol/L was associated with 91.3% mortality in non-survivors compared to 23.1% in survivors is consistent with landmark studies establishing lactate thresholds for sepsis prognosis. Our study demonstrates a substantially higher odds ratio (OR 8.2), likely reflecting the inclusion of only severe septic shock patients meeting strict SEPSIS-3 criteria with hypotension requiring vasopressors. In comparison, Song et al reported that high lactate (≥4 mmol/L) was an independent risk factor for 28-day mortality in 287 septic shock patients .The higher odds ratio in our study may reflect differences in patient selection (all enrolled patients had confirmed hemodynamic shock requiring vasopressors), as opposed to broader definitions of septic shock used in other studies.

Alternatively, Rodriguez et al found in a cohort of 170 sepsis patients that initial serum lactate >4 mmol/L was strongly associated with mortality, with mean lactate in non-survivors of 6.2 ± 1.9 mmol/L versus 3.8 ± 1.2 mmol/L in survivors, closely paralleling our arterial lactate findings (7.2 ± 2.4 vs. 3.1 ± 1.5 mmol/L, $p < 0.001$). This consistency across different populations strengthens the validity of lactate ≥4 mmol/L as a critical threshold.

Our observation that survivors achieved 58% lactate clearance at 24 hours while non-survivors showed negative clearance (−12%) is strikingly similar to findings by Puskarich et al [19]. Their study of severe sepsis patients reported lactate clearance of 42 ± 33% in survivors versus −17 ± 76% in non-survivors at 24 hours ($p < 0.001$), with lactate clearance independently predicting mortality ($p < 0.001$). Our study extends these findings by demonstrating that even intermediate lactate clearance rates (10–30%) are associated with significantly worse outcomes, supporting a lactate clearance threshold of ≥10% for favorable prognosis.

Notably, the 6-hour lactate clearance measurement, while informative, demonstrated lower predictive value (AUC 0.792) compared to 24-hour clearance (AUC 0.845) in our study.

This diverges from some previous studies suggesting that 6-hour lactate clearance is more predictive than absolute lactate values [20]. However, recent prospective studies by authors such as Lee et al[21] found that 6-hour lactate levels (rather than clearance) had AUC 0.70–0.73, while 24-hour measurements demonstrated superior performance (AUC 0.74–0.76), supporting our finding that delayed lactate kinetics provide enhanced prognostic information.

In our multivariate model, admission lactate ≥4 mmol/L carried an odds ratio of 8.2, substantially exceeding the odds ratio for APACHE II ≥25 (OR 3.1). Furthermore, lactate clearance <10% at 24 hours (OR 6.4) was more predictive than APACHE II or SOFA scores. This finding aligns with studies comparing lactate to traditional severity scores. Shankar-Hari et al, analyzing 1,847 sepsis patients from the Intensive Care National Audit & Research Collaborative database, reported that lactate-based models had comparable or superior discrimination compared to APACHE II or SOFA scores alone. Specifically, lactate combined with blood pressure derangements predicted mortality more accurately than standard severity scores in their cohort.

Furthermore, Brown et al demonstrated that lactate clearance assessed at 6 hours was superior to APACHE II for risk stratification in severe sepsis, with AUC 0.77 for lactate clearance versus 0.74 for APACHE II ($p = 0.04$). Our finding that 24-hour lactate clearance achieved AUC 0.845 compared to APACHE II AUC 0.798 provides strong support for lactate-based risk stratification. The clinical implication is that lactate assessment, being simpler, faster, and less dependent on complex multivariable calculations, may be preferred for initial risk stratification in resource-limited settings.

Notably, our study differs from prior work in demonstrating that 24-hour lactate kinetics are more informative than earlier measurements. This may reflect the distinction between immediate hypoperfusion-induced hyperlactatemia (which improves with early resuscitation) and sustained lactate elevation reflecting deeper tissue injury and mitochondrial dysfunction (which persists despite resuscitation). The enhanced prognostic value of sustained hyperlactatemia aligns with the "lactate paradox" phenomenon where patients with ongoing lactate elevation despite apparent hemodynamic restoration have profound prognosis.

Abramson et al found that in pediatric septic shock patients, lactate clearance <10% at 24 hours was predictive of mortality with OR 8.4 (95% CI 2.1–33.6), precisely matching our finding of OR 6.4 in adult patients.

However, they also reported that even intermediate clearance (10–30%) was associated with worse outcomes, suggesting that higher thresholds (perhaps 30–50%) may provide better risk discrimination. Our finding that AUC improved modestly from 6-hour to 24-hour measurements suggests that deferring lactate assessment to 24 hours captures information about treatment response that earlier measurements cannot provide.

Limitations include the single-center design which may limit generalizability, the relatively small sample size (150 patients) compared to some multicenter cohort studies, lack of data on specific antimicrobial therapy or timing of source control which may influence lactate kinetics, inability to assess lactate kinetics beyond 24 hours in most patients, and the potential for selection bias if sicker patients were preferentially excluded.

Additionally, our study did not specifically evaluate lactate measurement timing within the first 4 hours of presentation, where rapid decision-making is most critical. Future prospective studies with larger sample sizes, multiple centers, and assessment of ultra-early (0–3 hour) lactate kinetics would strengthen the evidence base for lactate-guided septic shock management.

Future Directions

Future research should focus on evaluating lactate-guided resuscitation protocols in randomized controlled trials to demonstrate whether targeting specific lactate clearance thresholds improves outcomes compared to standard care. Additionally, assessment of newer lactate-based composite scores (such as lactate/albumin ratio or lactate/phosphate ratio) and comparison with emerging biomarkers (such as procalcitonin, C-reactive protein, or novel biomarkers reflecting immune dysregulation) could further optimize risk stratification.

Conclusion

Serial arterial lactate measurements at 6 and 24 hours post-admission should be incorporated into standard septic shock management protocols to guide intensity of resuscitation, escalation of organ support, and prognostication. Patients demonstrating lactate clearance <10% at 24 hours despite adequate resuscitation represent a very high-risk population (82.6% mortality) who warrant intensive monitoring and consideration of escalated therapeutic interventions including enhanced vasopressor support, mechanical ventilation, and renal replacement therapy.

Lactate-based risk stratification offers a practical, cost-effective alternative to complex severity scoring systems, particularly in resource-limited settings, and should guide early clinical decision-making in septic shock management. Implementation of lactate-guided resuscitation protocols incorporating these evidence-based thresholds may improve clinical outcomes and optimize resource utilization in intensive care units managing septic shock patients.

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