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Original Article

Lactate measurements accurately predicts 1-week mortality in emergency department patients with acute kidney injury

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ABSTRACT

Background: Studies on prognostic indicators in patients with acute kidney injury are limited. This study investigated 1-week mortality, laboratory and clinical parameters according to the lactate levels in patients with acute kidney injury.

Methods: In this cross-sectional study, we compared the lactate levels on admission and follow-up in emergency department with vital findings, laboratory parameters, and 1-week mortality.

Results: Data of 3375 patients examined; 2681 patients excluded and 694 patients were included. Median lactate level on admission was 1.6 (1.1–2.5) mmol/L for patients who discharged from emergency department, 2.2 (1.3–3.4) mmol/L for patients admitted to the hospital wards, 3.7 (1.7–7.2) mmol/L for patients admitted to the intensive care unit and 4.4 (2.4–8.0) mmol/L for patients with mortality within 1-week of ED presentation. Mortality was 30.4% in patients with high lactate levels and 8.1% in patients with normal lactate levels on admission. ($p < 0.001$, odds ratio 5.0, 95% CI 3.2–7.7) Elevated lactate level was independent risk factor for 1-week-mortality. ($p < 0.001$, odds ratio 1.138, 95% CI 1.067–1.214) Patients with high lactate levels have low systolic blood pressure, diastolic blood pressure, oxygen saturation, pH, base deficit, and bicarbonate, and higher heart rate and respiratory rate. The mortality of patients with normal lactate levels on admission was 8.1%, while mortality rate increased to 19% if elevated lactate levels observed during emergency department follow-up.

Conclusions: Elevated lactate level predicts 1-week mortality in patients presenting with acute kidney injury in emergency department. Elevated lactate level were associated with poorer vital signs and abnormal laboratory results.

1. Introduction

Acute kidney injury (AKI) is one of the major cause of admission to the emergency department (ED) and it constitutes approximately 5.5% of all admission. The 30-day mortality of AKI was found to be up to 12%, in a large ED based cohort study.[1]

There is no high-risk criteria or decision rules for predicting the short-term mortality in patients with AKI. It was shown that elevated lactate levels associated with higher mortality in patients with shock, trauma, sepsis, and postcardiac arrest however, it was not studied in patients with AKI, extensively.[2–5]

The primary outcome of the study is to examine the association between lactate levels, measured during initial ED admission and follow-up in ED, and 1-week mortality in patients presenting with AKI. The secondary outcome is to reveal the relationship between lactate level and vital signs on ED admission and laboratory parameters including pH, bicarbonate, base excess (BE), creatinine, and potassium levels.

2. Methods

This is a retrospective cross-sectional study conducted at the Dokuz Eylül University, Department of Emergency Medicine between July 2016 and July 2017. Patients aged over 18 years who had the creatinine level higher than 1.2 mg/dL and increase more than 50% of the previously measured creatinine level, which is known or presumed to have occurred within the prior 7 days, and had an arterial or venous blood sample taken for lactate measurement were included in the study.

In our emergency medicine practice, in patients with AKI we routinely screen for pH, base excess (BE), and HCO_3 with blood gas

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analysis, so in this way lactate levels also measured. An arterial or venous blood sample taken for lactate measurement within few hours after ED admission. The highest lactate level was recorded as peak lactate level if there was a more than once measurement during ED follow-up. The exclusion criteria were as follows[1]: patients with chronic renal failure who received continuous renal replacement therapy[2]; patients whose laboratory data were missing[3]; patients who had a creatinine level of over 1.2 mg/dL but had an increase less than 50% of the previously measured creatinine level[4]; patients without prior creatinine measurement within prior last 7 days.

The demographic characteristics, vital signs, laboratory results, and clinical outcomes of the patients were screened in the electronic information management system and processed in the data recording form. The information about the mortality of patients who were referred another hospital or discharged to the home was obtained via the "national death notification system."

Lactate, bicarbonate, BE, and pH were measured with arterial or venous blood samples using a blood gas analyzer (Radiometer ABL800 basic instrument®), and the serum creatinine, blood urea nitrogen (BUN), and potassium were measured with venous blood samples using a Beckman Coulter AU5800 instrument®.

The lactate levels of the patients were divided into two groups, less than and more than 2.5 mmol/L, according to the cutoff value for our laboratory. Lactate levels compared with 1-week mortality, vital signs on admission and initial laboratory parameters. The study was started after the approval of the Local Ethics Committee.

2.1. Data analysis

The data recorded in the standard program "Statistical Package for Social Sciences for Windows 22.0." The Kolmogorov–Smirnov test was used for assessment of the homogeneity of variables. The continuous variables presented as median with IQR because of the abnormal distribution. The Mann Whitney *U* test and the chi-square test used to compare the continuous and categorical variables respectively. The variables with p value > 0.2 in univariate analysis were used in the multivariate logistic regression model for 1-week mortality. The Spearman test used for assessment of correlation between significant varibales for 1-week mortality. The Hosmer-Lemeshow test used for goodness of fit for logistic regression models and p value > 0.05 accepted as a fit for logistic regression model. P value < 0.05 were considered significant.

3. Results

3375 patients admitted to the ED with a creatinine level more than 1.2 mg/dL and whose lactate level was measured were screened. 2277 patients were excluded because of their creatinine level did not increase by 50% compared with previous creatinine level, the patients on the hemodialysis program (evaluated as chronic renal failure), the patients have no prior creatinine measurement and 6 patients were excluded because of laboratory data were missing. As a result, 694 patients were included in the study, 58.4% (n = 405) of were male and the median age was 74.0 (64.8–83.0) years. 354 of (51%) patients were discharged from the ED, 139 (20%) of were still in hospital ward at the end of 1-week, 84 (12.1%) of were still in the intensive care unit, and 117 of (16.9%) died. The median duration from ED admission to the first lactate measurement was 13 min (IQR 6–73.2), and the time from ED admission to peak lactate measurement was 506 min (IQR 252–936).

3.1. Outcomes according to lactate levels

The median lactate level was 2.5 (1.4–4.4) mmol/L in all patients, 1.6 (1.1–2.5) mmol/L in patients discharged from ED, 2.2 (1.3–3.4) mmol/L in the patients admitted to hospital ward, 3.7 (1.7–7.2) mmol/L in patients admitted to intensive care unit, and 4.4 (2.4–8.0) mmol/L in patients with 1 week mortality. The median lactate level was 1.8 (1.2–3.1) for survivors and 4.4 (2.4–8.0) mmol/L for non-survivors. (p < 0.001; 95% CI 2.73–5.06) Patients with a lactate level more than 2.5 mmol/L had a higher mortality rate than those with a normal lactate level on admission. (30.4% vs 8.1%; p < 0.001; OR 5.0; 95% CI 3.2–7.7) 1-week mortality was 7% (OR 1) for patients with lactate level < 2 mmol/L, 14.4% (OR 2.2, 95% CI 1.3–4) for patients with lactate level 2–4 mmol/L, 27.5% for patients with lactate level 4–6 mmol/L (OR 5, 95% CI 2.6–9.7), and 51.2% (OR 14, 95% CI 7.6–25.5) for patients with lactate level > 6 mmol/L.

Table 1
Vital signs and laboratory data of the patients according to the initial lactate levels.

	Lactate level		*p value*
	≤2.5 mmol/L Median (IQR)	> 2.5 mmol/L Median (IQR)	
Systolic blood pressure (mmHg)	126 (110–130)	117 (95–126)	< 0.001
Diastolic blood pressure (mmHg)	78 (65–82)	72 (60–82)	0.001
Pulse rate (beat/min)	82 (81–97)	94 (82–116)	< 0.001
Respiratory rate (breath/min)	16 (16–21.8)	16 (16–24)	0.009
Oxygen saturation (%)	97 (93–98)	95 (90–98)	< 0.001
Creatinine (mg/dL)	1.8 (1.5–2.3)	1.7 (1.5–2)	0.016
Blood urea nitrogen (mg/dL)	45.5 (30.1–69.7)	47.6 (34.0–68.6)	0.377
Potassium (mEq/L)	4.3 (3.9–4.9)	4.5 (3.9–5)	0.682
Sodium (mEq/L)	136 (133–140)	136.5 (131–142)	0.522
pH	7.39 (7.34–7.44)	7.36 (7.29–7.42)	< 0.001
Base excess (mEq/L)	−2.6 ([-5.8]-0.7)	−5.9 ([-9.9]-[-1.2])	< 0.001
HCO_3 (mEq/L)	22 (19.6–24.7)	19.2 (16.2–22.7)	< 0.001

Vital signs/laboratory data and clinical outcomes according to lactate levels shown in Table 1 and Table 2. Baseline characteristics of patients according to the 1-week mortality in univariate analysis shown in Table 3. Diastolic blood pressure, BE and HCO_3 did not included into logistic regression model because of the significant correlation (r > 0.6) with other variables. The final model with 10 variables found to be fit for multivariate analysis. (p = 0.354) Multivariate analysis revealed that advanced age, female sex, low systolic blood pressure and elevated lactate levels were the independent risk factors for 1-week mortality (Table 4).

In 387 (55.7%) patients, serial lactate levels had been measured during the ED follow-up. Median lactate level of the patients on admission was 2.5 (1.4–4.4) mmol/L, whereas the median of highest lactate level was 2.3 (1.5–3.9) mmol/L on ED follow-up. The mortality rate of patients with normal lactate levels (< 2.5 mmol/L) on admission was 8.1%, while in this group the mortality rate was 19% in patients with elevated lactate levels during ED follow-up. The mortality rate of patients with elevated lactate levels on admission was 30.4%, while in this group the mortality rate of patients who had normalized lactate levels during ED follow-up was 5.7%. 1-week mortality of patients

Table 2
Clinical outcomes of the patients according to the initial lactate levels.

Outcomes	≤2.5 mmol/L *n* (%)	> 2.5 mmol/L *n* (%)
Survivors	387 (91.9)	190 (69.6)
Discharged from ED	274 (70.8)	80 (42.1)
Admitted to hospital	82 (21.2)	57 (30)
Admitted to ICU	31 (8)	53 (27.9)
Non survivors	34 (8.1)	83 (30.4)
Odds ratio (95% CI) for 1 week mortality	1 (reference)	5.0 (3.2–7.7)

ED, Emergency Department; ICU, Intensive Care Unit.

Table 3
Univariate analysis of baseline characteristics of patients according to the 1-week mortality.

Variables	Survivors Median (IQR)	Nonsurvivors Median (IQR)	OR	95% CI	p value
Sex[a] (Male/Female)	346 (85.4)/231 (79.9)	59 (14.6)/58 (20.1)	1.472	0.988–2.194	0.057
Age (years)	74 (64–83)	78 (68–85)	1.015	1.000–1.030	0.056
Systolic blood pressure (mmHg)	126 (111–134)	106 (89–131)	0.979	0.971–0.987	< 0.001
Diastolic blood pressure (mmHg)	82 (70–82)	62 (52–82)	0.966	0.954–0.978	< 0.001
Pulse rate (beat/min)	82 (82–100)	101 (82–119)	1.023	1.015–1.032	< 0.001
Respiratory rate (breath/min)	16 (16–20)	20 (16–25)	1.093	1.052–1.136	< 0.001
Oxygen saturation (%)	97 (92–98)	94 (88–98)	0.949	0.923–0.976	< 0.001
Creatinine (mg/dL)	1.7 (1.5–2)	1.7 (1.5–2)	0.948	0.852–1.054	0.321
Blood urea nitrogen (mg/dL)	41 (29–63)	51 (35–72)	1.005	0.999–1.010	0.079
Potassium (mEq/L)	4.4 (4–5)	4.5 (3.8–4.9)	1.014	0.814–1.264	0.898
Sodium (mEq/L)	137 (133–140)	139 (134–145)	1.042	1.021–1.064	< 0.001
pH	7.39 (7.33–7.43)	7.34 (7.26–7.42)	0.005	0.001–0.023	< 0.001
Base excess (mEq/L)	−3.1 ([-6.7] - 0.1])	−5.9 ([-10.3] - [-1.7])	0.924	0.896–0.952	< 0.001
HCO_3 (mEq/L)	21.7 (18.8–24.4)	19.7 (15.6–22.7)	0.890	0.854–0.927	< 0.001
Lactate (mmol7L)	1.8 (1.2–3.1)	4.4 (2.4–8.0)	1.214	1.153–1.277	< 0.001

[a] n, (%).

Table 4
Multivariate logistic regression analysis for the prediction of 1-week mortality.

Variables	OR	95% CI	p value
Sex (Female)	1.570	0.933–2.642	0.09
Age (years)	1.030	1.008–1.052	0.008
Systolic blood pressure (mmHg)	0.982	0.973–0.991	< 0.001
Pulse rate (beat/min)	1.009	0.999–1.019	0.091
Respiratory rate (breath/min)	1.046	0.993–1.101	0.089
Oxygen saturation (%)	0.983	0.945–1.023	0.401
Blood urea nitrogen (mg/dL)	1.002	0.995–1.010	0.576
Sodium (mEq/L)	1.024	0.997–1.050	0.078
Base excess (mEq/L)	0.976	0.993–1.020	0.275
Lactate (mmol7L)	1.138	1.067–1.214	< 0.001

according to the initial and serial lactate levels shown in Table 5.

4. Discussion

This study examined the relationship between the lactate level of patients with AKI (on both admission and ED follow-up) and 1-week mortality, initial vital signs and laboratory results. Patients with higher lactate levels were have a higher 1-week mortality and higher ICU admission rates. We found that elevated lactate level is independent risk factor for the 1-week mortality. In addition, as the lactate levels increased, the mortality rate also increased. The laboratory parameters and vital findings were worse in patients with high lactate levels. The study concluded that lactate level should be use as a prognostic parameter in patients with AKI in ED's.

It was shown that, high lactate levels associated with higher mortality rate in patients with trauma, sepsis, and burn.[2–5] We found only 4 studies focusing lactate levels and prognosis of AKI in Medline.[6–8] These studies have a various limitations for the generalization of their results to emergency medicine practice such as; carrying of the study in non ED environment, enrollment of only pediatric or cirrhotic patients, patients treated with hemodialysis or patients who developed AKI due to sepsis. Our study novel in this field, as the AKI etiology and prognosis of adult patients admitted to the ED are different from the patients in the intensive care unit and pediatric population. In ED, AKI have a various etiology such as a severe dehydration, nephrotoxic agents, and obstruction, but not only the sepsis. The main outcomes, results, limitations of these studies with the current study presented in Table 6.

Another parameter that differentiated this study from previous studies was that the lactate levels measured on ED admission and ED follow-up. The mortality rate is diminished 30.4%–5.7% in patients with elevated lactate levels on admission but then normalized in the ED follow-up. Patients with normal lactate levels on ED admission (at the first sample) but had elevated lactate level in ED course had higher mortality rate than who showed normal lactate measurement on follow-up. Improving or worsening lactate levels is seems to more accurate tool for estimating 1-week mortality than the initial measurement. Probably serial lactate measurements reflected patient's response to the initial ED resuscitation. Therefore, we suggested that serial lactate measurements rather than a single measurement should perform to in patients with AKI.

We showed that more than half of the patients had been died within 1-week, when they had a lactate level higher than 6 mmol/L on admission. OR for predicting mortality is 14 in this group. Sun et al. showed that patients with cirrhosis with AKI, mortality rate is 75.9% for patients with lactate level > 4.1 mg/dl. Therefore, emergency physician should be alarmed for early admission to the ICU and aggressive resuscitation for patients with lactate level > 6 mmol/L.

We also compare the lactate levels with initial vital parameters and laboratory results. As the lactate levels increased, patients also have a poorer vital parameters (blood pressure, heart rate, respiratory rate, oxygen saturation) and more abnormal pH, base deficit, and bicarbonate level.

In patients with AKI and have high lactate levels, more aggressive treatment, and early admission to the ICU should considered in the ED management due to poorer prognosis.

Table 5
Mortality rates according to the initial ED admission and serial lactate levels on ED follow-up.

Lactate level on admission	Mortality rate *n* (%)	Lactate level in ED follow-up[a]	Mortality rate *n* (%)
< 2.5 mmol/L, (*n* = 421)	34 (8.1%)	≤ 2.5 mmol/L (*n* = 162)	13 (8%)
		> 2.5 mmol/L (*n* = 42)	8 (19%)
> 2.5 mmol/L, (*n* = 273)	83 (30.4%)	≤2.5 mmol/L (*n* = 53)	3 (%5.7)
		> 2.5 mmol/L (*n* = 130)	47 (36.2%)

[a] The highest lactate level recorded if there was a more than once measurement during ED follow-up.

Table 6
Comparison of several studies that examined the lactate level as a prognostic marker in patients with acute kidney injury, including the current study.

Authors and title	Study design, n	Patients characteristics	Limitations	Main outcome	Main Results
Linares et al.[6] Risk factors associated to hospital mortality in patients with acute kidney injury on hemodialysis	Retrospective cohort, 169	Adult patients	Patients underwent to hemodialysis had been enrolled into study. (Patients treated without hemodialysis was not included) No serial lactate measurement Mortality according to lactate categories was not calculated Single center study	28 day mortality	The mean lactate levels were found to be higher in patients with mortality. (2.3 mmol/L vs 1.3 mmol/L) Adjusted relative risk for mortality was 1.09 ($p < 0.05$) in patients with elevated lactate levels
Passos et al.[7] A clinical score to predict mortality in septic acute kidney injury patients requiring continuous renal replacement therapy: the HELENICC score	Prospective cohort, 186	ICU patients Sepsis related AKI	Only AKI patients who require continuous renal replacement therapy enrolled into study Only septic patients enrolled into study No serial lactate measurement Mortality according to lactate categories was not calculated Single center study	1-week mortality	The mean lactate level was 3 mmol/L in non-survivors vs 1.8 mmol/L in survivors Multivariate analysis showed that high lactate levels associated 1-week mortality ($p < 0.001$; OR 1.6)
Choi et al.[8] Factors Associated With Mortality in Continuous Renal Replacement Therapy for Pediatric Patients With Acute Kidney Injury	Retrospective, cross-sectional, 123	Pediatric intensive care unit patients	Patients underwent to hemodialysis had been enrolled into study. No serial lactate measurement Mortality according to lactate categories was not calculated Single center study	In hospital mortality	The mean lactate levels were much higher in non-survival. (2.8 mmol/L vs 1.4 mmol/L, $p < 0.001$) Multivariate logistic regression analysis showed that high lactate level has not been associated in-hospital mortality ($p < 0.958$; OR 1.005)
Sun et al.[9] Serum lactate level accurately predicts mortality in critically ill patients with cirrhosis with acute kidney injury	Retrospective, cross-sectional, 480	ICU patients with cirrhosis	ICU based study Only patients with cirrhosis enrolled into study No serial lactate measurement Single center study	In hospital mortality	Non-survivors had higher serum lactate levels. Mortality rate increased progressively as the serum lactate level increased (56% for patients with lactate level < 1.8 mg/dl, 62% for 1.9–2.4 mg/dl, 73% for 2.5–4.0 mg/dl, and 75.9% for > 4.1 mg/dl)
The current study	Retrospective, cross-sectional, 694	Adult ED patients with AKI	Single center study Other potential risk factors contributing to the mortality has not been investigated. (as with other studies listed above)	1-week mortality	Elevated lactate level is independent risk factor for the mortality. The median lactate level was 1.8 mmol/L for survivors and 4.4 mmol/L for non-survivors. ($p < 0.001$) Patients with a high lactate level had a higher mortality rate (30.4% vs 8.1%; $p < 0.001$; OR 5), had a higher ICU admission rate (8% vs 27.9%) and had a poor vital signs and more abnormal laboratory parameter. Serial lactate measurements give additional clues for the estimation of mortality rate.

AKI: Acute kidney injury; OR: odds ratio.

4.1. Limitations

This study carried out only in one center. Our results cannot be generalize for pediatric patient and patients with chronic renal failure. The patients whose laboratory data is missing were excluded from the study. This may have caused to the selection bias.

5. Conclusions

Elevated lactate levels associated with high mortality rate, poor vital signs and abnormal laboratory results in patients presented to the ED with AKI. As the lactate level increased, the mortality rate also increased. Serial lactate measurement is more accurate prognostic tool for estimating mortality. Lactate measurement should be use as a prognostic parameter in patients with AKI in ED.

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