

# Is Lactate Clearance Useful in Predicting Cardiopulmonary Resuscitation Outcome and 48-Hour Mortality?

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## ABSTRACT

**Objective:** To investigate the predictive value of lactate clearance ( $\Delta L$ ) in witnessed cardiac arrest patients in the emergency department (ED) at two time points: Cardiopulmonary resuscitation (CPR) outcome and 48-hour mortality.

**Study Design:** Observational study.

**Place and Duration of the Study:** Department of Emergency Medicine, Duzce University, Duzce, Turkiye, from July 1 to December 31, 2023.

**Methodology:** Patients aged 18 years and older presenting with cardiac arrest in the ED, whose relatives signed the informed consent form, were included. Out-of-hospital cardiac arrest, trauma-related cardiac arrest, major bleeding, and known malignancy were excluded from the study. All patients who met the criteria were included. All data were recorded prospectively. Receiver operating characteristic (ROC) analysis and risk analysis were performed for lactate clearance ( $\Delta L$ ) and 20-minute

**Results:** The predictive power of  $\Delta L$  at 10 minutes ( $\Delta L_{0-10}$ ), 20 minutes ( $\Delta L_{0-20}$ ), and between 10 and 20 minutes ( $\Delta L_{10-20}$ ) was found to be significantly high for both the likelihood of no-ROSC (return of spontaneous circulation) and 48-hour mortality across all patients. The AUC values for  $\Delta L$  at first 10 minutes, 20 minutes, and within 10-20 minutes were 0.991, 0.997, and 0.944, respectively for the no-ROSC group, and 0.942, 0.947, and 0.882, respectively for 48-hour mortality in the ROSC group. ROSC was not achieved in any patient with  $\Delta L_{0-20}$  value of  $\leq -0.15$ .  $\Delta L$  below the calculated thresholds increased the risk of not achieving ROSC and 48-hour mortality by tenfold.

**Conclusion:**  $\Delta L$  during CPR is a useful tool to predict the outcome of CPR and 48-hour mortality. The  $\Delta L_{0-20}$  value was evaluated as a valuable parameter that can be used after the 20<sup>th</sup> minute of CPR when deciding whether to continue or terminate CPR.

**Key Words:** Emergency department, In-hospital cardiac arrest, Lactate clearance, Mortality, CPR outcome.

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## INTRODUCTION

Cardiac arrest is a critical concern due to its high mortality rate and the need for rapid intervention in the emergency department (ED). In the United States of America (USA), more than 200,000 cases of in-hospital cardiac arrest (IHCA) are seen each year, which corresponds to a rate of 1.6 per 1,000 hospital admissions.<sup>1</sup> The annual incidence of out-of-hospital cardiac arrest (OHCA) is around 67-170/100,000 and it is thought that only 50-60% of these patients have access to appropriate healthcare services.<sup>2</sup> In recent years, the improved quality of cardiopulmonary resuscitation (CPR) and post-resuscitation (post-ROSC) care have led to some reduction in the mortality of IHCA patients, though overall mortality still remains high.<sup>1</sup> It has been reported that 18% of IHCA patients survive and are discharged home.<sup>1,3</sup> In OHCA patients, the survival rate at discharge is around 8%.<sup>4</sup> Approximately 10-20% of the IHCA occur in the ED.<sup>5</sup>

Lactate is formed in tissues due to the activation of anaerobic metabolism.<sup>6</sup> Lactate level increases in conditions such as sepsis and cardiogenic shock where tissue perfusion is impaired, and in respiratory failure leading to hypoxaemia.<sup>7</sup> It is known that elevated lactate levels are associated with high mortality in sepsis and critical care patients.<sup>8</sup> In cardiac arrest patients, lactate level has been evaluated as a mortality predictor, and the relationship between lactate levels and mortality in post-CPR patients has also been demonstrated by several studies and high lactate levels have been associated with high mortality rates.<sup>9,10</sup> The relationship of lactate levels analysed during CPR with the return of spontaneous circulation (ROSC) and mortality has also been investigated in previous studies. High lactate levels were also associated with high mortality rates.<sup>3,9,11-13</sup>

The aim of early and effective CPR is to ensure tissue and organ perfusion and to minimise damage due to hypoxia.<sup>4</sup> In patients in whom early intervention is provided and effective CPR is performed, lactate production is expected to decrease with the decrease in tissue hypoxia. The predictive value of lactate level and lactate clearance ( $\Delta L$ ) for IHCA in the ED remains underexplored. The change in subsequent lactate levels during CPR may be a potential parameter indicating the quality of CPR and the metabolic response of the patient to CPR.

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This study aimed to assess the predictive value of  $\Delta L$  in patients with witnessed cardiac arrest in the ED at two time points i.e. CPR outcome and 48-hour mortality.

## METHODOLOGY

It was a single-centre, observational study, conducted prospectively in the Department of Emergency Medicine of Duzce University, Duzce, Turkey, with approximately 100,000 admissions per year. The study was initiated after the local Ethics Committee approval (Approval ID: 2023/96, Dated: 19 June, 2023) was obtained. The results of other studies in the literature were taken as reference in determining the minimum sample size to be included in the study.<sup>14</sup> Sample size was calculated with Gpower software version 3.1.9.4. The minimum number of patients to be included in the study was determined to be 50. The study was conducted with patients admitted to the ED during a six-month period between 1 July and 31 December 2023 and who developed cardiac arrest during ED stay.

In the ED, blood gas analysis (BGA) was performed every 10 minutes from the arterial blood of patients undergoing CPR.<sup>15</sup> For BGA, arterial blood was drawn from the radial artery or femoral artery. The personnels drawing the BGA sample were emergency physicians with at least two years of experience. Sample drawing took an average of 10 seconds, using a pre-heparinised syringe. Blood samples were rapidly delivered to the laboratory. The laboratory where the samples were analysed was on the upper floor of the ED. The specimens were wrapped in ice moulds and sent by a pneumatic transfer system. It took an average of three minutes for BGA samples to reach the laboratory. Samples with insufficient blood volume and clotted samples were not analysed. BGA samples were not taken again for patients whose blood samples could not be analysed and these patients were excluded from the study. For analysis, a radiometre ABL 800 BG device was used and results were obtained in an average of five minutes. The BGA includes pH, partial carbon-dioxide pressure as mmHg ( $pCO_2$ ), bicarbonate level as mmol/L ( $HCO_3$ ), and lactate levels as mg/dL. The first measurement is performed at the start of cardiac arrest ( $L_0$ ), this includes the most recent lactate levels obtained just before the cardiac arrest, and repeated measurements continued at 10-minute intervals. Three samples were drawn for all patients,  $L_0$ ,  $L_{10}$  (lactate after 10 minutes of CPR), and  $L_{20}$  (lactate after 20 minutes of CPR). CPR is performed by the physicians of the patients in accordance with the European Resuscitation Council and American Heart Association guidelines.<sup>2,16</sup>

Age and gender information, systolic (SBP) and diastolic (DBP) non-invasive blood pressures, pulse rate (HR), and BGA results at 0, 10, and 20 minutes were recorded on the dedicated study proforma. A study proforma is a one-page document created by the authors that contains the data scanned in the study. Data were prospectively recorded on the proformas by emergency physicians as soon as they were obtained. Proformas were given to the researchers after all requested data were noted.

Inclusion criteria were patients aged 18 years or older, cardiac arrest in ED, consent of the patients' relatives to participate in the study (reading and signing of the informed consent form by the patients' first-degree relatives), and CPR was performed for at least 20 minutes. Exclusion criteria were OHCA, cardiac arrest due to major bleeding such as gastrointestinal tract bleeding, intra-abdominal bleeding or haemothorax, trauma-related cardiac arrest, pregnancy, known case of malignancy, recurrent cardiac arrests, and whose BGA results were not available due to coagulation or other technical reasons.

The results of BGA of the patients at the initiation of CPR were recorded as pH- $T_0$ ,  $pCO_2$ - $T_0$ ,  $HCO_3$ - $T_0$ , and L- $T_0$ . The results of the 10<sup>th</sup> and 20<sup>th</sup>-minute analyses were similarly noted as  $T_{10}$  and  $T_{20}$ . This data were compiled and studied on statistical software SPSS version 23 (SPSS Inc., Armonk, NY). The difference between the results of the analyses in terms of lactate value was indicated by  $\Delta L$ .  $\Delta L_{0-10}$  indicated the difference between the lactate results of the analyses taken at 0 and 10 minutes,  $\Delta L_{0-20}$  indicated the difference between the lactate results of the analyses taken at 0 and 20 minutes, and  $\Delta L_{10-20}$  indicated the difference between the lactate results of the analyses taken at 10<sup>th</sup> and 20<sup>th</sup> minutes.  $\Delta L$  values were calculated by subtracting the next result from the previous result using a simple calculator / formula. Negative  $\Delta L$  values indicate increases in lactate level, while positive  $\Delta L$  values indicate decreases. Clinical parameters including arterial blood pressure and HR of the patients were also recorded on SPSS.

The 48-hour mortality of the patients included in the study was monitored and recorded using the hospital's electronic medical record (EMR) system. ED physicians followed up the patients after admission and collected all the relevant data. If patients hospitalised in intensive care or other wards after CPR died, the time of death was instantly recorded in the hospital system. If there was an update in patients whose 48-hour mortality was monitored due to the study, emergency physicians noted this and recorded it on the study proforma. The relatives of the patients whose mortality results could not be accessed through the computer system were called from the registered telephone numbers and the mortality results were obtained. The relatives of five patients whose mortality results could not be accessed were called by phone. It was found that two of these patients were still hospitalised in different intensive care units. The relatives of three patients could not be reached, and these patients were not included in the study.

Descriptive statistics were generated for demographic data, vital signs, BGA results, and  $\Delta L$  outcomes of the patients included in the study. Mortality groups were defined based on CPR outcomes and 48-hour mortality results. Comparative statistics were performed between mortality based on demographic data, vital signs, BGA results, and  $\Delta L$  outcomes.

Continuous variables were summarised as median (interquartile range [IQR], 25<sup>th</sup> and 75<sup>th</sup> percentiles) and categorical data as frequency and percentage. Conformity to normal distribu-

tion was evaluated by the Shapiro-Wilk's test, Kolmogorov-Smirnov test, and histogram analysis. Continuous data were compared between two groups by the Mann-Whitney U test. The relationship between two categorical variables was analysed using the Pearson's chi-square test or Fisher's Exact test. Statistical software SPSS version 23 (SPSS Inc., Armonk, NY) was used for these analyses. The receiver operating charac-

teristics (ROC) curve was analysed using the Rstudio version (pROC package). Sensitivity, specificity, area under the curve (AUC), positive predictive value (PPV), and negative predictive value (NPV) were calculated. Optimal cut-off values were determined using the Youden's index. J-point analysis and risk assessment were performed. Odds ratios (OR) with 95% confidence intervals (CI) were calculated using MedCalc version 23.0.5. A significance level of  $p < 0.05$  was considered.

**Table I: Comparison of study characteristics and  $\Delta L$  values among the two groups i.e. non-survivors (non-ROSC) and survivors (ROSC).**

Parameters	Non-ROSC (n = 33)	ROSC (n = 18)	p-value
Age (years)	67.00 (58.50 - 79.50)	69.50 (66.00 - 75.00)	0.540
Gender (female), n (%)	14 (42.4)	9 (50)	0.603
Systolic blood pressure (mmHg)	80 (70 - 94)	97 (80 - 101)	0.156
Diastolic blood pressure (mmHg)	50 (40 - 63)	62 (46 - 67)	0.410
Heart rate (bpm)	120 (86 - 135)	100 (83 - 118)	0.142
pH-T <sub>0</sub>	7.136 (6.891 - 7.259)	6.986 (6.877 - 7.102)	0.067
pCO <sub>2</sub> -T <sub>0</sub>	53.30 (38.25 - 70.00)	47.20 (26.82 - 79.50)	0.354
pHCO <sub>3</sub> -T <sub>0</sub>	14.30 (8.40 - 19.20)	10.00 (8.32 - 12.30)	0.030
L-T <sub>0</sub>	9.50 (6.05 - 12.85)	11.90 (9.52 - 16.25)	0.018
pH-T <sub>10</sub>	6.980 (6.880 - 7.176)	7.030 (6.913 - 7.093)	0.984
pCO <sub>2</sub> -T <sub>10</sub>	60.00 (43.15 - 78.65)	56.70 (44.12 - 81.00)	0.828
HCO <sub>3</sub> -T <sub>10</sub>	10.20 (7.90 - 14.75)	10.60 (7.90 - 13.17)	0.875
L-T <sub>10</sub>	12.50 (9.25 - 15.00)	10.85 (6.97 - 14.12)	0.364
pH-T <sub>20</sub>	6.956 (6.886 - 7.117)	7.042 (6.944 - 7.206)	0.270
PCO <sub>2</sub> -T <sub>20</sub>	58.00 (36.75 - 73.35)	57.10 (52.95 - 70.82)	0.701
HCO <sub>3</sub> -T <sub>20</sub>	9.40 (7.20 - 11.85)	13.10 (9.07 - 16.57)	0.042
L-T <sub>20</sub>	14.00 (10.65 - 18.00)	8.65 (5.30 - 12.72)	0.007
$\Delta L_{0-10}$	-2.10 (-3.95 - -0.70)	1.3 (0.70 - 2.82)	<0.001
$\Delta L_{0-20}$	-3.6 (-6.1 - -2.2)	3.35 (2.05 - 4.75)	<0.001
$\Delta L_{10-20}$	-1.00 (-2.10 - 0.60)	1.65 (0.20 - 2.35)	<0.001

ROSC = Return of spontaneous circulation; L = Lactate;  $\Delta L$  = Lactate clearance;  $\Delta L_{0-10}$  = Lactate clearance in first 10 minutes of CPR;  $\Delta L_{10-20}$  = Lactate clearance between 10<sup>th</sup> and 20<sup>th</sup> minutes of CPR;  $\Delta L_{0-20}$  = Lactate clearance between 0<sup>th</sup> and 20<sup>th</sup> minute of CPR.  $p < 0.05$  was considered statistically significant.

**Table II: Comparison of study characteristics and  $\Delta L$  values between 48-hour mortality groups. The 48-hour mortality group included patients who did not achieve ROSC and those who died within 48 hours of achieving ROSC.**

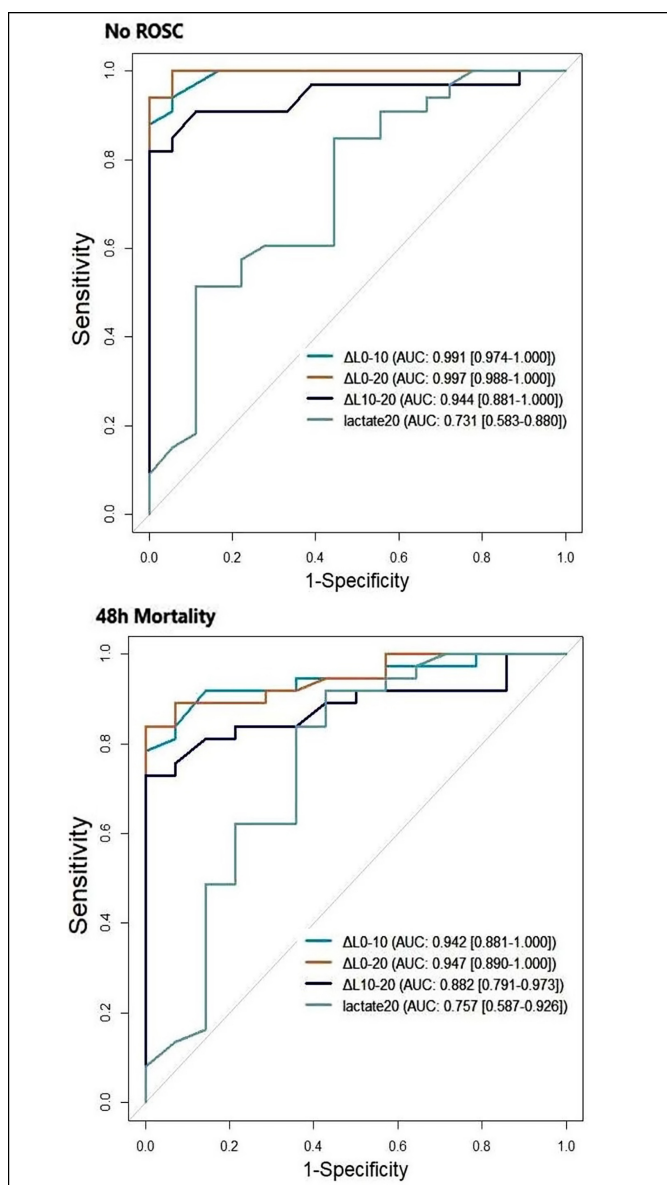
Parameters	48 Hours survival (n = 14)	48 Hours mortality (n = 37)	p-value
Age (years)	69.50 (62.75 - 73.25)	67.00 (60.50 - 79.50)	0.916
Gender (female), n (%)	7 (50)	16 (43.2)	0.665
Systolic blood pressure (mmHg)	100 (94 - 102)	80 (70 - 92)	0.010
Diastolic blood pressure (mmHg)	64 (60 - 69)	50 (40 - 61)	0.048
Pulse (BPM)	100 (90 - 126)	120 (58 - 132)	0.321
pH-T <sub>0</sub>	7.008 (6.902 - 7.104)	7.100 (6.871 - 7.238)	0.311
pCO <sub>2</sub> -T <sub>0</sub>	47.20 (26.82 - 79.50)	53.30 (37.75 - 70.00)	0.473
pHCO <sub>3</sub> -T <sub>0</sub>	10.35 (9.12 - 12.57)	12.90 (8.35 - 18.90)	0.201
L-T <sub>0</sub>	11.40 (8.87 - 15.50)	9.70 (6.50 - 14.40)	0.202
pH-T <sub>10</sub>	7.051 (6.971 - 7.093)	6.980 (6.847 - 7.143)	0.493
pCO <sub>2</sub> -T <sub>10</sub>	55.35 (44.12 - 71.00)	62.10 (43.15 - 80.00)	0.562
HCO <sub>3</sub> -T <sub>10</sub>	11.20 (8.30 - 13.75)	10.00 (7.65 - 14.55)	0.547
L-T <sub>10</sub>	9.45 (5.85 - 14.12)	12.70 (9.35 - 15.00)	0.126
pH-T <sub>20</sub>	7.068 (6.956 - 7.212)	6.959 (6.886 - 7.117)	0.191
PCO <sub>2</sub> -T <sub>20</sub>	58.60 (49.50 - 87.22)	56.50 (37.85 - 67.85)	0.348
HCO <sub>3</sub> -T <sub>20</sub>	14.00 (9.07 - 16.77)	9.50 (7.20 - 11.85)	0.036
L-T <sub>20</sub>	7.60 (3.75 - 12.50)	12.90 (10.65 - 17.50)	0.005
$\Delta L_{0-10}$	1.30 (0.70 - 2.95)	-2.00 (-3.65 - 0.45)	<0.001
$\Delta L_{0-20}$	3.35 (1.77 - 4.97)	-3.40 (-5.60 - 1.55)	<0.001
$\Delta L_{10-20}$	1.55 (0.17 - 2.05)	-0.90 (-2.00 - 0.05)	<0.001

L = Lactate;  $\Delta L$  = Lactate clearance;  $\Delta L_{0-10}$  = Lactate clearance in first 10 minutes of CPR;  $\Delta L_{10-20}$  = Lactate clearance between 10<sup>th</sup> and 20<sup>th</sup> minutes of CPR;  $\Delta L_{0-20}$  = Lactate clearance between 0<sup>th</sup> and 20<sup>th</sup> minute of CPR.  $p < 0.05$  was considered statistically significant.

**Table III: Performance, risk ratio, specificity, sensitivity, and predictive value data of  $\Delta L$  and 20<sup>th</sup>-minute lactate values.**

Parameters	AUC	OR (95% CI)	Sensitivity	Specificity	PPV	NPV	p-value
No: ROSC							
$\Delta L_{0-10} \leq -0.10$	0.991	263.50 (22.23-3122.26)	93.90%	94.40%	96.88%	89.47%	<0.001
$\Delta L_{0-20} \leq -0.15$	0.997	781.66 (30.23-20208.99)	100.00%	94.40%	97.06%	100.00%	<0.001
$\Delta L_{10-20} \leq 0.05$	0.944	80 (12.09-529.16)	84.80%	88.90%	93.75%	84.21%	<0.001
$L_{20} \geq 9.20$	0.731	7.00 (1.85 - 26.47)	84.80%	55.60%	77.78%	66.67%	0.004
48 Hours: Mortality							
$\Delta L_{0-10} \leq -0.35$	0.942	100.64 (5.42-1867.37)	78.40%	100.00%	100.00%	63.64%	0.002
$\Delta L_{0-20} \leq -0.80$	0.947	140.53 (7.40-2666.32)	83.80%	100.00%	100.00%	70.00%	<0.001
$\Delta L_{10-20} \leq -0.40$	0.882	75.95 (4.14-1390.79)	73.00%	100.00%	100.00%	58.33%	<0.001
$L_{20} \geq 8.05$	0.757	15.11 (3.09-73.77)	91.89%	57.14%	85.00%	72.73%	<0.001

AUC = Area under the curve; OR = Odds ratio; CI = Confidence interval; PPV = Positive predictive value; NPV = Negative predictive value. L = Lactate;  $\Delta L$  = Lactate clearance;  $\Delta L_{0-10}$  = Lactate clearance in first 10 minutes of CPR;  $\Delta L_{10-20}$  = Lactate clearance between 10<sup>th</sup> and 20<sup>th</sup> minutes of CPR;  $\Delta L_{0-20}$  = Lactate clearance between 0<sup>th</sup> and 20<sup>th</sup> minute of CPR.  $p < 0.05$  was considered statistically significant.



**Figure 1: Receiver operating characteristic (ROC) curves of  $\Delta L$  and 20<sup>th</sup>-minute lactate values for no ROSC and 48 hours mortality.** AUC = Area under the curve; L = Lactate;  $\Delta L$  = Lactate clearance;  $\Delta L_{0-10}$  = Lactate clearance in first 10 minutes of CPR;  $\Delta L_{10-20}$  = Lactate clearance between 10<sup>th</sup> and 20<sup>th</sup> minutes of CPR;  $\Delta L_{0-20}$  = Lactate clearance between 0<sup>th</sup> and 20<sup>th</sup> minute of CPR.

## RESULTS

Out of a total of 64,264 ED admissions during the study period, 651 suffered from a cardiac arrest. Of these, 51 patients fulfilled the inclusion criteria and were included in the study. The median age of 51 patients included in the study was 68 years (62 - 78), of whom 54.9% ( $n = 28$ ) were males and 45.1% ( $n = 23$ ) were females. The median SBP was 85.00 (70.25 - 100.75) mmHg and the median DBP was 60.00 (40.00 - 64.75) mmHg. The median heart rate (HR) was 117 (87 - 130) bpm.

ROSC was achieved in 35.3% ( $n = 18$ ) of the patients.  $L_{20}$  was statistically significantly higher in the no-ROSC group (14.00 [10.65 - 18.00]), as compared to the ROSC group 8.64 [5.30 - 12.72]) ( $p < 0.05$ ). In the no-ROSC group,  $\Delta L_{0-10}$  was statistically significantly lower (-2.10 [-3.95 - 0.70]) as compared to ROSC group 1.3 [0.70 - 2.82]) ( $p < 0.05$ ). There was a similar difference in  $\Delta L_{0-20}$  and  $\Delta L_{10-20}$  between ROSC and no-ROSC groups.  $\Delta L$  values were statistically significantly lower in the no-ROSC group ( $p < 0.05$ ). Comparisons between groups with and without ROSC are shown in Table I.

Thirty-seven (72.5%) of the patients died within 48-hours. The 20<sup>th</sup>-minute lactate level was significantly higher in patients who died within 48-hour (12.90 [10.65 - 17.50]) as compared to 48-hour survivors group 7.60 [3.75 - 12.50]) ( $p < 0.05$ ). In 48-hour non-survivors group,  $\Delta L_{0-10}$  was statistically significantly lower (-2.00 [-3.65 - -0.45]) as compared to 48-hour survivors group 1.30 [0.70 - 2.95]) ( $p < 0.05$ ). There was a similar difference in  $\Delta L_{0-20}$  and  $\Delta L_{10-20}$  between 48-hour non-survivors group and 48-hour survivors group.  $\Delta L$  values were statistically significantly lower in the 48-hour non-survivors group ( $p < 0.05$ ). Comparisons between the groups of patients who died within 48-hour and those who did not die are shown in Table II.

AUC values for  $\Delta L_{0-10}$ ,  $\Delta L_{0-20}$ , and  $\Delta L_{10-20}$  were 0.991, 0.997, and 0.944, respectively.  $\Delta L_{0-10} \leq -0.10$  increased the risk of not achieving ROSC 263.50 (27.23- 3122.26) times.  $\Delta L_{0-20} \leq -0.15$  increased the risk of not achieving ROSC by 781.66 (30.23- 20208.99) fold, and  $\Delta L_{10-20} \leq 0.05$  increased the risk



of not achieving ROSC by 80.00 (12.09 - 529.16) fold.  $\Delta L_{0-10}$ ,  $\Delta L_{0-20}$ , and  $\Delta L_{10-20}$  values were also found to be very successful in predicting the risk of 48-hour mortality, with AUC values of 0.942, 0.947, and 0.882, respectively. A  $\Delta L_{0-10} \leq -0.35$  increased the 48-hour mortality risk 100.64 (5.42-1867.37) times.  $\Delta L_{10-20} \leq -0.80$  increased the 48-hour mortality risk 140.53 (7.408- 2666.32) times, and  $\Delta L_{10-20} \leq -0.40$  increased the 48-hour mortality risk 75.95 (4.14-1390.79) times. The performance, sensitivity, specificity, positive, and negative predictive values, cut-off values, and odds ratio values of  $\Delta L_{0-10}$ ,  $\Delta L_{0-20}$ ,  $\Delta L_{10-20}$ , and 20-minute lactate values in predicting failure to achieve ROSC in ED and 48-hour mortality are shown in Table III. The ROC curves of  $\Delta L_{0-10}$ ,  $\Delta L_{0-20}$ , and  $\Delta L_{10-20}$  and 20-minute lactate values in terms of failure to achieve ROSC and 48-hour mortality are shown in Figure 1.

## DISCUSSION

In this study, IHCA was addressed as an understudied subject in the ED.  $\Delta L_{0-20}$  was evaluated as a parameter that helps clinicians in decision-making whether to terminate or continue CPR. It was revealed that  $\Delta L_{0-20}$  was effective in predicting CPR outcomes.

Studies investigating the effect of  $\Delta L$  on mortality in the follow-up of patients who achieved ROSC show that a decrease in lactate levels was associated with a better prognosis.<sup>10,17</sup> In a study conducted with patients undergoing extracorporeal CPR, mortality was found to be lower in patients with a decrease in lactate level during the procedure, and  $\Delta L$  was emphasised as a good predictor of survival in patients undergoing extracorporeal CPR.<sup>18</sup> The present study was conducted with patients who underwent conventional CPR, but similar results were obtained with the extracorporeal CPR study in terms of the effect of  $\Delta L$  during intervention on mortality. All three of the  $\Delta L_{0-10}$ ,  $\Delta L_{0-20}$ , and  $\Delta L_{10-20}$  values calculated in the present study were statistically significantly lower both in the group in which no-ROSC and in the group of patients who died within 48-hour.

Cardiac arrest is a medical condition with a high mortality rate. In previous studies, mortality rates were found to be 92% for OHCA and 82% for IHCA at hospital discharge.<sup>1,3,4</sup> Higher chances of early intervention, ease of access to necessary medical equipment and trained personnel can be listed as factors that decrease the mortality rate in IHCAs.<sup>19,20</sup> In the study conducted with IHCA patients, 64.7% (n = 33) of the patients died at the end of CPR and 72.5% of total patients (n = 37) died within 48 hours. One reason for the lower mortality rate (72.5%) in this study compared to the literature data (82%),<sup>3</sup> is the exclusion of patient groups with a low probability of ROSC, such as patients with cardiac arrest due to trauma, patients with major bleeding, and patients diagnosed with malignancy.

In previous studies, it is observed that the lactate level at the beginning of CPR generally does not show a significant difference between short-term (at hospital discharge) mortality

groups,<sup>9,11-13</sup> whereas there are studies in which the initial lactate value was found to be high in the group of patients who died in the hospital discharge.<sup>3,10</sup> In this study, the  $L_0$  level in IHCA patients was found to be statistically significantly higher in the ROSC group, but no significant difference was observed between the 48-hour mortality groups. The findings of the present study suggest that initial lactate level is not reliable marker for an at-hospital discharge mortality in patients undergoing CPR.

In a study conducted with 83 OHCA patients, it was found that the  $L_{20}$  value was statistically significantly higher in the group in which ROSC was not achieved.<sup>11</sup> Similarly, in this study, the  $L_{20}$  value was significantly high both in the group without ROSC and the group of patients who died within 48 hours. The  $L_{20}$  is considered more valuable by the authors as it will reflect the patients' response to CPR.

Studies investigating the predictive power of lactate for the outcome of CPR and mortality after ROSC were generally performed with a single lactate value obtained or with  $\Delta L$  calculated after ROSC was achieved, and the change in lactate level during CPR was excluded from the evaluations.<sup>3,9-11</sup> The difficulty of repeated lactate measurements during CPR may be one reason for this. The need for rapid analysis of the BGAs and rapid comparison of the measurements made in a short period of time also makes it difficult to perform studies with repeated measurements. The change in lactate level is considered as a parameter indicating an increase or decrease in tissue hypoxia.<sup>21,22</sup> It is thought that the change in consecutive lactate levels measured during CPR administration will predict the response to intervention and prognosis more strongly than a single lactate level measured at any minute. In this study, ROC analyses performed with 20<sup>th</sup>-minute lactate level  $L_2$  and  $\Delta L_{0-20}$  values in terms of failure to achieve ROSC and 48-hour mortality gave results confirming this idea.

There is no clear information about the duration of CPR and the minute at which it should be terminated in case of no response. Decisions are made according to clinical indicators, the effectiveness of resuscitation efforts, and local protocols.<sup>4,16</sup> Various protocols have been developed for the decision to terminate resuscitation. Data, such as resuscitation time, characteristics of the first detected rhythm, and end-tidal carbon dioxide pressure have been used for this purpose.<sup>23-25</sup> In this study, ROSC was not achieved in any patient with a  $\Delta L_{0-20}$  value  $\leq -0.15$ . In light of the findings of the present study, it is thought that  $\Delta L$  during CPR may be a valuable parameter that can be used when deciding the duration of CPR. Multicentred studies with larger sample sizes will be useful in this regard.

The first limitation of the present study is that it is a single-centre study. The second limitation is the small sample size.

## CONCLUSION

$\Delta L$  during CPR is a potentially useful tool to predict the outcome of CPR and 48-hour mortality in patients suffering

from cardiac arrest in the ED. In terms of mortality prediction, it is more effective to use  $\Delta L$  rather than a single lactate value.  $\Delta L_{0-20} \leq -0.15$  increases the risk of failure to achieve ROSC and  $\leq -0.80$  increases the risk of 48-hour mortality. The  $\Delta L_{0-20}$  value was evaluated as a valuable parameter that can be used after the 20<sup>th</sup> minute when deciding whether to continue or terminate CPR.

### ETHICAL APPROVAL:

This study was initiated in the Department of Emergency Medicine, Duzce University, Duzce, Turkiye, following the Ethics Committee's approval. (Duzce University Non-Invasive Health Research Ethics Committee's approval with decision number: 2023/96, Dated: 19 June 2023).

### PATIENTS' CONSENT:

The study was explained to the eligible patients or their first-degree relatives and informed consent forms were given. Those who read the informed consent forms and signed that they approved to participate in the study were included.

### COMPETING INTEREST:

The authors declared no conflict of interest.

### AUTHORS' CONTRIBUTION:

ES, MCD, KS: Conceptualisation, data curation, investigation, methodology, project administration, supervision, writing of the original draft, reviewing of the manuscript, and editing. All authors approved the final version of the manuscript to be published.

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