ORIGINAL ARTICLE

Eastern Journal of Medicine
East J Med 28(4): 562-567, 2023
DOI: 10.5505/ejm.2023.08068

Prognostic Value of Admission Lactate Level in Patients With Myocardial Infarction With ST Segment Elevation

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ABSTRACT

Lactate is a product of anaerobic metabolism and increases in states of tissue hypoxia. Furthermore, it is demonstrated that lactate level is correlated with the extent of infarct area and short term (30-day) mortality rates in patients with acute coronary syndrome with ST segment elevation (STE-ACS). Therefore, we aimed to test the prognostic value of this easily obtainable parameter on outcomes in patients presenting with STE-ACS.

All adult patients who admitted with STE-ACS between 2019 and 2020 were screened. The cases with admission lactate levels were included. Patients were separated into two groups as low (<2mmol/l) and high (>2mmol/l) lactate groups.

A total of 70 patients were enrolled. The mean age of the study population was 62.3 ± 15.0 years and 53 (75.7%) of them were male. The most common infarct related artery was the left anterior descending (LAD) artery. The median lactate level was 2.5 (0.80-15.3) mmol/L. Malignant arrhythmia, contrast induced nephropathy (CIN), and in-hospital mortality rates were not different between the high and low lactate groups. However, all-cause mortality was significantly higher in the high lactate group during the follow-up (p=0.005). Among all included parameters; lactate level [OR:1.76, (CI: 1.28-2.42); p<0.001] and age [OR:1.10, (CI: 1.03-1.17); p=0.004] were predictors for all-cause mortality.

Admission lactate level can predict all-cause mortality in patients with STE-ACS. In addition, high admission lactate levels could help to raise more attention even if the patients have been discharged from the hospital.

Keywords: STE-ACS, lactate level, mortality, contrast-induced nephropathy, arrhythmia

Introductıon

Lactate is a product of glycolysis and is synthesized under anaerobic and, to a small extent, aerobic conditions. It is produced from tissue cells and transported back to the liver, transformed into pyruvate, and metabolized by pyruvate dehydrogenase in the Cori cycle (1). However, pyruvate's metabolism is impaired in hypoxia states, which is then oxidized to its alternate metabolite, lactate. A high circulating lactate concentration thus implies global inadequate tissue perfusion and oxygenation (2).

Since the clinical significance for revealing hypoxic states, lactate has been extensively used in critical care settings (3). Furthermore, the improvement of hyperlactatemia, in other words, lactate clearance, was demonstrated as a follow-up marker in different shock states (1,4,5). Hyperlactatemia is defined as a blood lactate level higher than the normal value of 2 mmol/liter (mM/L), and its elevation is an indicator of hemodynamic impairment even if the patient is hemodynamically stable (6,7). Independent of the type of shock, elevations in circulating lactate indicate the presence of anaerobic metabolism. In patients with cardiogenic shock, where the most frequent cause is acute myocardial infarction, lactate elevation is known to be associated with impaired tissue perfusion (8,9). Furthermore, previous studies have shown that the amount of circulating lactate has been demonstrated to correlate both with the severity and extent of the coronary artery disease (10). In a randomized controlled trial, Jansen and colleagues showed

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Received: 13.03.2023, **Accepted:** 18.07.2023

improved organ function and hospital mortality with early lactate clearance-guided therapy (11).

Even mild hyperlactatemia is related to increased mortality rates in shocks (12). However, the prognostic significance of admission lactate level on long-term survival and developing complications related to myocardial infarction with ST segment elevation (STEMI), which is an important predisposing factor for cardiogenic shock, is scarce and controversial. Therefore, this study aimed to establish the predicted value of arterial lactate levels in patients presented with STEMI. In addition, we examined whether patient characteristics and complications differ between low and high lactate levels at admission.

Materials and Methods

This is a retrospective study that enrolled 70 consecutive patients who admitted to our hospital with the diagnosis of STEMI and who have measured lactate level at admission between December 2019 and December 2020. The guideline of the American College of Cardiology Foundation/American Heart Association and European Society of Cardiology guidelines of STEMI was used as the diagnostic criteria for STEMI. The patients without a lactate level at hospital admission or prior to coronary angiography were excluded from the study. Age under 18 years, decompensated liver failure, presence of cancer diagnosis and pregnancy were other exclusion criterias. Ethical approval (Approval Number:321; approval date:13.01.2023) was obtained from the local ethics committee of the Gazi Yaşargil Training and Research Hospital.

Data Collection: The datas were obtained from the electronic database of the hospital. Demographic datas, comorbidities (hypertension, diabetes, chronic heart disease, etc.) and used medications, infarct-related artery, and in-hospital complications (malign arrhythmia, contrast-induced nephropathy) were all recorded.

Outcome and Follow-Up: The primary end-point was the occurence of STEMI-associated complications during the stay in the hospital. The secondary outcome was all-cause death during follow-up. Datas including in-hospital complications were collected from the hospital database and mortality datas were obtained via telephone calls with the relatives of the patients.

Statistics: Categorical variables were presented as number and percentage. Parametric numeric variables were expressed as mean ± standard deviation whereas non-parametric variables were presented as median (min-max) values. Student's t-test is used for comparing parametric variables and Mann-Whitney U test was used in order to compare non-parametric variables. Chi-squre test was used to examine the differences between categorical variables. ROC-curve analysis was performed to define cut-off values of lactate level for predicting outcomes. A two sided 0.05 p-value was regarded as statistically significant. SPSS 22.0 version was used for statistical analysis.

Results

A total of 70 patients were included in the study. The mean age of the study population was 62.3 ± 15.0 years, and 75.7% (n=53) were male. Hypertension was present in 52 (74.2%) patients, and diabetes was present in 40 (57.1%) cases. The median level of lactate was 2.5 (0.80-15.3) mmol/L, and the mean left ventricular ejection fraction was 48.8% ± 10.2. None of the cases were in cardiogenic shock at the admission; however, 12 (17.1%) cases required vasopressor treatment during hospitalization. Cardiac arrest developed after admission in 3 patients before PCI and all of them responded to short-term cardiopulmonary rescucitation. Patients were seperated into two groups based on lactate levels, and baseline characteristics were listed in Table-1.

Left anterior descending artery (LAD) was the most frequent involved culprit artery underlying the STEMI. Malignant arrhythmias occurred in 8 (11.4%) patients, and contrast-induced nephropathy developed in 15 (21.4%) cases during the hospital stay. In-hospital mortality occurred in 3 (4.2%) patients, and the total mortality rate after index admission was 27.1% (n=19) during the median 36.9 (0.13-39.0) months of follow-up. The incidence of malignant arrhythmia, contrast-induced nephropathy, and in-hospital mortality was similar between the two groups, while the all-cause mortality rate during follow-up was distinctly higher in patients with high lactate levels (6.8% vs. 0%; p=0.005). Outcomes were summarized in Table-2.

Logistic regression analysis was performed with regard to determine the predictors of all-cause mortality. Variables with p values <0.200 were included in multivariate regression analysis. Gender [OR:0.29, (CI:0.09-0.941); p=0.039], age [OR:1.04, (CI: 0.99-1.08); p=0.054], lactate level [OR:1.35, (CI:1.09-1.66); p=0.005], and diabetes [OR:2.69, (CI:0.84-8.58); p=0.094] were further included in multivariate analysis. Only lactate level

Table 1. Baseline Characteristics and Outcomes

	High lactate level (n=44)	Low lactate level n=26	p value
Age, years	61.9 ± 15.6	62.8 ± 14.2	0.810
Gender, male	33 (75%)	20 (76.9 %)	1.000
Hypertension	36 (81.8%)	16 (61.5%)	0.111
Diabetes mellitus	31 (70.4%)	9 (34.6%)	0.007*
LVEF	48.6 ± 10.9	49.2 ± 9.2	0.824
Hemoglobin, g/dL	14.3 ± 2.1	14.2 ± 2.2	0.802
GFR, mL/min/m²	73.8 ± 19.9	76.5 ± 21.1	0.598
Infarct related artery;			
-LAD	25 (56.8%)	10 (38.4%)	0.216
-Circumflex artery	13 (29.5%)	7 (26.9%)	1.000
-Right coronary artery	11 (25.0%)	12 (46.1%)	0.119

Abbreviations: LVEF: Left ventricular ejection fraction; GFR: Glomerular filtration rate; LAD: Left anterior descending artery

Table 2. Comparison of the Outcomes With Regard To The Lactate Levels

	High lactate level (n=44)	Low lactate level n=26	p value
Malignant arrhythmia	7 (15.9%)	1 (3.8%)	0.243
Contrast induced nephropathy	12 (27.2%)	3 (11.5%)	0.144
Mortality (Follow-up)	17 (38.6%)	2 (7.6%)	0.005*
In hospital mortality	3 (6.8%)	0 (0%)	0.289

Table 3. Cut-off Values of Lactate For Predicting Outcomes

Outcome	Cut-off value	Sensitivity (%)	Specifity (%)	Area under curve (AUC)	*p* value
Malignant arrhythmia	3.44	75	79	0.786	0.009
Contrast induced nephropathy	2.85	66	64	0.670	0.044
All-cause mortality	2.59	73	63	0.763	0.001

Abbreviations: AUC: Area under curve

[OR:1.76, (CI: 1.28-2.42); p<0.001] and age [OR:1.10, (CI: 1.03-1.17); p=0.004] were the predictors of all-cause mortality.

Cut-off values of lactate levels for predicting malignant arrhythmia, CIN, and all-cause mortality were determined by ROC analysis. The cut-off levels with the highest area under curve values are listed in Table-3.

Discussion

The current study found that high lactate levels on admission were related to high overall mortality in patients with STEMI. Interestingly, in-hospital mortality did not change if the cut-off level was adopted as >2 mmol/l. On the other hand, the risk of contrast-induced nephropathy and malign arrhythmia increased at cut-off levels of 2.8 mmol/l and 3.4 mmol/l, respectively. Moreover, diabetic patients were more prone to have high lactate concentrations.

The additional value of lactate measurement, notably in the early period of hospital admission, has been most pronounced in septic patients (13,14). In parallel, higher lactate levels have been demonstrated to be associated with worse outcomes in several other critical illnesses. The underpinning reason for this issue is that hypoperfusion or hypoxia dominates the lactate level. Sure enough, the development of severe hypoperfusion leads to ischemia-related complications. Under normal circumstances, the heart

is an essential net consumer of lactate that provides 10 to 40% of the myocardial energy supply. However, decreased oxygen delivery to the heart myocardium can lead the heart to become a lactate producer instead of a lactate consumer, as demonstrated in several models (15). Myocardial infarction is also characterized by hypoperfusion of the heart muscle, which takes the primary role in cardiovascular hemodynamics. In accordance with the pathophysiology, our study confirmed that increased lactate level is related to high mortality rates in STEMI patients. In other words, the level of increase in the surrogate parameter of global hypoperfusion secondary to heart dysfunction was correlated with reduced survival rates. Supportively, Vermeulen and colleagues evaluated 1176 patients and showed that higher lactate levels were correlated with a higher rate of hypotension and tachycardia in patients with STEMI. In parallel to our study, they also demonstrated that higher lactate level was associated with higher 30-day mortality, notably when the level increased more than 1.8 mmol/L. In addition to our study, they demonstrated that higher lactate levels indicate a worse response to percutaneous coronary intervention (8). The prognostic value of lactate is not limited only to the acute coronary syndromes and lactate levels may predict mortality in other vascular events such as stroke. It was reported that, 24th hour of an ischemic stroke episode lactate level was prominently higher in patients who died during follow-up than patients remained alive (16). These findings are crucial since admission lactate is an easily obtainable clinical parameter and could be involved in patient risk stratification systems (17). Moreover, lactate should be added in the routine laboratory markers measured in patients with STEMI at admission to the hospital. The main advantage could be that the patients with high admission lactate levels could be followed with more attention even they discharge from the hospital.

Former studies suggested that the clinical role of lactate level is precisely related to the specific disease. For instance, it was assumed that the cut-off value of 2 mmol/l lactate was not alarming in septic patients; it was clinically relevant in surgical patients. However, recent studies suggested that even a relative increase in lactate level is related to a higher risk of death (12). Furthermore, absolute lactate >2 mmol/l is strongly associated with higher hospital mortality. In the current study, the cut-off lactate level for mortality was found as 2.6 mmol/l, which is firmly in accordance with previous findings (18). In a study including 754 acute decompensated heart failure patients, lactate levels of >3.2 mmol/l on admission were related to worse in-hospital mortality rates, independent of accompanying acute coronary syndrome (19).

From a distinct perspective, absolute lactate level could help diagnose acute coronary syndromes in clinically relevant patients. For example, Schmiechen and colleagues evaluated 129 patients admitted to the emergency room due to chest pain and tested the value of blood lactate for diagnosing critical cardiac illnesses. They showed that while high lactate was correlated with severe cardiac illness, normal lactate ranges had a high negative predictive value for AMI diagnosis (20). In parallel, in another study, lactate measured at admission was found to be highly sensitive for AMI diagnosis in patients who had chest pain for more than two hours (21). Furthermore, Mavric and colleagues tested the ability of blood lactate levels to predict shock development in a group of 229 patients. They demonstrated that admission lactate level had a great predictive value for shock development (22). So, in combination with our study, lactate levels in admission could be a relevant diagnostic marker for detecting acute coronary patients.

The current study's other main findings are increased risk for complications, notably contrast-induced nephropathy, and malign arrhythmia. These findings are not unexpected since the common cause is hypoxia-induced organ dysfunction. For example, kidneys receive almost 20% of circulated blood flow but are pretty sensitive to hypoxia (23). So, the addition of any nephrotoxic medication would increase the risk of acute kidney injury. The current study's other crucial contribution is defining which cut-off level AKI risk rises in this population. In patients with lactate levels higher than 2.8 mmol/l, the clinician could be more alert for developing AKI, which might raise attention for avoiding hypo- and hypervolemia in these patients. Independent of the improvement in lactate level during follow-up, admission lactate is still invaluable due to a hypoxic hit, which can be enough for kidney ischemia (24). Similarly, our study demonstrated that the risk of malign arrhythmia increases in STEMI cases with lactate >3.4 mmol/l. The high lactate level is a surrogate marker for tissue hypoxemia and relevant acidosis, a precipitating factor for malign arrhythmias (18). Closely monitoring these patients in intensive care units could prevent undesirable arrhythmia-related complications.

The current study also has several limitations to be mentioned. Firstly, this is a retrospective study that leads to missing parameters and limits adding extra parameters to consider. Use of metformin and some other drugs may cause increased lactate levels however we could not reach the datas about the

medications. Secondly, a relatively low number of included patient population decreases the power of the research. Thirdly, one of the main issues regarding the interpreting the results of research performed with lactate evaluation is to clearly define the period from taking the blood sample to laboratory evaluation since the lactate levels may increase even 1.2 mmol/L if the blood sample is not analyzed around 1 hour (25). However, the samples are assessed in a very close field in the emergency department, and maximum attention is paid to these patients.

To conclude, admission serum lactate is an easily obtainable clinical parameter and a good predictor of complications and mortality in STEMI patients. If the admission level is high, more attention could be paid even if they have optimal macrohemodynamic parameters or improved lactate levels.

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