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Original Article

The 6-hour lactate clearance rate in predicting 30-day mortality in cardiogenic shock

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ABSTRACT

Background: Early evaluation of prognosis in cardiogenic shock (CS) is crucial for tailored treatment selection. Both lactate clearance and lactate levels are considered useful prognostic biomarkers in patients with CS. However, there is yet no literature comparing the 6-hour lactate clearance rate (Δ6Lac) with lactate levels measured at admission (L1) and after 6 h (L2) to predict 30-day mortality in CS.

Methods: In this observational cohort study, 95 patients with CS were treated at Department of Intensive Care Unit, Yiwu Central Hospital between January 2020 and December 2022. Of these, 88 patients met the eligibility criteria. The lactate levels were measured after admission (L1) as the baseline lactate value, and were measured after 6 h (L2) following admission. The primary endpoint of the study was survival rate at 30 days. A receiver operating characteristic curve was used for data analysis. Univariate and multivariate Cox regression analyses were performed based on Δ6Lac. Kaplan–Meier (KM) survival curves were generated to compare the 30-day survival rates among L1, L2, and Δ6Lac.

Results: The Δ6Lac model showed the highest area under the curve value (0.839), followed by the L2 (0.805) and L1 (0.668) models. The Δ6Lac model showed a sensitivity of 84.2% and specificity of 75.4%. The L1 and L2 models had sensitivities of 57.9% each and specificities of 89.9% and 98.6%, respectively. The cut-off values for Δ6Lac, L1, and L2 were 18.2%, 6.7 mmol/L, and 6.1 mmol/L, respectively. Univariate Cox regression analysis revealed a significant association between Δ6Lac and 30-day mortality. After adjusting for five models in multivariate Cox regression, Δ6Lac remained a significant risk factor for 30-day mortality in patients with CS. In our fifth multivariate Cox regression model, Δ6Lac remained a risk factor associated with 30-day mortality (hazard ratio [HR]=5.14, 95% confidence interval [CI]: 1.48 to 17.89, P=0.010) as well as L2 (HR=8.42, 95% CI: 1.26 to 56.22, P=0.028). The KM survival curve analysis revealed that L1 >6.7 mmol/L (HR=8.08, 95% CI: 3.23 to 20.20, P <0.001), L2 >6.1 mmol/L (HR=25.97, 95% CI: 9.76 to 69.15, P <0.001), and Δ6Lac ≤18.2% (HR=8.92, 95% CI: 2.95 to 26.95, P <0.001) were associated with a higher risk of 30-day mortality.

Conclusions: Δ6Lac is a better predictor for 30-day mortality in CS than lactate levels at admission. It has a predictive value equivalent to that of lactate level at 6 h after admission, making it an important surrogate indicator for evaluating the suitability as well as poor prognosis after CS treatment. We found that a cut-off value of 18.2% for Δ6Lac provided the most accurate assessment of early prognosis in CS.

Introduction

Cardiogenic shock (CS) is the most severe condition of heart failure, where insufficient cardiac function hinders blood circulation, resulting in inadequate oxygen supply to tissues and organs and hence, has a high mortality rate.[1–3] Delaying rescue treatment can result in a worse prognosis; for example, patients receiving extracorporeal cardiopulmonary resuscitation (ECPR) with delayed opening of their culprit vessels often experience poor neurological outcomes, leading to decreased 30-day survival.[4] The latest Society for Cardiovascular Angiography and Interventions (SCAI) clinical expert consensus statement has established new guidelines to evaluate shock severity. These guidelines require a regular reassessment of the patient's

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shock stage to determine the best treatment options, whether upgrading or downgrading, ultimately leading to an improved prognosis. Lactate level is an important factor in the evaluation process.[2] Elevated lactate levels, resulting from anaerobic glycolysis, are commonly observed in patients with circulatory failure.[5] Animal and clinical studies have demonstrated an association between lactate production and tissue hypoxia.[6,7] Park et al.[8] showed that prolonged hyperlactatemia can also reduce survival in patients with other medical conditions such as low blood pressure, while Datta et al.[9] identified a positive correlation between lactate levels and mortality in emergency admissions patients. Moreover, some investigations have concluded that a blood lactate level >4 mmol/L is a reliable predictor of outcomes in CS patients.[10] Therefore, baseline arterial lactate level is often used as a prognostic biomarker in critical care settings.[11,12] However, relying solely on the lactic acid level at a particular moment cannot accurately determine the severity of the disease and response to treatment. Therefore, it is necessary to identify better indicators in clinical practice.

A likely alternative is the lactate clearance rate, and the efficient removal of lactate from the body suggests better blood flow to tissues.[13] Recently, a decrease in lactate clearance rate and lactate levels in patients with CS has been associated with a worse prognosis.[14] Fuernau et al.[12] identified an 8-hour lactate clearance rate below 3.45% per hour as an independent predictor of survival in CS patients. However, limited research has been carried out on the correlation between the levels of 6-hour lactate clearance rate (Δ6Lac) and lactate upon admission, as well as at the 6-hour mark following admission, in patients experiencing CS.

Therefore, the aim of this study was to assess the predictive value of Δ6Lac in compensating for the initial lactate levels and lactate levels at the 6th hour. The primary objective was to establish definitive thresholds that can assist in making well-informed decisions to improve therapeutic strategies.

Methods

Data collection

Patients treated for CS at Department of Intensive Care Unit, Yiwu Central Hospital between 1st January, 2020, and 31st December, 2022 were enrolled in this study. Patients were diagnosed with CS if they had severe myocardial functional impairment leading to reduced end-organ perfusion.[2] The criteria for identifying CS were elevated serum lactate levels ≥2 mmol/L and a urine output of <0.5 mL/(kg·h). Patients aged ≤18 years or ≥90 years, who had undergone cardiopulmonary resuscitation for more than 30 min, had severe cerebral deficits, had mechanical causes of CS, and had severe hepatic insufficiency were excluded from this study. We gathered general patient characteristics, including age, sex, and previous underlying diseases such as hypertension, diabetes, and stroke. We also noted the causes of CS such as acute myocardial infarction, severe myocarditis, dilated cardiomyopathy, and malignant arrhythmia. Additionally, we recorded some important treatment interventions such as the proportion of coronary angiography, percutaneous coronary intervention (PCI), thrombolysis in myocardial infarction (TIMI) blood flow classification after PCI treatment, as well as mechanical ventilation (MV), intra-aortic balloon pump (IABP), and extracorporeal membrane oxygenation (ECMO). Furthermore, we collected laboratory examination results at admission, including NT-proBNP, troponin I level in the emergency room, serum creatinine, and alanine aminotransferase (ALT).

Measuring the lactate levels and lactate change

As a daily treatment standard for hemodynamic management in patients with CS, we require monitoring of lactate after admission and at the 6th hour after admission. We also monitored blood gas every 2–4 h. As the patients were already in CS upon admission to the intensive care unit (ICU), the lactate levels were measured after admission (L1) as the baseline lactate value, and we also measured lactate after 6 h (L2) following admission to our unit. Δ6Lac was determined for each patient using the following formula[15]:

$$\Delta 6\mathrm{Lac}(\%) = (\mathrm{L1} - \mathrm{L2})/\mathrm{L1} \times 100.$$

Statistical analysis

Patients were divided into those who survived for more than 30 days (30-day survival group) and those who survived for less than 30 days (non-survival group) following admission. Categorical variables were expressed as percentages. Normally distributed continuous variables are expressed as mean±standard deviation, while non-normally distributed variables are expressed as medians (interquartile ranges [IQR]). Pearson's chi-squared test or Fisher's exact test was used to compare categorical variables, whereas the Wilcoxon rank-sum test was used to compare continuous variables between the two groups. The area under the curve (AUC) of the receiver operating characteristic (ROC) curve was used to calculate the accuracy of the L1, L2, and Δ6Lac models in predicting the 30-day mortality. The cut-off values for predicting 30-day mortality for each model were calculated using the Youden index.

A univariate Cox regression model was used to determine the impact of age, sex, baseline serum creatinine, baseline hemoglobin, baseline bilirubin, heart rate, baseline ALT, N-terminal pro-B-type natriuretic peptide, cardiac troponin I, systolic blood pressure, history of hypertension, diabetes mellitus, prior stroke, prior myocardial infarction, PCI, mechanical circulatory support (MCS) including IABP and/or ECMO, MV at admission, lactate level at admission, lactate at the 6th hour of admission, and 6-hour lactate clearance on 30-day survival. Next, five multivariate Cox regression models were constructed to evaluate the adjusted relationship between 6-hour lactate clearance and survival. The choice of variables in the model was closely related to the treatment of clinical and prognostic CS. This method is based on an iterative process that starts with an empty model and sequentially adds variables to the model based on their statistical significance (P <0.05) or improvement in the model fit. Five multivariate Cox regression models were used to account for potential covariates for Δ6Lac. We also calculated the Akaike information criterion (AIC) and the Bayesian information criterion (BIC), when each model incorporated a new

variable then recalculated the AIC and the BIC to evaluate the model performance.

Finally, Kaplan–Meier (KM) analyses, according to Δ6Lac, L1, and L2 were performed.

R software (version 4.2.2) was used for all statistical analyses, and a *P*-value <0.05 was deemed statistically significant.

Results

Patient characteristics

A total of 95 patients with CS received treatment at our hospital between 1st January 2020 and 31st December 2022. However, three patients were excluded because of severe brain dysfunction, and four patients were excluded as they were ≥90 years old. Of the 88 patients included in the study, 69 (78.4%) survived to discharge beyond 30 days.

The baseline demographic and clinical characteristics of the patients who survived and those who did not 30 days after ICU admission are summarized in Table 1. The patients who survived beyond 30 days had a significantly higher incidence of TIMI grade flow 3 (63.8% *vs.* 31.6%; *P* <0.001) than the non-survivors.

In addition, the 30-day survivors were significantly less likely to receive MV (33.3% *vs.* 68.4%; *P*=0.013) and venoarterial ECMO (5.8% *vs.* 26.3%; *P*=0.020). There was no statistically significant difference between patients requiring IABP (27.9% *vs.* 42.1%; *P*=0.348) between the two groups (Table 1).

Association between survival and lactate levels and Δ6Lac

In the 30-day survival group, the median Δ6Lac was significantly higher than the non-survival group (37.5% [IQR: 20.0%–53.9%] *vs.* 7.9% [IQR: −30.6% to 17.2%], *P* <0.001). Conversely, the median L1 was significantly lower in the 30-day survival group than in the non-survival group (2.6 mmol/L [IQR: 1.4–4.0 mmol/L] *vs.* 7.2 mmol/L [IQR: 2.0–9.8 mmol/L], *P*=0.026), while the median L2 was also significantly lower in the 30-day survival group than in the non-survival group (1.6 mmol/L [IQR: 1.2–2.0 mmol/L] *vs.* 7.9 mmol/L [IQR: 1.7–11.0 mmol/L], *P* <0.001).

Regression and ROC analysis

The cut-off values for the prediction of Δ6Lac, L1, and L2 were 18.2% (sensitivity: 84.2%, specificity: 75.4%), 6.7 mmol/L

Table 1
Baseline demographic and clinical characteristics.

Baseline characteristics	Total (*n*=88)	30-day survival group (*n*=69)	30-day non-survival group (*n*=19)	*P*-value
Demographic characteristics				
Age (years)	61±15	61±16	67±10	0.109
Male sex	57 (64.8)	45 (65.2)	12 (63.2)	1.000
Heart rate (beats/min)	107±30	108±28	101±34	0.358
Systolic blood pressure (mmHg)	97±29	96±26	101±36	0.493
Comorbidity				
Hypertension	43 (48.9)	32 (46.4)	11 (57.9)	0.374
Diabetes mellitus	26 (29.5)	19 (27.5)	7 (36.8)	0.431
Prior stroke	4 (4.5)	2 (2.9)	2 (10.5)	0.202
History of myocardial infarction	5 (5.7)	4 (5.8)	1 (5.3)	1.000
Clinical features				
Myocardial infarction	67 (76.1)	52 (75.4)	15 (78.9)	1.000
Acute myocarditis	7 (8.0)	5 (7.2)	2 (10.5)	0.641
Ventricular tachycardia	11 (12.5)	8 (11.6)	3 (15.8)	0.697
Atrial fibrillation	6 (6.8)	5 (7.2)	1 (5.3)	1.000
Dilated cardiomyopathy	4 (4.5)	3 (4.3)	1 (5.3)	1.000
Valvular heart disease	1 (1.1)	1 (1.4)	0 (0)	1.000
Laboratory examination				
NT-proBNP at baseline (pg/mL)	2541 (575–5763)	1758 (209–5191)	4421 (988–8138)	0.131
Emergency cardiac troponin I (ng/mL)	13.8 (2.2–40.0)	13.6 (2.1–33.8)	25.0 (7.8–40.0)	0.147
Total bilirubin (μmol/L)	17.7 (11.4–26.7)	18.1 (12.6–26.6)	15.1 (9.1–32.0)	0.914
Baseline ALT (U/L)	60 (31–152)	52 (29–95)	183 (64–968)	0.007
Baseline serum creatine (μmol/L)	87.1 (67.4–132.3)	78.2 (66.9–113.0)	132.67 (118.5–150.1)	0.006
Special examination and intervention				
CABG	66 (75.0)	51 (73.9)	15 (78.9)	0.771
PCI	59 (67.0)	51 (73.9)	8 (42.1)	0.039
TIMI flow grade				<0.001
Grade 3	50 (56.8)	44 (63.8)	6 (31.6)	
Grade 1–2	6 (6.8)	4 (5.8)	2 (10.5)	
Grade 0	12 (13.6)	4 (5.8)	8 (42.1)	
Intervention means				
MV	36 (40.9)	23 (33.3)	13 (68.4)	0.013
IABP	27 (30.7)	19 (27.9)	8 (42.1)	0.348
ECMO	9 (10.2)	4 (5.8)	5 (26.3)	0.020
Prognostic indicators.				
Lactate levels measured upon admission (L1) (mmol/L)	2.6 (1.4–5.7)	2.6 (1.4–4.0)	7.2 (2.0–9.8)	0.026
Lactate levels measured after 6 h (L2) (mmol/L)	1.6 (1.2–2.8)	1.6 (1.2–2.0)	7.9 (1.7–11.0)	<0.001
The 6-hour lactate clearance rate (Δ6Lac)	29.3 (11.8–46.5)	37.5 (20.0–53.9)	7.9 (−30.6 to 17.2)	<0.001

Data are presented as mean±standard deviation, *n* (%), or median (interquartile range).
ALT: Alanine aminotransferase; CABG: Coronary angiography; ECMO: Extracorporeal membrane oxygenation; IABP: Intra-aortic balloon pump; MV: Mechanical ventilation; NT-proBNP: N-terminal pro-brain natriuretic peptide; PCI: Percutaneous coronary intervention; TIMI flow grade: Thrombolysis in myocardial infarction flow grade.

(sensitivity: 57.9%, specificity: 89.9%), and 6.1 mmol/L (sensitivity: 57.9%, specificity: 98.6%), respectively. The Δ6Lac model had the highest AUC (0.839, 95% confidence interval [CI]: 0.746 to 0.909), followed by the L2 (0.805, 95% CI: 0.707 to 0.882) and L1 (0.668, 95% CI: 0.560 to 0.765) models (Figure 1). The Δ6Lac model showed the highest sensitivity (84.2%) and specificity (75.4%). The sensitivities for the L1 and L2 models were 57.9% and 57.9%, and the specificities were 89.9% and 98.6%, respectively.

Univariate and multivariate Cox regression analyses

Univariate and multivariate Cox regression analyses resulted in the identification of five models (Table 2). Model 1 was adjusted for patient age and sex, indicating that Δ6Lac is a significant factor in predicting 30-day mortality (hazard ratio [HR]=9.11, 95% CI: 3.01 to 27.62, P <0.001).

The second model was adjusted for patients with elevated baseline ALT and serum creatinine levels above the upper limit of the normal values, and Δ6Lac remained a significant factor for predicting the 30-day mortality (HR=12.21, 95% CI: 3.85 to 38.76, P <0.001).

The third model was adjusted for patients receiving PCI and TIMI flow grade after PCI, which also indicated Δ6Lac as a significant predictor for 30-day mortality (HR=19.00, 95% CI: 5.95 to 60.61, P <0.001).

Model 4 was adjusted for patients receiving intubation or MCS support, which includes IABP and/or ECMO, and Δ6Lac achieved an HR of 14.36 and a 95% CI of 4.30 to 47.95, P <0.001.

In the fifth multivariate Cox regression model, Δ6Lac, L1, and L2 were analyzed. Δ6Lac remained a risk factor associated with 30-day mortality (HR=5.14, 95% CI: 1.48 to 17.89, P=0.01), and L2 was also a risk factor associated with 30-day mortality (HR=8.42, 95% CI: 1.26 to 56.22, P=0.028). However, L1 was no longer a risk factor (HR=2.08, 95% CI: 0.36 to 11.91, P=0.409).

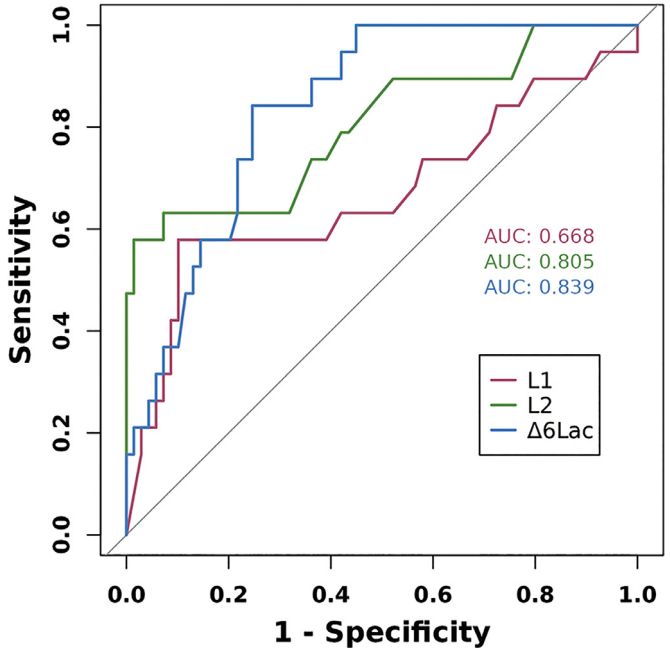

Figure 1. ROC curves show the predictive value of lactate level on 30-day mortality. ROC curves were calculated for 1-hour (L1) and 6-hour (L6) lactate levels and the 6-hour lactate clearance rate (Δ6Lac).
AUC: Area under curve; ROC: Receiver operating characteristics.

KM analysis for the 30-day mortality

Patients with a Δ6Lac ≤18.2% had significantly better survival than those with a Δ6Lac >18.2% (HR= 8.92, 95% CI: 2.95 to 26.95) (Figure 2). Patients with L1 ≤6.7 mmol/L had significantly better survival than those with L1 >6.7 mmol/L (HR= 8.08, 95% CI: 3.23 to 20.20) (Figure 3). Additionally, patients with L2 ≤6.1 mmol/L had significantly better survival than those with L2 >6.1 mmol/L (HR= 25.97, 95% CI: 9.76 to 69.15) (Figure 4).

Discussion

Our study revealed a significantly decreased Δ6Lac during the initial stage of CS in non-survivors. Furthermore, Δ6Lac

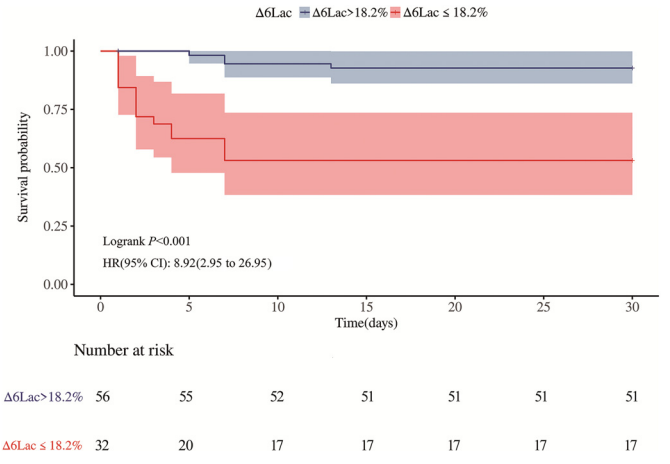

Figure 2. The 30-day Kaplan–Meier survival analysis comparing Δ6Lac for cut-off values above and below 18.2%.
Δ6Lac: The 6-hour lactate clearance rate; CI: Confidence interval; HR: Hazard ratio.

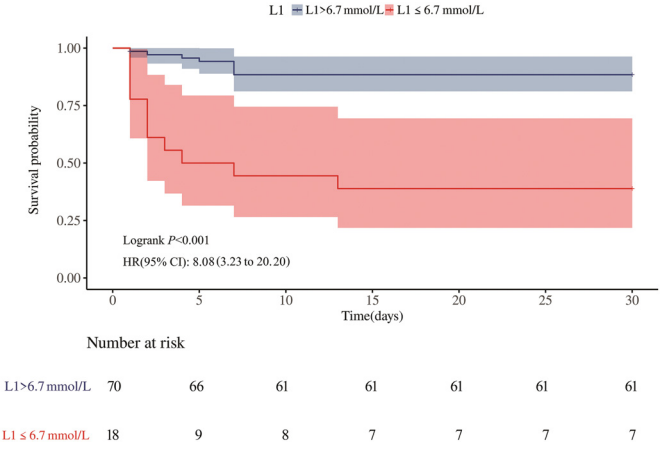

Figure 3. The 30-day Kaplan–Meier survival analysis comparing the L1 for cut-off values above and below 6.7 mmol/L.
CI: Confidence interval; HR: Hazard ratio; L1: Lactate levels measured upon admission.

Table 2
Univariate and multivariate Cox regression for 30-day mortality based on the Δ6Lac.

Model*	HR (univariable)	95% CI	*P*-value	AIC	BIC	HR (multivariable)	95% CI	*P*-value	AIC	BIC
Model 1										
Δ6Lac ≤18.2%	8.92	3.95 to 26.95	<0.001	147.95	148.89	9.11	3.01 to 27.62	<0.001	147.95	148.89
Age ≥60 years	2.77	0.92 to 8.35	0.070	163.70	164.65	3.08	0.97 to 9.78	0.057	145.79	147.68
Sex	0.92	0.36 to 2.35	0.869	167.55	168.50	1.21	0.46 to 3.21	0.701	147.64	150.48
Model 2										
Δ6Lac ≤18.2%	8.92	3.95 to 26.95	<0.001	147.95	148.89	12.21	3.85 to 38.76	<0.001	147.95	148.89
ALT >200 U/L	4.50	1.80 to 11.23	0.001	158.64	159.59	2.31	0.82 to 6.51	0.112	141.98	143.87
0<ΔCr≤+25%	2.07	0.38 to 11.33	0.400	49.58	49.37	3.85	0.67 to 22.13	0.131	135.21	139.93
+25%<ΔCr≤+50%	7.16	2.01 to 25.49	0.002	73.03	73.34	10.33	2.74 to 38.86	<0.001		
ΔCr>+50%	6.33	1.85 to 21.69	0.003	82.07	82.46	5.35	1.38 to 20.69	0.015		
Model 3										
Δ6Lac ≤18.2%	8.92	3.95 to 26.95	<0.001	147.95	148.89	19.00	5.95 to 60.61	<0.001	147.95	148.89
TIMI flow grade=0	4.01	1.52 to 10.57	0.005	157.37	158.31	9.72	3.50 to 27.01	<0.001	129.78	132.61
Model 4										
Δ6Lac ≤18.2%	8.92	3.95 to 26.95	<0.001	147.95	148.89	14.36	4.30 to 47.95	<0.001	147.95	148.89
IABP	1.67	0.67 to 4.16	0.268	166.39	167.34	2.38	0.90 to 6.29	0.081	148.75	150.64
ECMO	3.79	1.36 to 10.54	0.011	163.40	163.40	5.06	1.49 to 17.19	0.009	140.23	143.06
MV	3.90	1.48 to 10.26	0.006	159.25	160.19	3.26	1.13 to 9.39	0.029	137.35	141.13
Model 5										
Δ6Lac ≤18.2%	8.92	3.95 to 26.95	<0.001	147.95	148.89	5.14	1.48 to 17.89	0.010	147.95	148.89
L1 >6.7 mmol/L	8.08	3.23 to 20.20	<0.001	148.71	149.66	2.08	0.36 to 11.91	0.409	128.75	130.64
L2 >6.1 mmol/L	25.97	9.76 to 69.15	<0.001	129.88	130.82	8.42	1.26 to 56.22	0.028	126.11	128.95

*The models were adjusted for various clinical factors based on common clinical confounding factors, comprehensive professional assessment, and calculation of AIC and BIC values after the inclusion of each model parameter, including age, sex, ALT, ΔCr. Clinically important therapeutic interventions: TIMI grade flow, MV, IABP, ECMO, L1, lactate levels measured after 6 h L2. In all five models, Δ6Lac remained a significant predictor of the 30-day mortality rate in patients with CS. In each model, we attach the AIC and BIC values for the authoritative standard sensitivity analysis criteria.
Δ6Lac: The 6-h lactate clearance rate; ΔCr: Increase in creatinine from basal level; AIC: Akaike information criterion; ALT: Alanine aminotransferase; BIC: Bayesian information criterion; CI: Confidence interval; CS: Cardiogenic shock; ECMO: Extracorporeal membrane oxygenation; HR: Hazard ratio; IABP: Intra-aortic balloon pump; L1: Lactate levels measured upon admission; L2: Lactate levels measured after 6 h; MV: Mechanical ventilation; TIMI: Thrombolysis in myocardial infarction.

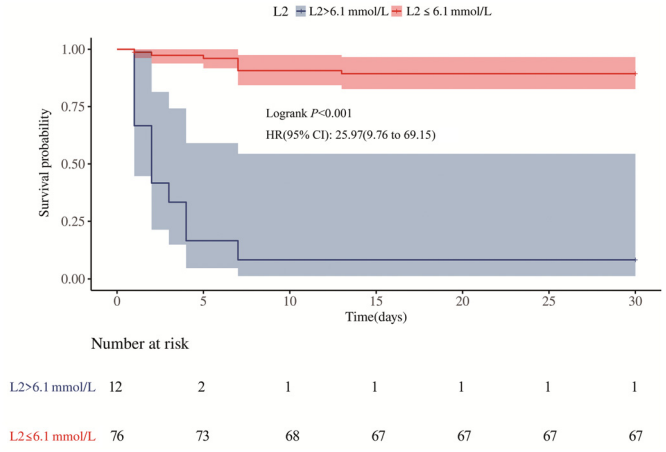

Figure 4. The 30-day Kaplan–Meier survival analysis comparing the L2 for cut-off values above and below 6.1 mmol/L.
CI: Confidence interval; HR: Hazard ratio; L2: Lactate levels measured after 6 h.

seems to be a more effective predictor of 30-day survival than baseline lactate levels, and its clinical significance was on par with the lactate level 6 h after CS treatment. We identified that a cut-off value of 18.2% for Δ6Lac provided the most accurate assessment of early prognosis in patients with CS.

Lactate is a metabolic marker that can indicate tissue hypoxia and serves as a valuable indicator of tissue metabolism. Therefore, serum lactate levels are often utilized to predict the clinical outcomes in critically ill patients. Smuszkiewicz et al.[16] discovered an association between serum lactate levels ≥4.5 mmol/L in category 2 upon admission and 28-day mortality in 78.94% of patients. Zhang et al.[17] also determined that ICU patients with high initial lactate levels and prolonged lactate normalization times had a higher mortality risk. High lactic acidosis was also found to be a strong predictor of mortality in patients with CS. However, when using lactate as an indicator, it is important to ascertain whether the increase in lactate levels is caused by hypoxia. Type A lactic acidosis is closely linked to tissue hypoxia and mortality, whereas type B lactic acidosis has been associated with other conditions (e.g., liver disease, multiple myeloma, diabetic ketoacidosis, and thiamine deficiency) and the administration of some drugs such as metformin and adrenaline; patients with type B lactic acidosis do not exhibit tissue hypoxia.[18,19]

Lactate clearance is an indicator of the improvement of tissue hypoperfusion and correction of tissue anaerobic metabolism. Rapid lactate clearance during the early stages of severe sepsis and septic shock is associated with increased tissue perfusion and reduced morbidity and mortality.[20–22] Based on these findings, some studies recommend detecting and managing tissue hypoperfusion within the first 6 h of resuscitation.[21] Limited studies have been performed to investigate earlier lactate clearance in patients with CS until Fuernau et al.[12] first discovered the meaningful impact of 8-hour lactate clearance on the prognosis of CS patients. A 4-hour lactate clearance could not provide sufficient prognostic information, while a 6–8 hour lactate clearance could provide adequate prognostic information.[12,14] We conducted a study on the Δ6Lac in patients with CS. We investigated the Δ6Lac as a potential excellent chemical biomarker for early prognostic assessment in CS. Our study suggests that it may be superior to baseline lactate levels.

Similar to our study, Marbach et al.[15] found that poor lactate clearance at 8 h, 12 h, and 24 h following admission was associated with increased in-hospital mortality and survival at all stages. However, the population characteristics of Marbach et al.'s[14] study were different from ours. In their study, patients with ischemic cardiomyopathy accounted for 66.2%, and

only 7.0% of patients were treated with IABP, only one patient was treated with ECMO, while in our study, the majority (76.1%) of patients had a myocardial infarction, and 30.7% received IABP.[14] Moreover, 10.2% of patients in our study received ECMO. Park et al.[8] found that patients with an initial 24-h lactate clearance rate of 64% or higher had a significantly lower incidence of in-hospital death. The percentage number of patients treated with ECMO in the study by Park et al.[8] was 40.2%.

Other studies have also supported this claim. Marbach et al.[15] conducted a meta-analysis of 1585 patients with CS and found that evaluating lactate clearance rates within 6–8 h post-admission could provide an insight into the prognosis. The average percentage lactate clearance difference within this time period was 17.3%, with a CI of 11.6% to 23.1% (P <0.001). However, the 4-hour lactate clearance did not offer prognostic value, as the HR for this factor was 0.80 (95% CI: 0.61 to 1.07, P=0.16). These findings suggest that lactate clearance within less than 6 h is not suitable for predicting short-term outcomes.

In this study, we found that Δ6Lac was superior to lactate level at admission. This finding can be explained by the fact that except for factors such as severe liver and kidney dysfunction, the early lactate clearance rate can reflect CS and is a highly sensitive indicator of shock improvement following clinical intervention, as compared to a single lactate value at an early stage. Upon admission to the hospital, the lactate levels in these patients were extremely high; however, after receiving comprehensive treatment, the levels dropped rapidly, with a 6-hour lactate clearance rate >18.2%. Consequently, these patients have a comparatively better prognosis.

The improvement of perfusion significantly impacts patient survival; hence, accurate assessment of the therapeutic effect after emergency treatment in critical illness is crucial. In a study by Fuernau et al.[12], they identified a lactate clearance rate at 8 h-admission below 3.45% per hour as a significant risk factor for 28-day mortality. Furthermore, stepwise multivariable Cox regression analysis identified an 8-hour lactate level ≥3 mmol/L as a better risk factor for predicting 30-day mortality. Building on their research, we also found that the 6-hour lactate clearance rate and the 6-hour lactate level after admission to the hospital for CS can predict its 30-day mortality. Additionally, our research showed that the AUC curve of Δ6Lac in predicting 30-day survival is better than that of L1 and L2.

In addition to Δ6Lac, we also identified a TIMI flow grade of 0, the use of IABP and/or ECMO, and abnormal baseline serum creatinine levels as risk factors for 30-day mortality. After considering these factors, particularly L1 and L2, which were strongly associated with patient prognosis, the Δ6Lac remained a key predictor of 30-day mortality. Our study found that the Δ6Lac was also a better predictor of 30-day survival than L1 >6.7 mmol/L, and a comparison of AUC curves suggested that the Δ6Lac model was better than the L2 model.

These findings suggest that Δ6Lac is a better indicator of treatment response and prognosis. It can provide more accurate parameters for early assessment of subsequent CS prognosis. Early recognition of tissue hypoperfusion improvement is crucial for administering advanced treatments. Accurately determining the fluid status of patients is essential for volume assessment, allowing clinicians to tailor fluid resuscitation strategies to individual needs. Furthermore, early recognition and prompt initiation of fluid resuscitation can prevent the progression of hypovolemia and associated complications.

Similarly, timely administration of inotropic agents provides additional support to patients with compromised cardiac function. These agents enhance myocardial contractility and improve cardiac output, thereby promoting end-organ perfusion. Inotropic agents have shown promising results in the management of conditions such as heart failure and septic shock. Additionally, it is important to consider other interventions such as MCS assistance and the early identification of potential complications that could adversely affect drug treatment outcomes, including myocardial infarction, pericardial effusion, and valve rupture.

Limitations

This study has some limitations. First, this study was conducted at a single center with a relatively small number of participants, which may undermine the generalizability of the results and introduce partial biases in the verification results. However, multivariable Cox regression analysis was used to adjust for potential confounding variables and minimize the introduction of partial biases into the results. In addition, patients with severe organ damage or liver and kidney dysfunction were excluded from this study, because these conditions may have decreased the lactate clearance rate and affected the accuracy of our experimental results. Further studies should focus on evaluating the impact of lactate clearance on the prognosis of patients with severe organ dysfunction. Finally, we only evaluated the impact of lactate clearance on survival at two-time points. Therefore, further studies evaluating lactate clearance at different time intervals (1 h, 2 h, or 4 h post-treatment) are recommended to assess its impact on predicting survival in patients with CS.

Conclusions

The Δ6Lac of ≤18.2% was found to be associated with a higher risk of 30-day mortality. This finding suggests that it can serve as a crucial indicator for early prognostic assessment of CS. Additionally, it was observed to be superior to the lactate level measured upon admission and had a predictive value comparable to the lactate level 6 h after admission.

Author Contributions

Junfeng Wang contributed to the study conception, design, material preparation, data collection, and analysis, and the first draft of the manuscript was written by **Junfeng Wang**. **Junfeng Wang** and **Mingxia Ji** read and approved the final manuscript.

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Ethics Statement

The study was approved by the Ethics Committee of Yiwu Central Hospital and conducted in accordance with the guidelines of the Declaration of Helsinki (ethics number: K2021-IRB-029). Each patient or legal representative provided written informed consent to participate in this study.

Conflict of Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Data Availability

All data generated or analyzed during this study are included in this published article and its supplementary information files. The additional datasets used and analyzed during the current study are available from the corresponding author upon reasonable request.

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