

# The effect of lactate levels on prognosis in patients with ST-segment elevation myocardial infarction

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## Abstract

**Aim:** The prognostic role of lactate for early mortality in patients with ST-segment elevation myocardial infarction (STEMI) submitted to primary percutaneous transluminal coronary angiography (PTCA) is not elucidated clearly. This study was conducted with patients that presented to the emergency department (ED) with STEMI and underwent PTCA to investigate whether the changes in lactate values from ED admission to 24 hours after PTCA affected mortality.

**Material and Methods:** This prospective observational study on 143 patients with STEMI was conducted at emergency service and tertiary-level cardiology clinic in a public university hospital. The documentation for each patient included detailed information on demographics, type of myocardial infarction according to electrocardiography and PTCA results, duration of hospital stay, vital signs, laboratory findings on admission, lactate levels 24 hours after PTCA, and outcome (hospital discharge or death).

**Results:** The lactate values are higher in non-surviving groups measured 24 hours after PTCA ( $P < 0.001$ ). The differences in the lactate levels from the time of admission to 24 hours after PTCA were significantly lower in the non-surviving group ( $P < 0.001$ ).

**Conclusion:** Among patients presenting to the ED with STEMI, a high lactate level is associated with mortality. Also, the difference between lactate values of the patients after PTCA is associated with the risk of mortality. Therefore, we consider that first lactate levels in ED and last lactate levels after PTCA in patients with STEMI can provide physicians with an insight into the possibility of mortality.

**Keywords:** Lactates; mortality; myocardial infarction; primary percutaneous transluminal coronary angiography

## INTRODUCTION

ST-segment elevation myocardial infarction (STEMI) is caused by a coronary vessel and thrombotic obstructions due to the rupture or erosion of a plaque. As a result of irregular blood flow, the oxygen demand of the myocardium is not met and myocardial damage occurs (1). The relative incidences of STEMI are increasing, respectively. STEMI accounted for 39% of all hospital admissions due to myocardial infarction and the 1-year mortality rate for STEMI patients was 10% in the World (2). Important elements from the current guidelines recommend that patients with STEMI should be reperfused by primary percutaneous transluminal coronary angiography (PTCA) performed (3).

The elevated serum lactate levels are associated with higher mortality even in hemodynamically stable patients

and may indicate hypoperfusion and hypoxia (4). The value of an early lactate measurement with regard to patient risk stratification is pronounced with elevated lactate levels in STEMI patients, as has been demonstrated in patients with ischemic diseases (5). In patients with STEMI, increased levels of lactate in venous circulation have been reported (6).

The aim of the study was determine to investigate the effect of lactate values changes from the time of admission to 24 hours after PTCA on mortality with patients that presented to the emergency department (ED) with STEMI and underwent PTCA.

## MATERIAL and METHODS

This prospective study was conducted in the ED of a University Hospital, Turkey. The university's Institutional Review Board approved the study design, and patients or

Received: 20.02.2020 Accepted: 06.04.2020 Available online: 06.07.2020

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their relatives provided written consent. The participants were 143 adult patients with STEMI who underwent PCCA between January 1, 2015, and March 31, 2016.

PTCA, percutaneous coronary interventions (PCIs), and other cardiac interventions, such as coronary artery bypass graft surgery, pacemaker, open-heart surgery, and intraaortic balloon pump were performed for 24 hours in our hospital by a team consisting of four cardiothoracic surgeons and six interventional cardiologists. Door-to-balloon (or device) time was less than 30 minutes. The inclusion criteria were being aged  $\geq 18$  years, having STEMI, and having undergone PTCA. These patients were selected by emergency physicians. The patients were excluded from the study if they were diagnosed with unstable angina or non-ST-segment elevation myocardial infarction. Emergency physicians or cardiologists have obtained the consent at ED before PTCA. All patients were followed until discharge from the hospital or in-hospital death.

Standard study forms were prepared to record the patient data daily, beginning from admission to the ED. Upon arrival at the ED, each patient who had chest pain was monitored. The patients were examined quickly, an ECG was performed immediately. If STEMI was detected in the patients' ECG, their pulse rate, arterial blood pressure, fever, respiratory rate, and oxygen saturation were recorded on the study form. An intravenous line was placed, and blood samples were collected to measure creatine kinase (CK), CK-MB, troponin I, lactate, and other laboratory parameters. After these procedures, resuscitation was conducted following the principles of the American Heart Association, and the patients underwent diagnostic and therapeutic procedures according to the existing protocol STEMI was defined according to a previous study.

Per this study, STEMI was diagnosed in the absence of left ventricular hypertrophy or left bundle-branch block as 1) new ST elevation at the J point in at least two contiguous leads of  $\geq 2$  mm (0.2 mV) in men or 2)  $\geq 1.5$  mm (0.15 mV) in women in leads V2–V3 and/or 3) of  $\geq 1$  mm (0.1 mV) in other contiguous chest leads or the limb leads. Also, a new or presumably new left bundle branch block was considered as a STEMI equivalent.

The documentation for each patient included detailed information on demographics (i.e., age, sex, and comorbidities), type of myocardial infarction according to ECG, results of PCCA, duration of hospital stay, vital signs, laboratory findings on admission, lactate level at 24 hours after PTCA, and outcome (discharge or death). According to PTCA, coronary artery disease was diagnosed as the presence of a  $\geq 70\%$  stenosis of diameter in any major vessel, and multi-vessel coronary artery disease as  $\geq 70\%$  stenosis of diameter in at least two major vessels.

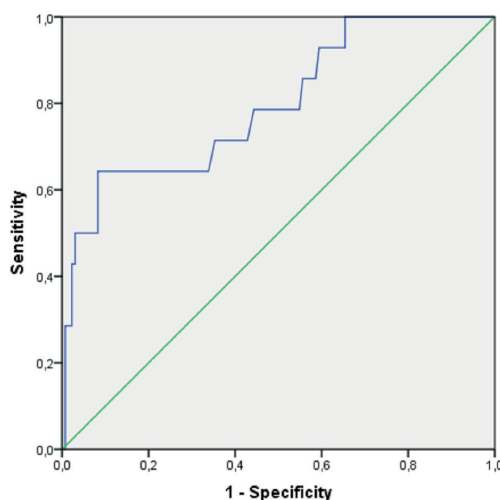
### Statistical analysis

The patients were categorized into surviving and non-surviving groups to analyze the findings. The Statistical Package for the Social Sciences for Windows version

20.0 (SPSS, Inc., Chicago, IL, USA) was used for statistical analysis. Descriptive statistics were reported, including mean, standard deviation and frequency values. Categorical data were analyzed using the chi-square or Fisher's exact test. Continuous data were analyzed using the unpaired T-test or Mann-Whitney U test, depending on whether the data were normally distributed. A risk analysis was conducted with the receiver operating characteristic (ROC) curve. The cut-off values were 33.3 for the first lactate level and 24.9 for the 24-hour lactate level. In all analyses, the difference or correlation was considered statistically significant when  $p$  was  $< 0.05$ .

## RESULTS

Table 1 lists the patient characteristics and other case details. The patients consisted of 119 males and 24 females with a median age of 61 years (interquartile range (IQR): 25-86). All the patients were transferred to a catheterization laboratory, and PCCA was performed. The mean age was significantly higher in the non-surviving group. Of the 143 patients in total, 131 (92%) underwent PCIs and three (2%) required emergent surgery (2%). According to ECG, the Most common myocardial infarctions were anteroseptal ( $n = 62$ , 44%), followed by inferior ( $n = 42$ , 29%), anterolateral ( $n = 13$ , 9%), and right inferior right ( $n = 10$ , 7%).



**Figure 1.** The sensitivity and specificity of the lactate level at the cut-off value of 33.3 at the time of admission (the area under the curve was 0.796; 95% confidence interval, 0.67-0.93)

Table 2 summarizes the patients' results concerning vital signs and laboratory findings while in the ED. On the surviving group's vital signs; the patient's mean systolic blood pressure was  $140 \pm 26$  mmHg, diastolic blood pressure was  $82 \pm 11$  mmHg and pulse rate was  $74 \pm 12$ /min. On the non-surviving group's vital signs; the patient's mean systolic blood pressure was  $129 \pm 26$  mmHg, diastolic blood pressure was  $78 \pm 15$  mmHg and the pulse rate was  $75 \pm 14$ /min. No significant difference was found when the vital signs of the living group were compared with the vital signs of the non-surviving group ( $p > 0.05$ ).

**Table 1. Patient characteristics and other case details**

	Surviving (n=129, 90%)	Non-surviving (n=14, 10%)	All patients (n=143)	p
<b>Age (years)</b>	61 (IQR: 25-86)	72 (IQR:60-82)	61 (IQR: 25-86)	<b>0.001</b>
<b>Gender</b>				0.188
Male	109 (84%)	10 (71%)	119 (83%)	
Female	20 (16%)	4 (29%)	24 (17%)	
<b>Presence of co-morbidities</b>	69 (53%)	9 (64%)	78 (55%)	0.315
<b>Results of ECG</b>				
Anteroseptal MI	57 (44%)	5 (36%)	62 (44%)	0.377
Inferior MI	37 (29%)	5 (36%)	42 (29%)	0.417
Anterolateral MI	11 (9%)	2 (14%)	13 (9%)	0.371
Inferior and right MI	9 (7%)	1 (7%)	10 (7%)	0.656
Lateral MI	10 (8%)	0 (0%)	10 (7%)	0.344
Inferolateral MI	3 (2%)	1 (7%)	4 (3%)	0.341
Posterior MI	2 (2%)	0 (0%)	2 (1%)	0.813
<b>Results of PTCA</b>				
Left anterior descending stenosis	92 (71%)	12 (86%)	104 (68%)	0.207
Right coronary artery stenosis	66 (51%)	7 (50%)	73 (50%)	0.578
Left circumflex artery stenosis	48 (37%)	10 (71%)	58 (33%)	<b>0.015</b>
Single vessel disease	64 (51%)	4 (29%)	68 (48%)	0.111
Multiple vessel disease	65 (10%)	10 (29%)	75 (12%)	0.111
<b>Treatments</b>				
PCIs	120 (93%)	11 (79%)	131 (92%)	0.097
Surgical	5 (4%)	3 (21%)	8 (6%)	0.032
Thrombolytic	1 (1%)	0 (0%)	1 (1%)	0.902
Medical	3 (2%)	0 (0%)	3 (2%)	0.732
<b>Duration of hospital stay (days)</b>	5 (IQR:1-17)	5 (IQR: 2-15)	5 (IQR: 1-17)	0.150

ECG: Electrocardiogram; MI: Myocardial Infarction; PTCA: Primary Percutaneous Coronary Angiography; PCIs: Percutaneous Coronary Interventions

**Table 2. Vital signs and laboratory findings at the time of ED admission**

	Surviving (mean±SD)	Non-surviving (mean±SD)	All patients (mean±SD)	p
<b>Vital signs</b>				
Systolic blood pressure (mmHg)	140±26	129±26	139±26	0.376
Diastolic blood pressure (mmHg)	82±11	78±15	82±58	0.512
Pulse rate (beat/min)	74±12	85±25	75±14	0.158
<b>Laboratory findings</b>				
Creatinine kinase (µgr/L )	274±465	343±347	281±455	0.313
CK-MB (µgr/L)	68±81	90±61	70±79	<b>0.047</b>
Troponin I (µgr/L)	0.53±1.6	0.74±1.23	0.55±1.6	0.073
<b>Lactate levels</b>				
Lactate level (mg/dL) at admission	30±121	46±32	32±115	<b>0.001</b>
Lactate level (mg/dL) at 24 hours after admission	21±60	46±34	24±58	<b>0.001</b>

The mean CK-MB values were significantly higher in the non-surviving group compared to the surviving group ( $p < 0.05$ ). The mean lactate level at admission was 30±121 mg/dL in the surviving group and 46±32 mg/dL in the non-surviving group. The mean lactate level at 24 hours

after admission was 21±60 mg/dL in the surviving group and 46±34 mg/dL in the non-surviving group. The mean lactate values at ED admission and 24 hours after PTCA were significantly higher in the non-surviving group compared to the surviving group ( $p < 0.001$  for both).

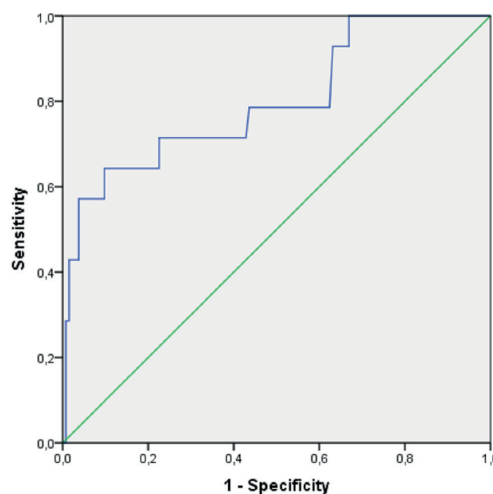
**Table 3. The differences in the lactate level from the time of admission to 24 hours after PTCA**

	Surviving (n=129) (95% CI)	Non-surviving (n=14) (95% CI)	P
Difference of Lactate Levels	8.6 ± 61.4 (-1.84,-19,23)	0.04 ± 34 (-19.59,19.67)	0.001

The mean difference of lactate levels was 8.6 ± 61.4 mg/dL in the surviving group and 0.04 ± 34 mg/dL in the non-surviving group. When the differences in the lactate levels from ED admission to 24 hours after PTCA compared the mean values for these differences were significantly lower in the non-surviving group ( $p < 0.001$ ) (Table 3).

At the cut-off value of 33.3 mg/dL, the lactate level had a sensitivity of 64.29, specificity of 91.73%, positive predictive value (PPV) of 44.90% (23.00-68.37%) and negative predictive value (NPV) of 96.06% (91.05-98.71%) at the time of ED admission (Table 4) (Figure 1).

At 24 hours after PTCA, at the cut-off value of 24.9 mg/dL, the lactate level had a sensitivity of 64.29%, specificity of 90.23%, PPV of 40.91% (20.71-63.65%) and NPV of 96.00% (90.92-98.69%) (Table 4) (Figure 2).



**Figure 2.** The sensitivity and specificity of the lactate level at the cut-off value of 24.9 at 24 hours after PTCA (the area under the curve was 0.799; (95% confidence interval, 0.66-0.98)

**Table 4. Specificity, sensitivity, positive predictive and negative predictive values for the lactate level at the time of admission and 24 hours after PTCA**

	Sensitivity	Specificity	Positive predictive value (95% CI)	Negative predictive value (95% CI)	OR
Lactate level at admission	64.29	91.73	44.90 (23.00-68.37)	96.06 (91.05-98.71)	0.796
Lactate level at 24 hours after PTCA	64.29	90.23	40.91 (20.71-63.65)	96.00 (90.92-98.69)	0.799

## DISCUSSION

Many studies conducted in the ED and intensive care unit have shown that a high level of lactate is an effective parameter in predicting early and late mortality in non-diabetic STEMI patients presenting with cardiogenic shock, traumatic shock, sepsis, and liver failure (7). At the same time, the effect of lactate levels on mortality in patients with STEMI and angina with acute coronary syndrome has been investigated in single- and multi-center studies (8).

In a study conducted with 129 patients presenting with chest pain, Schmiechen et al. reported that lactate levels could be used as a prognostic marker. When the lactate concentration was examined in patients who presented to the ED with myocardial infarction, chest pain, heart failure, and arrhythmia, it was observed that normal lactate values had a high NPV for the diagnosis of myocardial infarction (9). In our study, we found that the STEMI patients had high lactate levels at the time of ED presentation, and these elevated levels were associated with mortality in a parallel manner.

Some researchers suggest that a lactate level of 1.7 mm/L does not present a mortality risk in trauma or sepsis

patients, while others consider 4 mm/L as a threshold for this risk but note that a clinically significant lactate value for the indication of mortality remains controversial (10). In general, it is known that STEMI patients undergoing PTCA are at high risk and have high mortality in the presence of hyperlactatemia. Similarly, patients with increased acute decompensated heart failure (ADHF) were found to be having increased hospital mortality if their lactate value was above 3.2 mmol/L compared to those without ADHF (11). In contrast, Nichol et al. reported that patients with blood lactate concentrations above 0.75 mmol/L might have higher mortality (12). DeGreare et al. demonstrated that according to the historical Killip classification, lactate levels were closely associated with mortality in patients exposed to PTCA (13). In the current study, the blood lactate value of patients presenting to the ED with STEMI was 46 mg/dL (2.5mmol/L) at the time of admission. These findings are consistent with the literature; thus, we can state that STEMI cases presenting to the ED with high lactate levels may have a mortal course.

In another study evaluating the sensitivity, specificity and NPV of a high lactate level in predicting mortality, the values were reported as 92% (95% confidence interval [CI], 86-99%), 44% (95% CI, 40-48%) and

98% (95% CI, 97-99%), respectively (6). In our study, we found sensitivity as 64.29%, specificity as 91.7%, NPV as 99.06% (95% CI, 91-99%), and PPV as 45% (95% CI, 23-68%). Compared with the previous study, NPV was similar, but our sensitivity was lower and the specificity was higher.

In a study by Ludhmila et al. (14) the lactate values of the patients hospitalized in the intensive care unit were determined as 3 mmol/L and 2 mmol/L after six hours and 12 hours of admission, respectively, and the results of the area under the ROC curve were 0.72 (95% CI, 0.64-0.79;  $p < .001$ ) and 0.75 (95% CI, 0.66-0.83;  $p < .001$ ), respectively. In our study, similar results were obtained.

Lazzeri et al. conducted a study with 253 non-diabetic STEMI patients who underwent PTCA and found that the initial lactate level was a predictor of mortality in the intensive care unit (7). In a larger-scale study, the lactate levels of 803 non-diabetic STEMI patients who underwent PTCA were reported to be associated with early mortality according to the Killip classification (15). Another study determined that lactate clearance of less than 70% in the first 48 hours of PTCA was directly associated with hospital mortality among 96 STEMI cases (16). Similarly, Attana et al. detected an association between lactate clearance of less than 10% within the first 12 hours and early mortality in 51 patients with STEMI (17). In the current study, we observed that in cases where the difference between the lactate level at the time of admission and the lactate level after PTCA was high, the mortality rate was lower and these patients were discharged in a healthy state. In other words, mortality was decreased in parallel to the increase in lactate clearance.

High lactate values are associated with mortality. If the lactate level is high in STEMI patients, physicians should be more careful. Treatment of patients should be started as soon as possible, and treatments that decrease lactate values should be considered. There may be a significant decrease in lactate values after PTCA, and mortality is decreasing. Therefore, PTCA should be administered to STEMI patients as soon as possible.

## LIMITATIONS

This study was a single-center study. Therefore, our results cannot be generalized to all centers and erroneous/missing data may have affected our findings. Secondly, we researched the lactate levels 24 hours after PTCA. Different lactate levels can be measured at other hours. These are some limitations to our study.

## CONCLUSION

High lactate levels in patients presenting to the ED with STEMI are associated with mortality. The difference between the first and last lactate levels of patients undergoing PTCA also has an impact on mortality. Therefore, we consider that the lactate levels of STEMI cases presenting to the ED can provide physicians with an insight into the possibility of mortality.

When STEMI patients admitted to emergency departments lactate values should be requested in addition to routine examinations to predict the mortality of patients. So we can estimate an early mortality.

*Competing interests: The authors declare that they have no competing interest.*

*Financial Disclosure: There are no financial supports.*

*Ethical approval: The study was approved by the Inonu University Ethics Committee (No: 2014/231).*

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