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ORIGINAL RESEARCH

Association of Different Lactate Indices with 30-Day and 180-Day Mortality in Patients with ST-Segment Elevation Myocardial Infarction Treated with Primary Percutaneous Coronary Intervention: A Retrospective Cohort Study

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Long Hu[1]
Wei Lin[2]
Tiancheng Xu[1]
Dongjie Liang[1]
Guangze Xiang[1]
Rujie Zheng[1]
Changzuan Zhou[1]
Qinxue Dai[3]
Danyun Jia[3]

[1]Department of Cardiovascular Medicine, The Heart Center, The First Affiliated Hospital of Wenzhou Medical University, Wenzhou 325000, Zhejiang, People's Republic of China; [2]Department of Pediatric Intensive Care Unit, The Second Affiliated Hospital and Yuying Children's Hospital of Wenzhou Medical University, Wenzhou 325027, Zhejiang, People's Republic of China; [3]Department of Anesthesiology, The First Affiliated Hospital of Wenzhou Medical University, Wenzhou 325000, Zhejiang, People's Republic of China

Background: Admission lactate level has been reported as a useful marker of mortality. In this study, we compared the relative value of different lactate indices to predict survival in patients with ST-segment elevation myocardial infarction (STEMI) undergoing primary percutaneous coronary intervention (PCI).

Methods: This was a retrospective observational study including consecutive patients with STEMI undergoing primary PCI who admitted to the Coronary Care Unit of the First Affiliated Hospital of Wenzhou Medical University between 2014 and 2017. The predictive value of lactate indices for mortality was compared using receiver operator characteristic (ROC) analysis, and DeLong's test was used to compare the AUC. We compared the AUC between GRACE score and GRACE score + lactate index.

Results: A total of 1080 patients were included. Fifty-nine died in 30 days and 68 died in 180 days. Most lactate indices (Lac_{adm}, Lac_{24max}, Lac_{24min} and Lac_{24tw}) were significantly lower in survivors (all P<0.001). In Cox proportional hazards model, each lactate index showed as an independent factor of 30-day and 180-day mortality except Lac_{Δ}. Kaplan–Meier curves demonstrated that the patients of higher lactate indices group had higher rates of mortality (all P<0.0001, except Lac_{Δ} P=0.0485). In receiver operator characteristic analysis, Lac_{24max} was significantly larger than Lac_{adm}(P<0.001) while the AUC value for Lac_{adm} was similar to Lac_{24min} and Lac_{24tw}. Lac_{24tw} improved the predictive probability of 30-day mortality (P=0.0415). Lac_{24max} improved the predictive probability of GRACE score for both 30-day and 180-day mortality (P<0.05).

Conclusion: In patients with STEMI undergoing primary PCI, most lactate indices are all associated with 30-day and 180-day mortality except LacΔ. In prediction of both 30-day and 180-day mortality, Lac_{24max} is superior to Lac_{adm} and significantly enhances the ability of risk stratification and prognostic evaluation when adding Lac_{24max} to the GRACE score.

Keywords: STEMI, lactate indices, hyperlactatemia, mortality

Correspondence: Danyun Jia; Qinxue Dai
Department of Anesthesiology, The First Affiliated Hospital of Wenzhou Medical University, Nanbaixiang, Ouhai District, Wenzhou City 325000, Zhejiang Province, People's Republic of China
Tel/Fax +86-577-88581162
Email 529365150@qq.com; 653091408@qq.com

Introduction

Lactate plays an important role in critically ill patients' treatment for it may reflect the balance between the supply and consumption of oxygen. Over the past few decades, lactate has come to the forefront because of its good prediction of mortality in different patient populations: sepsis, trauma, surgery, multiple organ failure and heart failure

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patients.[1–6] Recently, admission lactate level has been reported as a clinically useful marker of increased risk of mortality in patients with acute coronary syndrome.[7] What's more, a previous study has shown good predictive power of admission lactate level for early mortality in patients with STEMI submitted to primary PCI.[8]

Most studies have focused on admission lactate level, while many studies have suggested that early changes in lactate concentration may be a useful sign in stratifying patients with higher death risk.[9–11] Thus, it may be more accurate and stable to predict patients' prognosis using other lactate indices instead of admission lactate level. Currently, it remains unclear which is the optimal lactate index when it comes to the assessment of mortality risk among STEMI patients.

In this study, we compared the relative value of different lactate indices (Lac_{adm}, Lac_{24max}, Lac_{24min}, Lac_{24tw} and Lac_{Δ}) to predict survival in patients with STEMI undergoing primary percutaneous coronary intervention (PCI). In addition, we investigated whether these lactate indices can be used to improve the accuracy of the GRACE score for overall survival risk estimation.

Methods

Population

From January 2014 to October 2017, 1411 consecutive patients with STEMI, who performed primary PCI, were admitted to the Coronary Care Unit of the First Affiliated Hospital of Wenzhou Medical University. The diagnostic criteria followed the American College of Cardiology Foundation/American Heart Association and European Society of Cardiology guidelines of STEMI.[12,13] In order to assess the dynamic change of lactate, those patients without more than two lactate values collected over the first 24 hours were excluded (n=331). Finally, a total of 1080 patients were enrolled for analysis. The study complied with the Declaration of Helsinki. This article was a clinical retrospective article, so the study was approved by the Ethics Committee of the First Affiliated Hospital of Wenzhou Medical University, which waived the need for informed consent.

Data Collection

The data used in this study were extracted from the database previously reported by us, and the details of data collection had been described in the previous study.[7] Briefly, we obtained demographic data, medical history, presentation characteristics and laboratory tests for each patient from the electronic data repositories, using the data previously collected.[7] The GRACE score was calculated as described previously.[14]

Lactate and Derived Variables

For each patient, admission lactate was regarded as Lac_{adm}. The maximal blood lactate concentration during the 24 hours after admission was recorded as Lac_{24max} while the minimal blood lactate concentrations within 24 hours were considered to be Lac_{24min}. As previously reported in other literature, Lac_{24TW} was calculated to avoid the potential effect of surveillance bias due to the increased blood lactate monitoring in more severely ill patients.[11,15] It is determined by summing the mean value between consecutive time points multiplied by the period of time between consecutive time points and then dividing by the total time, the same as the method in previous articles.[11,15] In addition, Lac_{Δ} was calculated by the last time lactate minus the admission lactate during 24 hours after admission.

Outcome and Follow-Up

The primary outcome was all-cause death from hospital admission, including 30-day and 180-day mortality. We tracked the patient's vital status for 180 days by viewing data from the hospital's medical database or contacting directly with the patient or next of kin on telephone calls. The end of follow-up was the date of the death or loss to follow-up.

Statistical Analysis

After testing for normality by the Kolmogorov–Smirnov test, quantitative data with normal distribution were presented as mean ± standard deviation, while those without normal distribution were presented as median (interquartile range). Categorical variables were presented as numbers (percentages). Patient characteristics were compared using Student's t-tests or Mann–Whitney *U*-test for continuous variables and using chi-square test or Fisher's exact test for categorical variables appropriately. In order to demonstrate the relationship between lactate indices (Lac_{adm}, Lac_{24max}, Lac_{24min}, Lac_{24tw} and Lac_{Δ}) and risk of mortality, we performed unadjusted and multivariable-adjusted Cox proportional hazard models. The confounders in the multivariable-adjusted model were selected on the basis of their associations with outcomes or a change in effect estimate of more than 10%. The outcomes were further evaluated by the Kaplan–Meier curve, and survival among groups was compared using the Log Rank test. To assess the predictive value of each lactate indices for 30-day and 180-day all-cause mortality, receiver operating characteristic (ROC) curves were performed. Discrimination was assessed by the area under ROC curve (AUC), DeLong's test was used to compare the AUC.[16] Finally, in order to evaluate whether each lactate index improves the predictive value of the GRACE score for 30-day and 180-day all-cause mortality, we compared the AUC between GRACE score and GRACE score + lactate index. Data analysis was performed using SPSS version 21.0 (Chicago, IL: SPSS, Inc.) and MedCalc version 15.2.2 (MedCalc Software bvba, Ostend, Belgium). A 2-sided p <0.05 was considered statistically significant in all analyses.

Results

Baseline Characteristics of Patients

Of the 1411 patients reviewed in this study, 1080 STEMI patients (age 64.4 ± 13.0 years, 78.7% male) with more than two times of lactate measurement were analyzed. Of these patients, 59 (5.5%) died in 30 days and 68 (6.3%) died in 180 days. The main demographic, clinical and laboratory data are depicted in Table 1. As compared to survivors, non-survivors were more likely to be male (P<0.001) and older (P<0.001). Non-survivors had a lower rate of smoking (P<0.001), higher values of admission heart rates (P<0.001), aspartate aminotransferase (AST) (P<0.001), creatinine (P<0.001), BNP (P<0.001) and hemoglobin (P<0.001). In addition, non-survivors seem to have a higher rate of previous coronary artery bypass grafting (CABG), lower levels of SBP (P<0.001) and DBP (P<0.001).

Most lactate indices (Lac_{adm}, Lac_{24max}, Lac_{24min} and Lac_{24tw}) were significantly lower in survivors than in non-survivors (all P<0.001), whereas there were no significant differences with regard to Lac_{Δ} (P=0.963).

Analysis of Each Lactate Factor Correlated with Clinical Outcomes

To determine the predictive value of each lactate indices (Lac_{adm}, Lac_{24max}, Lac_{24min}, Lac_{24tw} and Lac_{Δ}) for short-term mortality (30-day) and long-term mortality (180-day) , we performed unadjusted and multivariable-adjusted Cox proportional hazard models, respectively. For each Cox proportional hazard model, Lac_{adm}, Lac_{24max}, Lac_{24min}, Lac_{24TW} or Lac_{Δ} was entered individually. As shown in Table 2, the hazard ratios (HR) of each lactate indices in different models were displayed.

For short-term mortality (30 days), each lactate indices showed as an independent factor except Lac_{Δ}. In univariate analysis (Model 1) of 30-day all-cause death, the HR of 30-day mortality was 1.43 (95% CI 1.34–1.52) per 1 mmol/L increase in Lac_{adm}, 1.54 (95% CI 1.44–1.64) per 1 mmol/L increase in Lac_{24max}, 1.83 (95% CI 1.66–2.01) per 1 mmol/L increase in Lac_{24min} and 1.83 (95% CI 1.67–1.99) per 1 mmol/L increase in Lac_{24TW} (All P-value <0.001). After adjusting for sex, age (Model 2), the associations of these lactate indices with mortality remained significant. Finally, after progressive adjustment for other confounding variables (Model 3), the HR of 30-day mortality was 1.16 (95% CI 1.05–1.29; P-value = 0.005) per 1 mmol/L increase in Lac_{adm}; the HR of mortality for Lac_{24max}(1.34, 95% CI 1.21–1.48), Lac_{24min}(1.46, 95% CI 1.27–1.69), Lac_{24tw}(1.47, 95% CI 1.30–1.67) and Lac_{Δ}(1.20, 95% CI 1.08–1.34) was even greater.

The same results were found in long-term mortality (180 days). Model 1 displayed that the Lac_{adm} (HR 1.42, 95% CI 1.33–1.51), Lac_{24max} (HR 1.52, 95% CI 1.43–1.62), Lac_{24min} (HR 1.83, 95% CI 1.67–2.01) and Lac_{24tw} (HR 1.82, 95% CI 1.67–1.98) were risk factors for death (All P-value <0.001). Model 2 showed that each index was still strongly associated with 180-day all-cause death. When adjusted for other confounding variables in model 3, Lac_{adm}(HR 1.15 95% CI 1.04–1.26), Lac_{24max}(1.30, 95% CI 1.18–1.43), Lac_{24min} (1.48, 95% CI 1.30–1.69), Lac_{24tw}(1.46, 95% CI 1.30–1.64) and Lac_{Δ}(1.20, 95% CI 1.08–1.33) showed as an independent factor in predicting 180-day all-cause death, respectively.

Kaplan–Meier curves were constructed to further explore the discriminatory power of each lactate indices in predicting the mortality and survival among groups was compared using the Log Rank test (Figure 1). As the patients were divided into three groups according to the lactate indices, it is obvious that the patients of higher lactate indices group had higher rates of mortality (all P<0.0001, except Lac_{Δ} P=0.0485).

The Predictive Values of Lactate Indices (Lac_{adm}, Lac_{24max}, Lac_{24min}, Lac_{24TW} and Lac_{δ})

The predictive ability of lactate indices (Lac_{adm}, Lac_{24max}, Lac_{24min}, Lac_{24TW} and Lac_{Δ}) for 30-day mortality and 180-day mortality was assessed by ROC curves (Figure 2). Table 3 shows AUC of all these variables and P-values when compared to the AUC of Lac_{adm}. The Lac_{adm} was predictive of mortality and achieved AUC of 0.757 (95% CI, 0.731–0.783) for 30-day mortality and 0.751 (95% CI, 0.724–0.777) for 180-day mortality. The AUC value for

Table 1 Characteristics of Study Patients

Characteristics	All Patients	Survivors	Non-Survivors	P
N	1080	1012	68	
Lactate series index				
Lac_{adm}	2.3 (1.6–3.3)	2.3 (1.6–3.2)	4.4 (2.4–7.8)	<0.001
Lac_{24max}	2.8 (2.1–3.8)	2.7 (2.1–3.6)	5.7 (3.3–12.0)	<0.001
Lac_{24min}	1.8 (1.4–2.3)	1.7 (1.4–2.2)	2.5 (1.8–4.4)	<0.001
Lac_{24tw}	2.3 (1.8–3.0)	2.2 (1.8–2.8)	3.9 (2.4–6.2)	<0.001
Lac_{Δ}	−0.2 (−0.9–0.4)	−0.2 (−0.9–0.3)	−0.2 (−1.7–1.1)	0.963
Survival outcome				
30-Day Death	59 (5.5%)	0 (0.0%)	59 (86.8%)	<0.001
180-Day Death	68 (6.3%)	0 (0.0%)	68 (100%)	<0.001
GRACE score	163.4 ± 38.0	159.2 ± 34.0	226.2 ± 38.9	<0.001
Demographics				
Age (years)	64.4 ± 13.0	63.8 ± 13.0	73.8 ± 9.9	<0.001
Male	850 (78.7%)	813 (80.3%)	37 (54.4%)	<0.001
Medical history				
Hypertension	631 (58.4%)	584 (57.7%)	47 (69.1%)	0.065
Diabetes Mellitus	245 (22.7%)	223 (22.0%)	22 (32.4%)	0.049
Current Smoking	534 (49.4%)	517 (51.1%)	17 (25.0%)	<0.001
Current Drinking	263 (24.4%)	251 (24.8%)	12 (17.6%)	0.183
Previous MI	26 (2.4%)	25 (2.5%)	1 (1.5%)	0.603
Previous PCI	51 (4.7%)	47 (4.6%)	4 (5.9%)	0.641
Previous CABG	2 (0.2%)	1 (0.1%)	1 (1.5%)	0.011
Previous Stroke	63 (5.8%)	59 (5.8%)	4 (5.9%)	0.986
Presentation characteristics				
SBP (mmHg)	123.5 ± 22.3	124.3 ± 22.0	111.7 ± 23.0	<0.001
DBP (mmHg)	74.9 ± 14.9	75.3 ± 14.9	68.5 ± 14.3	<0.001
HR (beats/min)	82.1 ± 18.5	81.1 ± 17.7	97.4 ± 21.8	<0.001
Killip class II–IV	258 (23.9%)	206 (20.4%)	52 (76.5%)	<0.001
Laboratory tests				
AST (U/l)	250.0 (126.0–410.0)	240.5 (122.0–392.2)	369.5 (233.0–686.5)	<0.001
BNP (ng/l)	117.0 (44.8–318.8)	110.0 (40.8–288.5)	368.0 (123.2–1243.2)	<0.001
Hs-cTnI (ng/l)	43.0 (12.1–50.0)	41.1 (11.5–50.0)	50.0 (37.4–50.0)	0.011
Creatinine (mmol/l)	68.0 (57.0–85.2)	67.0 (56.0–83.0)	108.0 (75.8–160.2)	<0.001
Hemoglobin (g/l)	131.5 (119.0–143.0)	240.5 (122.0–392.2)	369.5 (233.0–686.5)	<0.001

Notes: Continuous variables are presented as mean (SD) for normally distributed variables or median (interquartile range) for non-normally distributed variables, whereas categorical variables are presented as number (percentage).

Abbreviations: Lac_{adm}, lactate at admission; Lac_{24max}, maximal lactate during 24h after admission; Lac_{24min}, minimum lactate during 24h after admission; Lac_{24tw}, time-weighted lactate during 24h after admission; Lac_{Δ}, lactate at 24h after admission minus lactate at admission; MI, myocardial infarction; PCI, percutaneous coronary intervention; CABG, coronary artery bypass grafting; SBP, systolic blood pressure; DBP, diastolic blood pressure; HR, heart rate; AST, aspartate aminotransferase; BNP, brain natriuretic peptide; Hs-cTnI, high-sensitivity troponin I.

Lac_{adm} was similar to Lac_{24min} and Lac_{24tw} (The P values for comparison were not statistically significant). Notably, Lac_{24max} had the highest AUC value (30-day 0.812, 95% CI 0.787–0.835; 180-day 0.803, 95% CI 0.778–0.826) and was significantly larger than Lac_{adm} (The comparison P values for 30-day mortality and 180-day mortality were 0.0070 and 0.0060, respectively). In addition, the predictive ability of Lac_{Δ}(30-day 0.554 and 180-day 0.518, P values for comparison were all significant) was not as good as the Lac_{adm}.

Table 2 Association of Lactate Series with the All-Cause Mortality

Variables	Model 1		Model 2		Model 3	
	Hazard Ratio (95% CI)	P value	Hazard Ratio (95% CI)	P value	Hazard Ratio (95% CI)	P value
30-day mortality						
Lac_{adm}, mmol/L	1.43 (1.34, 1.52)	<0.001	1.40 (1.30, 1.49)	<0.001	1.16 (1.05, 1.29)	0.005
Lac_{24max}, mmol/L	1.54 (1.44, 1.64)	<0.001	1.50 (1.40, 1.60)	<0.001	1.34 (1.21, 1.48)	<0.001
Lac_{24min}, mmol/L	1.83 (1.66, 2.01)	<0.001	1.73 (1.57, 1.91)	<0.001	1.46 (1.27, 1.69)	<0.001
Lac_{24tw}, mmol/L	1.83 (1.67, 1.99)	<0.001	1.72 (1.57, 1.88)	<0.001	1.47 (1.30, 1.67)	<0.001
Lac_{Δ}, mmol/L	1.07 (0.89, 1.29)	0.460	1.06 (0.89, 1.25)	0.530	1.20 (1.08, 1.34)	<0.001
180-day mortality						
Lac_{adm}, mmol/L	1.42 (1.33, 1.51)	<0.001	1.39 (1.30, 1.48)	<0.001	1.15 (1.04, 1.26)	0.005
Lac_{24max}, mmol/L	1.52 (1.43, 1.62)	<0.001	1.48 (1.39, 1.58)	<0.001	1.30 (1.18, 1.43)	<0.001
Lac_{24min}, mmol/L	1.83 (1.67, 2.01)	<0.001	1.73 (1.57, 1.91)	<0.001	1.48 (1.30, 1.69)	<0.001
Lac_{24tw}, mmol/L	1.82 (1.67, 1.98)	<0.001	1.70 (1.56, 1.85)	<0.001	1.46 (1.30, 1.64)	<0.001
Lac_{Δ}, mmol/L	1.01 (0.86, 1.18)	0.910	1.00 (0.86, 1.16)	0.986	1.20 (1.08, 1.33)	<0.001

Notes: Model 1 adjust for: None. Model 2 adjust for: gender and age. Model 3 adjust for: gender; age; current smoking; current drinking; hypertension; diabetes mellitus; prior stroke; prior myocardial infarction; prior CABG; creatinine; hemoglobin; systolic blood pressure; heart rate and Killip class at admission 2–4.
Abbreviations: PCI, prior percutaneous coronary intervention; AST, aspartate aminotransferase; BNP, brain natriuretic peptide; Hs-cTnI, high-sensitivity troponin I.

Combination of GRACE Risk Score with Lactate Indices

The incremental value of different lactate index over the GRACE score among STEMI patients is demonstrated in Figure 3 and Table 4. The AUC of GRACE score in predicting mortality for 30-day mortality and 180-day mortality were both 0.893 (95% CI 0.873–0.911). When Lac_{24max} was incorporated into the model, the predictive probability improved to 0.914 (95% CI 0.896–0.930, p =0.0112) for 30-day mortality and 0.910 (95% CI 0.-891–0.926, p =0.0281) for 180-day mortality. Interestingly, the predictive probability of 30-day mortality improved when Lac_{24tw} was incorporated into the GRACE score (0.913, 95% CI 0.894–0.929, p=0.0415) while there

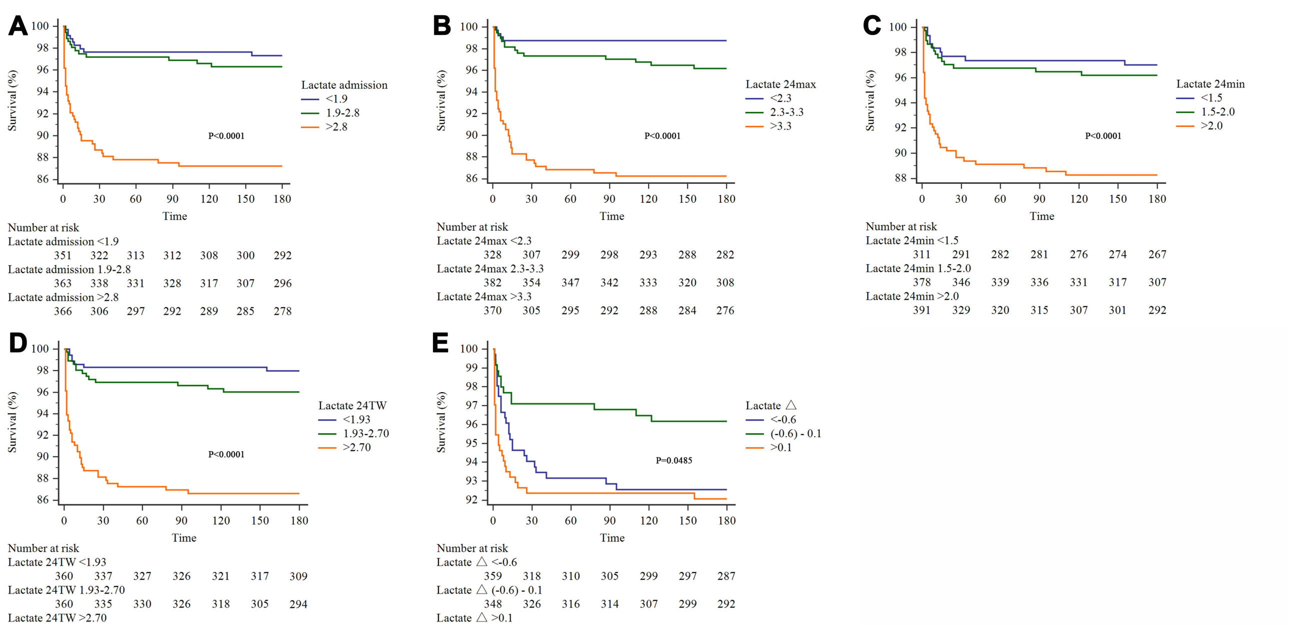

Figure 1 Kaplan–Meier survival curves of all-cause mortality according to lactate indices. Panels (**A**–**E**) Indicate Lacadm, Lac24max, Lac24min, Lac24TW and LacΔ, respectively. **Notes:** The red line, the low lactate indices; the green line, the middle lactate indices; the blue line, the high lactate indices.

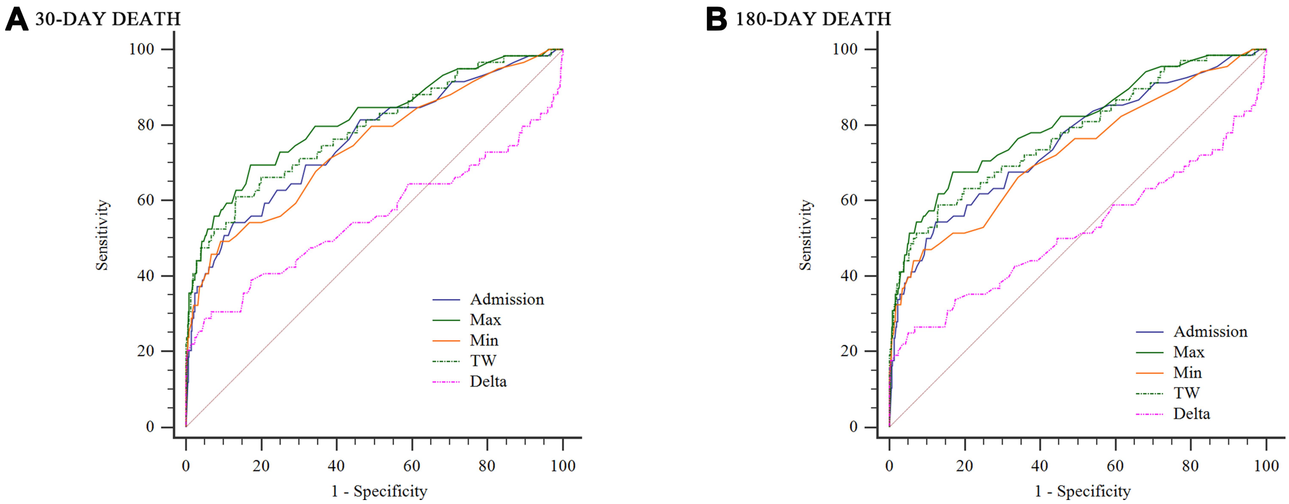

Figure 2 Receiver operating characteristic (ROC) analysis for lactate indices. Panel (**A**) is the 30-day mortality rate, and Panel (**B**) is the 180-day mortality rate.

was no such association in 180-day mortality (P=0.1098). As presented, the adding of other lactate indices to the GRACE score did not significantly enhance the prediction ability of mortality among STEMI patients.

Discussion

In this retrospective study of patients with STEMI undergoing primary PCI, we examined and compared the prognostic values of lactate indices (Lac_{adm}, Lac_{24max}, Lac_{24min}, Lac_{24TW} and Lac_{Δ}) for 30-day and 180-day mortality. The results were similar in both short-term and long-term deaths. We found that Lac_{adm}, Lac_{24max}, Lac_{24min} and Lac_{24TW} were all associated with 30-day and 180-day mortality, while Lac_{Δ} did not show the same association. For every one-unit increase in Lac_{adm}, Lac_{24max}, Lac_{24min} and Lac_{24TW}, the risk of 30-day death increased by 16%, 34%, 46% and 47% and the risk of 180-day death increased by 15%, 30%, 48%, and 46%, respectively.

In the ROC analysis, Lac_{adm} is of satisfactory predictive value with AUC more than 0.75. Among all lactate indices, Lac_{24max} shows its best predictive power and a statistically significant difference in survival compared to Lac_{adm}. However, Lac_{24min} and Lac_{24TW} were not superior in predicting mortality compared with Lac_{adm}. Furthermore, Lac_{Δ} was far less capable of predicting prognosis than Lac_{adm}. When adding lactate index to the GRACE score, only Lac_{24max} significantly enhances the prediction ability of mortality among STEMI patients undergoing primary PCI.

Many studies have demonstrated that the Lac_{adm} is a prognostic indicator in risk stratification among the diverse patient population. Among trauma patients, Lac_{adm} could identify the patients with serious injuries.[1] In patients with severe sepsis, Lac_{adm} was associated with mortality no matter whether patients were with clinically apparent organ dysfunction and shock.[2–4] What's more, Lac_{adm} has been reported may reflect inadequate tissue perfusion, so it can be an early indication of poor prognosis in patients with acute heart failure or patients after cardiac surgery.[5,6,17] Lac_{adm} is widely used in clinical critical patients and has been gradually extended to other

Table 3 The Area Under ROC Curve (AUC) for Lactate Indices

Variables	30-Day Death		180-Day Death	
	AUC (95% CI)	**P-value***	**AUC (95% CI)**	**P-value***
Lac_{adm}	0.757 (0.731–0.783)		0.751 (0.724–0.777)	
Lac_{24max}	0.812 (0.787–0.835)	0.0070	0.803 (0.778–0.826)	0.0060
Lac_{24min}	0.742 (0.715–0.768)	0.5729	0.725 (0.697–0.752)	0.3535
Lac_{24tw}	0.786 (0.760–0.810)	0.2057	0.775 (0.749–0.800)	0.2344
Lac_{Δ}	0.554 (0.523–0.584)	0.0041	0.518 (0.487–0.548)	0.0004

Note: *Compared to Lac_{adm}.

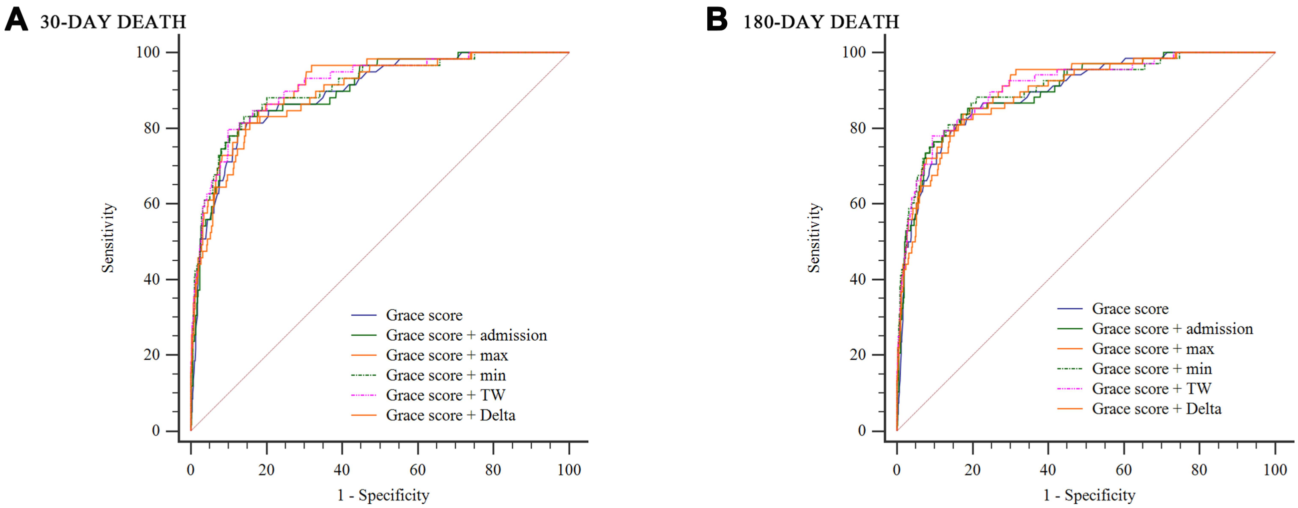

Figure 3 Receiver operating characteristic (ROC) analysis for GRACE score +lactate indices. Panel (**A**) is the 30-day mortality rate, and Panel (**B**) is the 180-day mortality rate.

populations. In patients with cirrhosis with acute kidney injury, Lac_{adm} was an excellent independent predictor of mortality.[18] A prospective cross-sectional study verified the role of Lac_{adm} in predicting pneumonia patient's mortality risk.[19] Recently, Lac_{adm} has been reported as clinically useful markers of increased risk of mortality in patients with acute coronary syndrome.[7] What's more, a previous study has shown good predictive power of admission lactate level for early mortality in patients with STEMI.[8] Our results were consistent with previous studies showing that Lac_{adm} is a good survival predictor of STEMI patients undergoing primary PCI.

Although a lot of studies have focused on the admission lactate level, some studies indicate that lactate concentration changed in early time after admission may be useful in stratifying patients with higher death risk.[9–11] It makes sense that both the magnitude and the duration of lactate derangement act on the prognosis of patients. Our results support this view for that Lac_{24TW} is closely related to survival outcomes. However, we did not find the superiority of dynamic lactate measures (Lac_{24TW} or Lac_{Δ}) over static lactate measures (Lac_{adm}) in helping to identify patients at higher risk of death. This phenomenon has also been mentioned in the previous study that individual dynamic measures did not outperform the currently used static measures of lactate.[11]

To speak of, the peak of blood lactate is a very powerful indicator to predicts mortality.[20–22] In our study, Lac_{24max} has been shown to be an independent predictor of both short-term and long-term mortality and superior to Lac_{adm} according to the comparison results of ROC. A retrospective study put forward that a score consists of lactate and the qSOFA perform better than the qSOFA alone in predicting mortality.[23] Similarly, we found that Lac_{24max} significantly enhances the ability of risk stratification and prognostic evaluation among STEMI patients undergoing primary PCI when adding Lac_{24max} to the GRACE score. Grace score is a score composed of many indicators but not including any lactate index, which is widely used in mortality risk prediction.[14] Indeed, the

Table 4 The Area Under ROC Curve (AUC) for GRACE Score + Lactate Index

Variables	30-Day Death		180-Day Death	
	AUC (95% CI)	P-value*	AUC (95% CI)	P-value*
GRACE score	0.893 (0.873–0.911)		0.893 (0.873–0.911)	
$+Lac_{adm}$	0.899 (0.880–0.917)	0.0756	0.898 (0.878–0.915)	0.1450
$+Lac_{24max}$	0.914 (0.896–0.930)	0.0112	0.910 (0.891–0.926)	0.0281
$+Lac_{24min}$	0.906 (0.888–0.923)	0.0855	0.903 (0.884–0.920)	0.1781
$+Lac_{24tw}$	0.913 (0.894–0.929)	0.0415	0.907 (0.888–0.924)	0.1098
$+Lac_{\Delta}$	0.890 (0.870–0.908)	0.7413	0.891 (0.871–0.909)	0.7387

Note: *Compared to GRACE score.

combination of Lac_{adm} and GRACE score was not superior to the original GRACE score in our study, which may be the reason why the lactate was not initially included in the GRACE score when originally created. To our knowledge, this study is the first to propose a combination of Lac_{24max} and grace score to predict the risk of death for STEMI patients.

According to previous studies, lactate is a stable indicator that can be used to predict both short-term and long-term mortality. The similar results in our study confirmed this standpoint and filled in the data gaps for the prediction of short-term and long-term mortality of lactate index in STEMI patients with primary PCI. This study brings a novel perspective to the role of lactate monitoring, especially focused on the peak of lactate (Lac_{24max}) in 24 hours after admission.

Several limitations of this study deserve consideration as well. First of all, despite routinely measuring lactate for each patient at admission, there was no predefined interval between the acquisitions of lactate after admission. Therefore, we did not calculate the value of lactate clearance, which is known as a predictor of mortality in critically ill patients.[24] However, there are two reasons not to calculate this indicator. One is that the previous study mentioned that lactate clearance was only useful in patients with hyperlactatemia and the patients included in this study were not all with hyperlactatemia.[25] The other is that some studies reported that lactate clearance may not superior to initial lactate in predicting mortality. Second, doctors may perform more frequent lactate tests on patients with poor situations, resulting in selection bias, leading to more lactate samples for patients with higher mortality. Furthermore, this retrospective study is based on a single-center cohort, which limits the generalization of the findings. Thus, further studies are needed to determine whether our findings can be accurately applied to these patients.

Conclusions

In patients with STEMI undergoing primary PCI, Lac_{adm}, Lac_{24max}, Lac_{24min} and Lac_{24TW} are all associated with 30-day and 180-day mortality, while Lac_{Δ} do not show the same association. In prediction of both 30-day and 180-day mortality, Lac_{24max} is superior to Lac_{adm} and significantly enhances the ability of risk stratification and prognostic evaluation when adding Lac_{24max} to the GRACE score.

Abbreviations

ACS, acute coronary syndrome; CCU, coronary care unit; ROC, receiver operator characteristic; HRs, hazard ratios; Lac_{adm}, lactate at admission; Lac_{24max}, maximal lactate during 24 h after admission; Lac_{24min}, minimum lactate during 24 h after admission; Lac_{24tw}, time-weighted lactate during 24 h after admission; Lac_{Δ}, lactate at 24 h after admission minus lactate at admission; MI, myocardial infarction; PCI, percutaneous coronary intervention; CABG, coronary artery bypass grafting; SBP, systolic blood pressure; DBP, diastolic blood pressure; HR, heart rate; AST, aspartate aminotransferase; BNP, brain natriuretic peptide; Hs-cTnI, high-sensitivity troponin I.

Ethical Statement

This article is a clinical retrospective article. All patient data is guaranteed to be anonymous or confidential.

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Disclosure

The authors state that they have no conflicts of interest.

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