




ORIGINAL STUDIES

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The prognostic value of initial serum lactate for survival in postcardiac arrest patients undergoing cardiac catheterization

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Abstract

Objectives: We sought to investigate the prognostic value of serum lactate on survival in patients postcardiac arrest.

Background: Patients who experience cardiac arrest, in- or out-of-hospital, may have a poor outcome. Initial electrocardiograms may suggest ischemia as an underlying cause and urgent referral for catheterization occurs. It remains unclear which of these patients may suffer a poor outcome.

Methods: We retrospectively reviewed all patients at our institution taken for urgent catheterization after cardiac arrest between January 2014 and September 2018. Three hundred and eighty four patients were referred urgently to the cath lab during this period, 50 with prior arrest.

Results: Sixty six percent underwent coronary intervention. The mean age of the entire cohort was 57 years. Thirty four percent were female, 40% had a history of coronary artery disease, and 94% were intubated at the time of cardiac catheterization. Overall survival to discharge was 40%. Survival in patients who underwent coronary intervention compared with those who did not was similar (45.5 vs. 29.4%, $p = .27$). Mean lactate level in survivors versus nonsurvivors was 4.7 ± 3.8 and 9.8 ± 4.7 mmol/L, respectively ($p < .05$). When divided into tertiles by serum lactate (< 4.5 , $4.5-9$, 9 mmol/L), survival to discharge was 75, 29.4, and 17.6%, respectively ($p < .05$). Initial serum lactate and age were independent predictors of in-hospital mortality.

Conclusions: In patients undergoing cardiac catheterization following cardiac arrest, routine measurement of serum lactate is a useful and available laboratory test that may help identify patients at risk for a poor outcome.

KEYWORDS

in-hospital cardiac arrest, lactic acid, out-of-hospital cardiac arrest, resuscitation

1 | INTRODUCTION

Cardiac arrest remains the leading cause of death in the United States, with approximately 350,000 individuals suffering out-of-hospital cardiac arrest (OHCA) and 210,000 in-hospital cardiac arrest (IHCA) annually.¹ Recent advances in early intervention with automated defibrillators^{2,3} and therapeutic hypothermia after resuscitation^{4,5} have improved survival rates after cardiac arrest, but despite these improvements reported survival to discharge in out-of-hospital cardiac is 9.6%.⁶

Initial electrocardiogram (ECG) postcardiac arrest may suggest myocardial ischemia as a potential precipitating factor. In the absence of ST-segment elevation, interpretation of the initial ECG is often confounded by the effects of prolonged resuscitation, including acidosis or electrolyte abnormalities.⁷ While several studies have demonstrated improved survival with routine cardiac catheterization (cath) in all-comers post-arrest patients,^{8,9} it remains difficult to reliably predict which of these patients are destined to experience a poor outcome. This is particularly true in those patients who may potentially have anoxic brain injury. Therefore, a reliable, rapidly available, and easily reproducible test is needed to help better risk stratify those patients who undergo urgent catheterization immediately following cardiac arrest.

Serum lactate has been used as a surrogate for tissue perfusion in the postarrest period, and has been demonstrated to be a stronger predictor of outcome after cardiac arrest than time to return of spontaneous circulation.^{10,11} Effective lactate clearance has also been associated with decreased mortality.¹²⁻¹⁴ We sought to investigate the utility of initial serum lactate as a predictor of outcome in the post-arrest patient when management strategy incorporates urgent cardiac catheterization.

2 | MATERIALS AND METHODS

2.1 | Patient selection

This study was a single center retrospective study. We identified all adult (age ≥ 18) patients for whom there was either a ST-elevation myocardial infarction (STEMI) or urgent activation of the cardiac catheterization lab between January 1, 2014 and October 1, 2018, further limiting our cohort to those who suffered an immediately preceding OHCA or IHCA. The decision to urgently take the patient to the cath lab was at the discretion of the operator on call at the time. Patients who had cardiopulmonary resuscitation (CPR) with return of spontaneous circulation (ROSC) prior to cardiac catheterization were included, irrespective of their level of consciousness. Patients who did not have serum lactate drawn prior to cardiac catheterization were excluded. The study was approved by the Temple University (IRB), and informed consent waived due to the retrospective nature of this study.

2.2 | Data collection

Data were abstracted from the electronic medical record. Baseline demographic characteristics were recorded as well as initial cardiac

arrest rhythm, left ventricular ejection fraction, in-hospital versus out-of-hospital arrest, and outside-hospital transfer status. The use of therapeutic hypothermia, cardiac catheterization data including time to device, type of intervention, culprit vessel and number of culprit lesions, presence of nonculprit disease, use of mechanical circulatory support (MCS), and intracatheterization CPR were also recorded. Culprit lesion was defined as the lesion felt to be involved in the initial acute myocardial infarction and subsequent cardiac arrest. Time to device for OHCA was conventional door to device time; for IHCA this was defined as the time from urgent cath lab activation to device deployment. In-hospital mortality, as well as cause of death, were noted. Initial serum lactate level was drawn after the arrest in either the emergency room or the cardiac cath lab, prior to catheterization.

3 | STATISTICAL ANALYSIS

The primary outcome measure was in-hospital mortality, defined as death from any cause during the index hospitalization. Secondary endpoints were effect of potential predictors on in-hospital mortality. We performed univariate logistic regression on initial serum lactate—defined as first lactate drawn after ROSC—as well as previously documented predictors of outcome including age, cardiac arrest setting, initial rhythm, type of intervention, and left ventricular ejection fraction. On the basis on univariate regression, we performed multivariate logistic regression with forward selection to identify predictors and evaluate their impact on in-hospital mortality.

To assess the ability of lactate to predict mortality, we created the receiver operating characteristic (ROC) curve and calculated the area under the curve (AUC) using serum lactate and in-hospital mortality as the test and state variables, respectively. In a separate analysis, patients were divided into three tertiles based on initial serum lactate (< 4.5 , $4.5-9$, and > 9 mmol/L).

384: Patients referred for urgent cardiac catheterization between January 2014 and September 2018

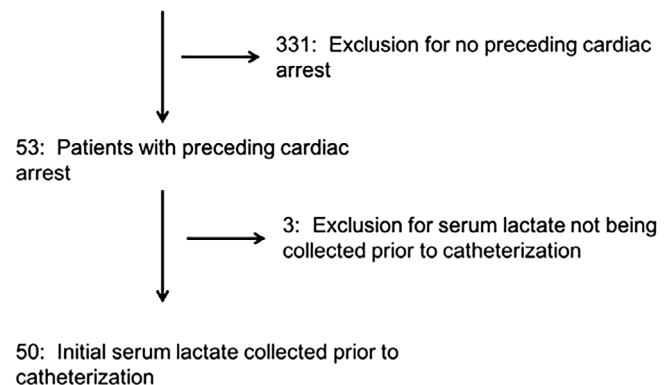


FIGURE 1 Identification of study population using single center patient cohort. Data are *n* patients at each phase of inclusion and exclusion

	Total (n = 50)	Survivors (n = 20)	Nonsurvivors (n = 30)	p value
Mean age, years	57 ± 12	54 ± 10	58 ± 13	.18
Female	17 (34)	9 (45)	8 (27)	.23
Race				
White	13 (26)	5 (25)	8 (27)	.9
Black	24 (48)	11 (55)	13 (43)	.42
Other	13 (26)	4 (20)	9 (30)	.43
BMI, kg/m ²	29.5 ± 5.8	30.2 ± 6.6	29.0 ± 5.2	.50
Medical history				
Diabetes	15 (30)	6 (30)	9 (30)	1.00
Hypertension	32 (64)	13 (65)	19 (63)	.76
Current smoker	19 (38)	10 (50)	9 (30)	.24
Previous stroke	9 (18)	3 (15)	6 (20)	.72
Previous MI	3 (6)	0 (0)	3 (10)	.27
CAD	19 (38)	7 (35)	12 (41)	.77
CHF	7 (14)	1 (5)	6 (20)	.22
Prior PCI	7 (14)	4 (20)	3 (10)	.42
Intubation at Cath	47 (94)	17 (85)	30 (100)	.06
Cardiac arrest setting				
				.04*
OHCA	38 (76)	12 (60)	26 (87)	
IHCA	12 (24)	8 (40)	4 (13)	
Shockable rhythm	42 (84)	18 (90)	24 (83)	.69

TABLE 1 Baseline characteristics of patients

Note: Data are n (%) or mean ± SD.

Abbreviations: BMI, body mass index; CAD, coronary artery disease; CHF, congestive heart failure; IHCA, in-hospital cardiac arrest; MI, myocardial infarction; OHCA, out-of-hospital cardiac arrest; PCI, percutaneous coronary intervention.

* $p < .05$.

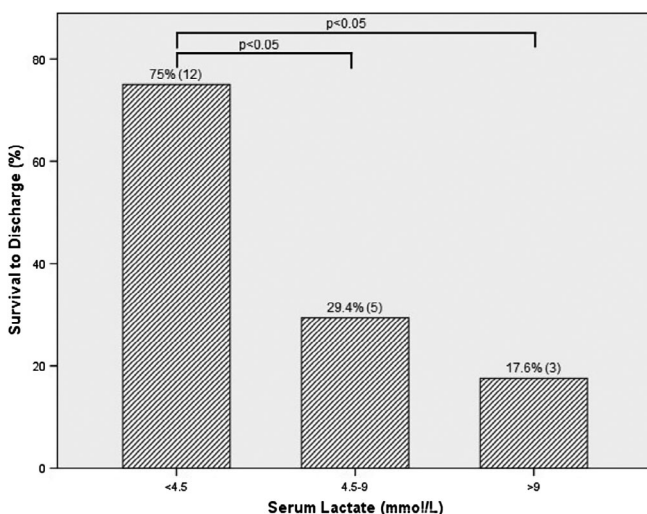


FIGURE 2 Tertiles of initial serum lactate. Data are percentage survival (n) within each tertile. Significant differences were found between the first tertile (lactate < 4.5) with both the second (lactate 4.5-9) and third (lactate >9) tertiles

Categorical variables were presented as number (percentage) and continuous variables as mean ± SD. Differences in categorical variables were evaluated using Chi-square tests, and those in continuous

variables were evaluated using t tests. Data from univariate analysis were presented as odds ratio (OR) with 95% confidence intervals (CIs). Data from the multivariate analysis were presented as adjusted odds ratio (aOR) with 95% CI. Analyses were performed using statistical package for social sciences for Windows, version 22.0. All statistical tests were performed at a two-tailed significance level of .05.

4 | RESULTS

A total of 384 patients underwent cardiac catheterization for STEMI or other urgent cardiac condition during the study period, 53 of whom suffered an immediately preceding cardiac arrest. There were a total of 805 OHCA and 2,278 IHCA over that study period. Three patients who did not have initial serum lactate drawn were excluded (Figure 1). Patients were divided into two groups, survivors versus nonsurvivors. Baseline characteristics for these patients are shown in Table 1. Patients in both groups had similar age and risk factors for coronary artery disease including diabetes and hypertension. More than 90% of the overall patients were intubated at the time of cardiac catheterization. Shockable rhythm was present in 84% of participants, and 56% underwent therapeutic hypothermia. Rates of coronary intervention, culprit vessel, door to balloon times, and percentage of patients who were transferred from another hospital were

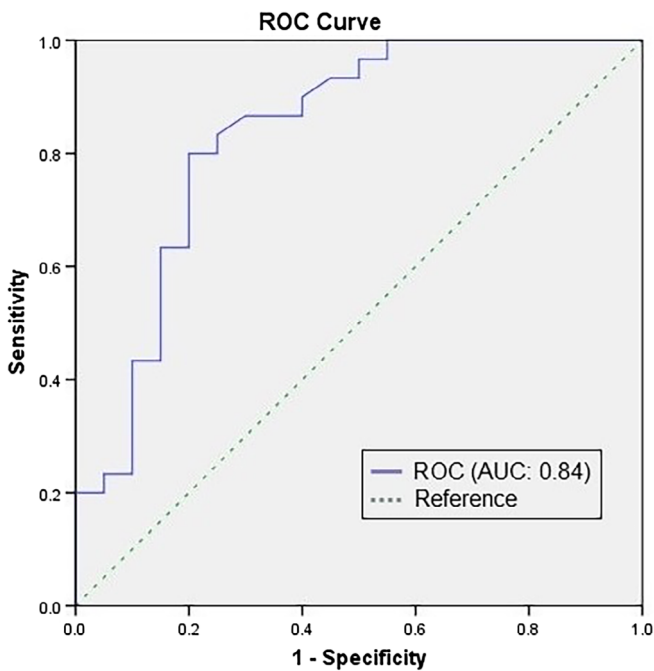


FIGURE 3 ROC curve generated using initial serum lactate and in-hospital mortality as test and state variables, respectively. Blue line represents the ROC curve with an AUC of 0.84 (95% CI: 0.73–0.96, $p < .01$). Green line represents the line of no discrimination. AUC, area under the curve; CI, confidence interval; ROC, receiver operating characteristic [Color figure can be viewed at wileyonlinelibrary.com]

similar between groups. Significantly more nonsurvivors suffered OHCA than IHCA compared to the survivors, (87 vs. 60%, respectively, $p = .04$). Overall survival to discharge was 40%. Primary causes of death were cardiogenic shock (30%), cardiac arrest (26.7%), and anoxic brain injury (20%).

Survivors had lower initial serum lactate than nonsurvivors (4.7 ± 3.8 vs. 9.8 ± 4.7 mmol/L, $p < .01$). When divided into tertiles of < 4.5 , 4.5 – 9 , and > 9 mmol/L serum lactate, survival to discharge was 75, 29.4, and 17.6%, respectively ($p < .05$) (Figure 2).

The AUC calculated for the ROC curve was 0.84 (0.73–0.96, $p < .01$) (Figure 3). Using lactate of 4.55 mmol/L as the cutoff value of the test, the sensitivity was 87% and specificity was 60%. At the level of 6.55 mmol/L, the sensitivity was 80% and specificity was 80%. At 9.45 mmol/L, the sensitivity was 43% and specificity was 85%.

In the initial analysis, lactate on admission and cardiac arrest setting (outside-hospital cardiac arrest) were the only two variables with statistical significance with at least one observation in both groups (Table 2). The OR associated with lactate on admission was 1.39 (1.13–1.71), and that of arrest setting 4.33 (1.09–17.25). On the basis of univariate regression, we performed multivariate logistic regression with the variables evaluated including lactate on admission, and arrest setting, age, sex, shockable rhythm, type of coronary intervention, and ejection fraction (Table 3). After forward selection, age and initial serum lactate were the only variables included in the model. The aOR associated with age was 1.09 (1.01–1.17), and that of lactate on admission was 1.56 (1.19–2.05).

5 | DISCUSSION

Patients with cardiac arrest, whether occurring in- or out-of-hospital have poor survival. ECG abnormalities suggesting ischemia are common in the immediate postarrest period and may or may not be due to active ischemia precipitating the arrest. In addition, a percentage of these patients may have anoxic brain injury and are unlikely to benefit from revascularization. Several important trends emerge from our registry.

We observed baseline lactate to be an independent predictor of survival. Previous studies have evaluated the impact of lactate on all comers with cardiac arrest.^{10–16} However, the prognostic value of lactate in patients who undergo urgent catheterization post-arrest to our knowledge has not been reported. Within our cohort, two important groups emerged, those with lactate greater than 9 and less than 4.5. Despite early invasive angiography and intervention when indicated, patients with a baseline lactate greater than 9 mmol/L continued to have a high mortality. It is imperative to note that despite markedly elevated lactate, these patients can still survive and catheterization did not necessarily represent futile care. The high lactate level is likely a result of multiple peri-arrest factors, but may represent more severe systemic tissue hypoxia and coronary reperfusion would not completely eliminate this initial insult. Conversely, those with low serum lactate, < 4.5 mmol/L, were significantly more likely to survive to discharge. This is similar to previously published studies suggesting that serum lactate and lactate clearance are inversely proportional to survival after cardiac arrest.^{10,12,14–16} Donnino et al¹³ reported that initial serum lactate was no different between survivors and nonsurvivors of cardiac arrest, but overall lactate values in both groups were significantly higher than those in this study, suggesting a sicker overall population.

Patients in the nonsurvivor group were more likely to have an OHCA, despite similar time to device and shockable rhythm in both groups. Our data are similar for all comers who have a cardiac arrest while hospitalized versus those which occur outside of a hospital setting.¹⁷ CPR with or without rescue breaths continues to remain an important intervention to improve survival for those patients who suffer out of hospital cardiac arrest.¹⁸

Anoxic brain injury (ABI) was the cause of death in 20% of patients in our cohort. While recommendations for emergent cardiac catheterization in those with electrocardiographic evidence of an ischemic etiology are well established,^{19,20} initial neurologic assessment in patients post-arrest is challenging, as the majority—such as in our cohort—are intubated and sedated. It is no surprise that previous studies have described a bias in providers' willingness to take post-arrest patients for catheterization based on known predictors of positive outcome such as neurologic status or presenting rhythm.²¹ Recommendations for formal brain death assessment in comatose survivors of cardiac arrest mandate performance of brain death testing occur at least 72 hr after arrest.²² This is far beyond the time period of salvageable myocardium, particularly in those patients who present with STEMI. Recent evidence from the coronary angiography after cardiac arrest without ST-segment elevation trial showed similar

TABLE 2 Procedural characteristics

	Total (n = 50)	Survivors (n = 20)	Nonsurvivors (n = 30)	p value
Number of culprit lesion				
0	14 (28)	3 (15)	11 (37)	
1	33 (66)	16 (80)	17 (57)	
2	1 (2)	0 (0)	1 (3)	
3	2 (4)	1 (5)	1 (3)	.29
Culprit vessel				
LAD	17 (34)	8 (40)	9 (30)	.55
Cx	11 (22)	7 (35)	4 (13)	.09
RCA	9 (18)	3 (15)	6 (20)	.72
Left main	2 (4)	1 (5)	1 (3)	1.00
Ramus intermedius	2 (4)	0 (0)	2 (7)	.51
PCI status				
Coronary intervention performed	33 (66)	15 (75)	18 (60)	
No intervention	17 (34)	5 (25)	12 (40)	
Type of intervention				
Stent	28 (56)	12 (60)	16 (53)	.77
Balloon	27 (54)	11 (55)	16 (53)	1.00
Thrombectomy	23 (46)	11 (55)	12 (40)	.39
Time to device, minutes	108 ± 63	90 ± 51	123 ± 69	.16
CPR in Cath lab	5 (10)	0 (0)	5 (17)	.08
Transferred from outside hospital	6 (12)	2 (10)	4 (14)	1.00
Support device used				
No device used	30 (60)	15 (75)	15 (50)	.14
IABP	10 (20)	5 (25)	5 (17)	.49
Impella	10 (20)	0 (0)	10 (33)	< .01*
ECMO	4 (8)	0 (0)	4 (13)	.14
Ejection fraction, %	32.4 ± 19.6	38.8 ± 18.8	27.8 ± 19.1	.06
Therapeutic hypothermia	28 (56)	8 (40)	20 (67)	.09
Initial serum lactate	7.8 ± 5.0	4.7 ± 3.8	9.8 ± 4.7	< .01*

Note: Data are n (%) or mean ± SD.

Abbreviations: CPR, cardiopulmonary resuscitation; Cx, circumflex; ECMO, extracorporeal membrane oxygenation; IABP, intra-aortic balloon pump; LAD, left anterior descending; PCI, percutaneous coronary intervention; RCA, right coronary artery.

* $p \leq .05$.

	Odds ratio	p value	Adjusted odds ratio	p value
Age	1.04 (0.99–1.10)	.17	1.09 (1.01–1.17)	.03*
Initial serum lactate	1.39 (1.13–1.71)	<.01*	1.56 (1.19–2.05)	<.01*
Male	2.25 (0.68–7.44)	.18		
Shockable rhythm	0.53 (0.10–3.07)	.48		
Type of coronary intervention				
Balloon	0.94 (0.30–2.91)	.91		
Stent	0.76 (0.24–2.40)	.64		
Thrombectomy	0.55 (0.17–1.71)	.30		
OHCA	4.33 (1.09–17.25)	.04*		
Ejection fraction	0.97 (0.939–1.00)	.06		

Note: Data are n (%) or mean ± SD.

Abbreviations: OHCA, out-of-hospital cardiac arrest.

* $p \leq .05$.

TABLE 3 Univariate and multivariate analysis of predictors of in-hospital mortality

90-day outcomes in patients undergoing immediate versus delayed angiography.²³ Hence, in patients with suspected ABI and elevated lactate, a deferred catheterization strategy may be appropriate, to await neurologic recovery.

Two important but not-statistically significant trends emerge from our data. There was a nonsignificant but considerable difference in time to device between survivors and nonsurvivors, indicating that longer delays to coronary angiography decrease survival. The highest cause of death in this cohort died from cardiogenic shock and likely represents those most likely to benefit from early revascularization. We also demonstrate a trend toward greater usage of MCS devices in patients who did not survive. Previous studies have demonstrated improved outcomes in IHCA^{24,25} and OHCA²⁶ when MCS is used. Caution should be exercised with associating higher mortality and MCS use in this small study. One possible explanation for this difference is that use of mechanical support may have been a marker for patients who were sicker, as there was a nonsignificant trend toward higher rates of CPR in the cath lab and lower ejection fraction in the nonsurvivor population. Further research into the role of mechanical support in patients with cardiac arrest in the form of randomized trials is therefore warranted.

Our study had several limitations. This is a retrospective observational study, and patients suffering both IHCA and OHCA are a heterogeneous group. We controlled for variables that are known to be associated with survival after cardiac arrest, but it is possible unmeasured confounders influenced our results. Measurement of lactate was not part of the postarrest protocol, and was left to the discretion of the treating provider. Therefore, the rapidity of lactate collection after ROSC may have varied. Despite this, only three patients were excluded from our cohort due to a failure to collect of initial serum lactate. Some parameters not included in our study were time from arrest to both ROSC and initial serum lactate due to lack of reliable arrest time documentation for the majority of our cohort. We did not include initial neurologic status—although we did not exclude any participant based on their initial neurologic status—and did not include any neurologic outcome data due to our inability to reliably define their discharge neurologic status in this retrospective cohort analysis.

6 | CONCLUSION

Patients that present with IHCA or OHCA are challenging to manage, particularly as many of them have electrocardiographic abnormalities, which may or may not be associated with coronary artery disease prompting referral for cardiac catheterization. Elevation of serum lactate, as demonstrated in this small, single-center study, may help stratify those patients who are at risk of a poor outcome and help determine the timing of cardiac catheterization.

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