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Identifying high-risk undifferentiated emergency department patients with hyperlactatemia: Predictors of 30-day in-hospital mortality

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Abstract:

BACKGROUND: Hyperlactatemia has been recognized as a significant prognostic indicator in critically ill patients. Nonetheless, there remains a gap in understanding the specific risk factors contributing to increased mortality among undifferentiated emergency department (ED) patients presenting with elevated lactate levels.

OBJECTIVES: The objective of the study is to investigate potential risk factors for 30-day in-hospital mortality in ED patients with hyperlactatemia.

METHODS: All nontraumatic adult presentations to the ED who had a lactate level of ≥ 2.5 mmol/L were included. Comorbidities, vital signs, lactate levels, lactate clearance, lactate normalization, and final diagnosis were compared with 30-day in-hospital mortality.

RESULTS: A 30-day in-hospital mortality rate of 10.4% was observed in 979 patients. The mortality rate was higher in hypotensive patients (odds ratio [OR] 4.973), in nursing home patients (OR 5.689), and bedridden patients (OR 3.879). The area under the curve for the second lactate level (0.804) was higher than the first lactate level (0.691), and lactate clearance (0.747) for in-hospital mortality. A second lactate level >3.15 mmol/l had a sensitivity of 81.3% in predicting in-hospital mortality. The OR for mortality was 6.679 in patients without lactate normalization. A higher mortality rate was observed in patients with acute renal failure (OR 4.305), septic shock (OR 4.110), and acute coronary syndrome (OR 2.303).

CONCLUSIONS: A second lactate measurement more accurately predicts in-hospital mortality than lactate clearance and the first lactate level in ED patients. Nursing home patients, bed-ridden patients, hypotensive patients on initial ED presentation, patients without lactate normalization, and patients with a final diagnosis of acute renal failure, septic shock, and acute coronary syndrome had a higher mortality rate.

Keywords:

Emergency departments, hyperlactatemia, lactate clearance, lactate normalization, lactates, lactic acid, mortality, prognosis

Introduction

Lactate is the end-product of the anaerobic energy pathway in cells, and

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its levels increase in patients with systemic hypoperfusion.^[1] The lactate level is often measured during the first few hours of emergency department (ED) presentation to detect circulatory shock in critically ill

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Box-ED Section**What is already known on the study topic?**

- It is known that elevated lactate is associated with increased mortality in critically ill emergency department (ED) patients.

What is the conflict on the issue? Has it importance for readers?

- However, the relationship between lactate clearance, lactate normalization, vital signs and comorbidities, and 30-day in-hospital mortality in undifferentiated ED patients with high lactate levels has not been adequately studied. Moreover, optimal treatment targets for the reduction of lactate levels in this patient population have yet to be established.

How is this study structured?

- This is a single-center observational study that includes data from 979 ED patients.

What does this study tell us?

- We revealed that the second lactate level predicts 30-day in-hospital mortality more accurately than the first lactate level and lactate clearance. Second lactate level of >3.15 mmol/l has a sensitivity of 81.3%, and a specificity of 69.7% in predicting mortality. Patients who did not achieve lactate normalization on the second measurement exhibited a mortality rate exceeding six times that of individuals who achieved lactate normalization. Nursing home patients, bedridden patients, hypotensive patients on initial ED presentation, patients without lactate normalization, and patients with a final diagnosis of acute renal failure, septic shock, and acute coronary syndrome had a higher mortality rate.

patients. Numerous studies have shown that high lactate levels are associated with poor prognosis in conditions such as septic shock, trauma, cardiogenic shock, obstructive shock, mesenteric ischemia, acute respiratory distress syndrome, and acute renal failure.^[1-3] However, despite hyperlactatemia, the mortality rate remains relatively low in patients with mild-to-moderate volume loss or patients presenting with seizures.^[4,5] Therefore, it is essential to determine which undifferentiated ED patients with elevated lactate levels have a higher mortality risk on initial presentation. Most studies that investigate lactate elevation as a prognostic marker were conducted in intensive care units (ICUs) or in specific patient groups in the ED.^[1,6-9]

In this study, we included all undifferentiated ED patients with hyperlactatemia, regardless of etiology. We aimed to identify factors associated with in-hospital mortality that had not been comprehensively investigated

previously, such as comorbidities, vital signs, and lactate normalization.

Methods

This was a cross-sectional retrospective study conducted at the tertiary level ED of Dokuz Eylül University Hospital. Patients aged 18 and over who were admitted to the monitored beds of the ED between October 2021 and January 2022 and had lactate levels ≥ 2.5 mmol/L were included in the study. The study was approved by the Ethics Committee of Dokuz Eylül University (Decision number: 2022/13-17, date: June 04, 2022).

First, patients with lactate levels ≥ 2.5 mmol/L were identified from the hospital information management system. "The study team reviewed electronic records of patients who underwent lactate level measurement within the 1st h following their presentation to the ED." Patients were excluded if they met any of the following criteria: (1) trauma-related presentations, (2) lactate level measured 1 h after ED presentation, (3) patients who left ED voluntarily before the completion of full ED evaluation, and (4) patients with insufficient data in their electronic files. The demographic characteristics of the patients, comorbidities, chronic illness, vital signs at initial ED presentation, laboratory results, final diagnoses, and outcomes of the patients were recorded.

Lactate levels were measured from both arterial and venous blood samples using a Beckman Coulter LH780® blood gas analyzer. In patients who had more than one lactate measurement in the ED, the second lactate level was also recorded. Lactate clearance was calculated using the following formula: lactate clearance = $([\text{first lactate level} - \text{second lactate level}] / \text{first lactate level}) \times 100$. When the lactate level was < 2.5 mmol/L on the second measurement, this was considered lactate normalization.

The primary endpoint for hospitalized patients was the 30-day in-hospital mortality rate. Patients discharged from the ED after full evaluation were considered alive. The national death notification system was used to determine the mortality status of patients who were transferred to another hospital.

Statistical analysis

The statistical analysis was performed using the SPSS version 26.0 (IBM® Corp, Armonk, New York, USA) program. The homogeneity of variables was tested using the Kolmogorov–Smirnov test. Data that had a normal distribution were represented by the mean and standard deviation, while those with an abnormal distribution were represented by the median and interquartile range (IQR). If the continuous data

were normally distributed, Student's *t*-test analysis was performed, while the Mann-Whitney *U*-test was used for data that were not normally distributed. Categorical variables were compared using Fisher's exact test and Chi-square test. The sensitivity and specificity of the first lactate level, lactate clearance, and second lactate levels in detecting 30-day in-hospital mortality were assessed using a receiver operating characteristic (ROC) analysis, and the area under the curve (AUC) was provided. Odds ratios (ORs) and 95% confidence intervals (CI) were used to evaluate predictor factors related to 30-day in-hospital mortality. Statistical significance was defined as a *P* < 0.05.

Results

Between study periods, 5976 patients were admitted to the monitored beds of the ED. Among these patients, 1,198 had lactate levels ≥ 2.5 mmol/l. Two hundred and nineteen of the patients were excluded from the study: 84 patients left the ED voluntarily before complementation of full ED evaluation, 68 patients were admitted due to trauma-related admission, there was not enough data in the electronic files of 51 patients, and the first lactate level was measured in 16 patients after the 1st h of ED presentation. As a result, 979 patients were included in the study.

The median age was 72 (60–80) years, and 56.7% of the patients were male. A 30-day in-hospital mortality occurred in 10.4% of the patients. 9% of males and 12.3% of females died. The mean age of survivors was 71 (IQR

59–79) years, while the mean age of nonsurvivor was 80 (IQR 72–89) years (*P* < 0.001).

The relationship between the comorbidities, vital signs, and the 30-day in-hospital mortality rate is shown in Tables 1 and 2. The mortality rate was higher in nursing home patients (OR 5.689, CI 95% 3.292–9.832), hypotensive patients on initial presentation (OR 4.973, CI 95% 3.094–7.992), bedridden patients (OR 3.879, CI 95% 2.120–7.098), and patients aged ≥ 75 years (OR 3.583, CI 95% 2.300–5.581).

The mean of the first lactate level was 5.06 ± 3.49 mmol/l. The lactate level of 53.2% of the patients was 2.5–4 mmol/l, 25.9% was 4–6 mmol/l, 11.9% was 6–10 mmol/l, and 9.1% was ≥ 10 mmol/l. Lactate level was measured for the second time in 685 patients (69.9%). Venous blood samples were used in 83.6% (*n* = 818) of the patients in the first measurement and 46.9% (*n* = 321) in the second measurement. The median time between measurements was 170 (110–299.3) min. The time elapsed between two measurements was <1 h in 7.7% of patients, 1–3 h in 43.7%, 3–12 h in 44.1%, and >12 h in 4.4%.

The relationship between first lactate level, bicarbonate, pH, lactate clearance, Δ lactate, and 30 days in-hospital mortality is shown in Table 3. pH and HCO₃ levels were lower and lactate levels were higher in both the first and second measurements in nonsurvivors. The median value of lactate reduction (Δ lactate) in nonsurvivors was 0.3 mmol/l (lactate clearance 5.9%), while it was

Table 1: Patient's vital signs on emergency department admission, comorbidities, and 30-day in-hospital mortality

Vital signs on admission	Median (IQR)		<i>P</i>
	Survival	Nonsurvival	
Systolic blood pressure (mmHg)	135 (116–154)	105.5 (88–130)	<0.001
Diastolic blood pressure (mmHg)	81.5 (70–90)	64.5 (48–86)	<0.001
Shock index (min/mmHg) (pulse rate/systolic blood pressure)	0.68 (0.56–0.90)	0.88 (0.70–1.20)	<0.001
Pulse rate (/min)	89.5 (82–113)	102 (81.5–120)	0.261
Peripheral oxygen saturation (%)	96 (90–98)	90 (80–95.5)	<0.001
Respiratory rate (/min)	16 (16–20)	19 (16–24.5)	<0.001
Temperature (°C)	36 (36–36)	36 (36–36)	0.795
Comorbidities, <i>n</i> (%)			
All patients	877 (89.6)	102 (10.4)	-
Diabetes	299 (91.4)	28 (8.6)	0.178
Chronic heart failure	142 (84.5)	26 (15.5)	0.018
Chronic obstructive pulmonary disease	96 (81.4)	22 (18.6)	0.002
Chronic renal impairment	49 (83.1)	10 (16.9)	0.090
Renal replacement therapy	27 (84.4)	5 (15.6)	0.327
Hypertension	500 (90.9)	50 (9.1)	0.124
Active malignancy	103 (86.6)	16 (13.4)	0.249
Bedridden patients	43 (71.7)	17 (28.3)	<0.001
Nursing home patients	45 (65.2)	24 (34.8)	<0.001
Chronic liver failure	26 (89.7)	3 (10.3)	0.989

IQR: Interquartile range

1.6 mmol/l (lactate clearance 42.3%) in survivors. Lactate normalization was observed in 337 (49.2%) of the patients. First lactate levels, lactate normalization, lactate clearance, and the 30-day in-hospital mortality rate are shown in Table 4.

When a decrease in lactate level $\geq 50\%$ was accepted as the reference, OR for mortality was 2.851 in patients whose lactate level decreased by 10%–49%, OR 7.047 in those with an increase or decrease of $<10\%$, OR 9.737 in

those with an increase of 10%–49%, and OR 18.4 in those with an increase of more than 50%. The mortality rate in those without lactate normalization was higher (OR 6.679, CI 95% 3.455–12.912) than in those with lactate normalization.

In ROC analysis, the AUC of the first lactate level to predict 30-day in-hospital mortality was 0.691 (95% CI 0.627–0.755, $P < 0.001$); 0.804 (95% CI 0.748–0.861, $P < 0.001$) for second lactate level; and 0.747 (0.691–0.802,

Table 2: Relationship between vital signs, comorbidities, and 30-day in-hospital mortality

	n (%)	Mortality, n (%)	OR	CI 95%	P
Hypotension on admission*	123 (12.8)	34 (27.6)	4.973	3.094–7.992	<0.001
Abnormal pulse rate [†]	429 (44.5)	56 (13.1)	1.964	1.273–3.028	0.002
Temperature $>38^{\circ}\text{C}$	12 (1.2)	1 (8.3)	0.849	0.108–6.649	0.876
Respiratory rate $>20/\text{min}$	230 (23.9)	36 (15.7)	2.198	1.406–3.435	0.001
Peripheral oxygen saturation $<90\%$	232 (24.1)	43 (18.5)	3.094	1.996–4.796	<0.001
Bedridden patients	60 (6.1)	17 (28.3)	3.879	2.120–7.098	<0.001
Nursing home residents	69 (7.0)	24 (34.8)	5.689	3.292–9.832	<0.001
Age ≥ 75 years	413 (42.2)	71 (17.2)	3.583	2.300–5.581	<0.001
Chronic heart failure	168 (17.2)	26 (15.5)	1.771	1.096–2.862	0.018
Chronic obstructive pulmonary disease	118 (12.1)	22 (18.6)	2.237	1.334–7.753	0.002

*Systolic blood pressure <90 mmHg or diastolic blood pressure <60 mmHg, [†]Pulse rate <60 beats/min or ≥ 100 beats/min. OR: Odds ratio, CI: Confidence interval

Table 3: Relationship between first (on admission), and second blood gas analysis parameters and 30-day in-hospital mortality

Parameters of blood gas analysis	Survival (n=877)	Nonsurvival (n=102)	P
Lactate (mmol/L), median (IQR)			
First measurement	3.6 (2.9–5.2)	6.1 (3.98–11.75)	<0.001
Second measurement	2.3 (1.67–3.6)	6.1 (3.3–10.1)	<0.001
pH, median (IQR)			
First measurement	7.36 (7.3–7.4)	7.23 (7.07–7.33)	<0.001
Second measurement	7.38 (7.33–7.42)	7.2 (7.02–7.28)	<0.001
HCO ₃ (mmol/L), median (IQR)			
First measurement	22 (19–24)	15 (11.5–20)	<0.001
Second measurement	22 (20–24)	16 (11–18)	<0.001
Δ lactate* (mmol/L), median (IQR)	1.6 (0.8–2.7)	0.3 (–2–2)	<0.001
Lactate clearance [†] (%), median (IQR)	42.3 (19.5–60)	5.9 (–21.1–34.2)	<0.001

* Δ lactate: First lactate level–second lactate level, [†]Lactate clearance: [(First lactate level) – (second lactate level)]/(first lactate level) $\times 100$. IQR: Interquartile range

Table 4: Comparison of first lactate levels, lactate normalization, lactate clearance with 30-day in-hospital mortality

	n	Mortality, n (%)	OR	CI 95%
First lactate level (mmol/L)				
2.5–4	521	25 (4.8)	Reference	
4–6	253	24 (9.5)	2.079	1.162–3.720
6–10	116	18 (15.5)	3.644	1.915–6.935
≥ 10	89	35 (39.3)	12.859	7.164–23.084
Lactate normalization				
Patients with lactate normalization*	337	11 (3.3)	Reference	
Patients without lactate normalization	348	64 (18.4)	6.679	3.455–12.912
Lactate clearance				
$\geq 50\%$ decrease	250	9 (3.6)	Reference	
10%–49% decrease	291	28 (9.6)	2.851	1.319–6.164
10% decrease or increase	72	15 (20.8)	7.047	2.936–16.910
10%–49% increase	45	12 (26.7)	9.737	3.812–24.870
$\geq 50\%$ increase	25	11 (40.7)	18.410	6.666–50.846

*Lactate normalization: Lactate levels <2.5 mmol/L on the second measurement

$P < 0.001$) for lactate clearance. A second lactate level >3.15 mmol/l had a sensitivity of 81.3% and a specificity of 69.7% in predicting 30-day in-hospital mortality.

The study team categorized the patients into 11 groups based on the most common final diagnosis recorded in the ED [Table 5]. Compared to all patients, patients with a final diagnosis of acute coronary syndrome, septic shock, and acute renal failure had a higher mortality rate, whereas patients with a final diagnosis of decompensated heart failure had a lower mortality rate. Patients with a final diagnosis of syncope and seizures had no mortality.

Discussion

A linear relationship has been shown between lactate elevation and the mortality of many critical diseases.^[1] Most studies investigating mortality-related factors have been conducted on ICU patients.^[1,3,7,8] ED-based studies were frequently performed in specific patient groups such as sepsis and trauma.^[1,2,9] We investigated 30-day in-hospital mortality- and mortality-related factors in nonclassified ED patients who had elevated lactate levels, regardless of their final diagnosis. This approach allowed us to identify patients who may benefit from more aggressive diagnostic and therapeutic interventions in nonselected ED settings. We also had the chance to compare the in-hospital mortality of different patient groups with high lactate levels.

In critically ill ED patients, lactate levels can be measured by blood gas analyzers within a few minutes during initial resuscitation. When lactate elevation is detected, emergency physicians often have no other data except for the patient's vital signs, chief complaint, examination findings, and comorbidities to predict the prognosis of patients in clinical practice. In most cases, the clinical diagnosis of the patient, comprehensive laboratory

results, and imaging are not obtained at this stage. Therefore, we also aimed to investigate whether the limited data available at that critical time could predict the patient's risk of death.

We have shown that in-hospital mortality increased more than threefold in nursing home patients, those with hypotension, bedridden patients, patients aged ≥ 75 years, and those with a peripheral oxygen saturation of $<90\%$ on initial presentation. While the mortality of all study patients was 10.6%, it was 15.5% in those with a history of heart failure, 18.6% in those with chronic obstructive pulmonary disease, 28.3% in bedridden patients, and 34.8% in nursing home patients. As expected, the higher the patient's initial lactate level, the higher the mortality, especially at lactate levels above 10 mmol/l, where the mortality rate reached 40%.

In clinical practice, it is essential to monitor lactate level changes in repeated measurements in addition to the initial lactate level. The Third International Consensus Definitions for Sepsis and Septic Shock (Sepsis-3) targeted at least a 10% reduction in lactate level within the first 2 h as a treatment goal.^[10] However, there is no consensus on the management target in critically ill ED patients with hyperlactatemia. Based on the data obtained from our study, the following issues should be discussed: (1) in our study, lactate clearance was 5.9% in nonsurvivors and 42.3% in survivors. The OR for predicting mortality is 7.047 in patients whose lactate level remained relatively stable ($<10\%$ increase or decrease), and OR 2.851 in patients whose lactate level decreased 10%–49% relative to the reference ($\geq 50\%$ clearance) lactate level. Therefore, achieving $\geq 50\%$ reduction of the initial lactate level can be considered a treatment goal in critically ill ED patients. (2) $\geq 50\%$ lactate clearance may not be an effective treatment goal in patients with moderate-to-severe hyperlactatemia. The second lactate level >3.15 mmol/l is 81.3% sensitive

Table 5: Mortality rates of patients according to final diagnosis

ED final diagnosis	n (%)	Mortality rate, n (%)	OR	CI 95%	P
All patients	979 (100)	102 (10.4)	-	-	-
Acute coronary syndrome*	60 (6.1)	12 (20)	2.303	1.180–4.495	0.015
Decompensated heart failure	97 (9.9)	2 (2.1)	0.165	0.040–0.678	0.013
Pulmonary†	204 (20.8)	23 (11.3)	1.120	0.684–1.832	0.653
Cerebrovascular accident‡	70 (7.2)	4 (5.7)	0.502	0.179–1.406	0.189
Seizure	59 (6)	0	-	-	-
Gastrointestinal bleeding	54 (5.5)	6 (11.1)	1.079	0.450–2.588	0.864
Septic shock	159 (16.2)	40 (25.2)	4.110	2.641–6.394	<0.001
Syncope	39 (4)	0	-	-	-
Acute renal failure	25 (2.6)	8 (32)	4.305	1.809–10.245	0.001
Malignancy related admission	29 (3)	2 (6.9)	0.630	0.148–2.687	0.532
COVID-19 pneumonia	53 (5.4)	3 (5.7)	0.501	0.153–1.637	0.253

*ST elevated acute myocardial infarction, non-ST elevated acute myocardial infarction, unstable angina pectoris, †Pneumonia without septic shock, acute exacerbation of chronic obstructive pulmonary disease, acute asthma attack, idiopathic pulmonary fibrosis, pulmonary embolism, pleural effusion, ‡Ischemic stroke, transient ischemic attack, hemorrhagic stroke. OR: Odds ratio, CI: Confidence interval, ED: Emergency department

and 69.7% specific in predicting mortality. If lactate normalization could not be achieved in the second measurement, the mortality rate increased more than sixfold (OR 6.7). For example, in patients who had a first lactate level of ~10 mmol/l and a second lactate level of ~5 mmol/l after initial resuscitation, lactate clearance reached 50%. However, according to our results, this patient is still in the danger zone. Therefore, lactate normalization should be considered a primary target rather than ~50% lactate clearance in patients with moderate to severe hyperlactatemia.

No mortality was observed in 59 patients whose final diagnosis was seizures and 39 patients with syncope in our study. Haas *et al.* reported that mortality did not develop in 8 patients diagnosed with seizures in ICU patients with a lactate level >10 mmol/l.^[4] Similarly, Gharipour *et al.* did not report mortality in four seizure patients with a lactate level >10 mmol/l in the ICU.^[5] Elevated lactate levels may predict seizure recurrence in ED follow-up, but it should not be considered a poor prognostic factor.^[11] It seems that an increase in lactate production during excessive muscle activity is often self-limiting. We also found a lower 30-day in-hospital mortality rate in patients with COVID-19 pneumonia (OR 0.501), active malignancy (OR 0.630), cerebrovascular accident (OR 0.502), and decompensated heart failure (OR 0.165) than in other critical ED patients with hyperlactatemia.

The mortality rate in patients with acute renal failure (32%, OR 4.305) is much higher than in patients with septic shock (25.7%, OR 4.110) and acute coronary syndrome (20%, OR 2.303). We previously reported that the mortality rate of 694 acute renal failure patients with lactate levels >2.5 mmol/l was 30.4%.^[2] The mortality rate was 7% (OR 1) in patients with a lactate level <2 mmol/l, 14.4% (OR 2.2) in patients with 2–4 mmol/l, 27.5% (OR 5) in patients with 4–6 mmol/l, and 51.2% (OR 14) in patients with a lactate level >6 mmol/l.^[2] The relationship between hyperlactatemia and increased mortality in patients with acute renal failure has been examined in a limited number of studies. Considering the data of these two studies, lactate elevation can be used as a prognostic marker in patients with acute renal failure in the ED.

There have been many studies examining the relationship between lactate elevation and mortality. Mortality rates may be anticipated to be higher among patients in the ICU compared to those in the ED due to the increased prevalence of critical etiologies such as septic shock, multiorgan failure, and traumatic/postoperative hemorrhagic shock. Therefore, it may not be practical to compare our results with data from studies conducted in the ICU. However, the study reported by Chebl

et al. is quite similar in many respects to our study.^[12] They categorized 450 ED patients, regardless of their etiology (including traumatic admissions), according to their lactate levels and examined in-hospital mortality. The most common final diagnosis of patients (80.2%) was an infection. In-hospital mortality was 2.7% in the lactate <2 mmol/l group, 12% in the 2–4 mmol/l group, and 40.7% in the >4 mmol/l group. They reported a higher mortality rate in patients with lactate levels >4 mmol/l than in patients in our study. This may be explained by the higher rate of septic patients in their study population. Surprisingly, they reported that the mortality rate was not increased in older patients (>65 years) or hypotensive (systolic blood pressure <90 mmHg) patients. We found that the OR for mortality was 4.973 in hypotensive patients and 3.583 for those aged ≥75 years.

Finally, according to our results, 30-day in-hospital mortality is higher in the following ED patients with elevated lactate levels, which might indicate the need for more aggressive treatments/interventions: (1) patients who do not show lactate normalization on the second measurement; (2) patients with a lactate level >3.15 mmol/l on second measurement; (3) patients with lactate clearance <50%; (4) patients with comorbidities such as nursing home residents, bedridden patients, and those older than 75 years; (5) hypotensive patients on initial measurement; and (6) patients with a final diagnosis of acute renal failure, septic shock, or acute coronary syndrome.

Limitations

One of the major limitations of this study is that the mortality rate in hospitalized patients was followed for only 30 days. Monitoring of mortality should continue throughout the patient's hospital stay. The main reason why we limited the mortality follow-up to 30 days is that mortality may be due to additional complications that may occur during long hospital follow-up, rather than the high lactate level at the time of admission to the ED.

In addition, patients who were discharged from the ED after a full evaluation were considered alive. In general, patients who were not found to have any life-threatening conditions after a comprehensive evaluation in the ED were discharged. Despite this, mortality may have occurred in discharged patients due to a critical illness that was missed in the ED management.

Another limitation of our study is its retrospective, single-centered design. Due to the retrospective nature of the study, the nonstandardization of lactate measurement times may have limited the ability to get a clear idea of lactate clearance. Furthermore, we do

not know if lactate normalization was not seen because the second measurement was taken early. Lactate normalization may have occurred in the subsequent lactate measurements of some patients who did not have lactate normalization in the period between the first and second lactate level measurements. In future studies, evaluating all lactate measurements during the follow-up of patients may eliminate this limitation.

Moreover, we only included patients who were admitted to monitored ED beds, which may have led to selection bias, as there may have been patients with hyperlactatemia in nonmonitored ED beds.

Conclusions

The second lactate level predicts 30-day in-hospital mortality more accurately than the first lactate level and lactate clearance in ED patients with elevated lactate levels. The second lactate level of >3.15 mmol/l has a sensitivity of 81.3% and a specificity of 69.7% in the prediction of mortality. Nursing home residents, bed-ridden patients, patients aged ≥ 75 years, hypotensive patients, and patients with a final diagnosis of acute renal failure, septic shock, or acute coronary syndrome have a higher mortality rate.

Author contributions statement

- AAK: Conceptualization, Data curation, Methodology, Project administration, Supervision, Visualization, Writing – original draft, Writing – review and editing
- EA: Conceptualization, Methodology, Project administration, Supervision, Visualization, Writing – original draft, Writing – review and editing
- BB: Conceptualization, Formal analysis, Methodology, Supervision, Visualization, Writing – original draft, Writing – review and editing
- EK: Conceptualization, Data curation, Supervision, Writing – original draft
- BEG: Conceptualization, Data curation, Supervision, Writing – original draft.

Conflicts of interest

None declared.

Ethical approval

The study was approved by the Ethics Committee of Dokuz Eylül University (Decision number: 2022/13-17, date: June 04, 2022).

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