Correlation of Venous Lactate and Time of Death in Emergency Department Patients with Noncritical Lactate Levels and Mortality from Trauma

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Abstract

Background: Serum venous lactate (LAC) levels help guide emergency department (ED) resuscitation of patients with major trauma. Critical LAC level (CLAC, ≥4.0 mmol/L) is associated with increased disease severity and higher mortality in injured patients. The characteristics of injured patients with non-CLAC (NCLAC) (<4.0 mmol/L) and death have not been previously described. Objectives: (1) To describe the characteristics of patients with venous NCLAC and death from trauma. (2) To assess the correlation of venous NCLAC with time of death. Methods: A retrospective cohort study at an urban teaching hospital between 9/2011 and 8/2014. Inclusion: All trauma patients (all ages) who presented to the ED with any injury and met all criteria: (1) Venous LAC drawn at the time of arrival that resulted in an NCLAC level; (2) were admitted to the hospital; (3) died during their hospitalization. Exclusion: CLAC. Outcome: Correlation of NCLAC and time of death. Data were extracted from an electronic medical record by trained data abstractors using a standardized protocol. Cross-checks were performed on 10% of data entries and inter-observer agreement was calculated. Data were explored using descriptive statistics and Kaplan–Meier curves were created to define survival estimates. Data are presented as percentages with 95% confidence interval (CI) for proportions and medians with quartiles for continuous variables. Kaplan–Meier curves with differences in time to events based on LAC are used to analyze the data. Results: A total of 60 patients met the inclusion criteria. The median age was 52 years (quartiles: 30, 75) and 73% were male (age range 2–92). The median LAC in the overall cohort was 1.9 mmol/L (quartiles: 1.5, 2.1). Sixteen patients (27%) died during the first 24 h with 5 (31%) due to intracranial hemorrhage. The median survival time was 5.6 days (134.4 h) (95% CI: 2.3–12.6). Conclusions: In trauma patients with NCLAC who died during the index hospitalization, the median survival time was 5.6 days, approximately one-third of patients died within the first 24 h. These findings indicate that relying on a triage NCLAC level alone may result in underestimating injury severity and subsequent morbidity and mortality.

Keywords: Emergency department, lactate, noncritical lactate, predicting factors for death, trauma

INTRODUCTION

Trauma is a substantial public health burden accounting for over 5 million annual deaths worldwide, and 16% of all global disabilities.1 Predicting death or severe disabilities early is crucial in managing emergency department (ED) patients with severe trauma. Existing indicators for identifying patients at high risk of death, such as the mechanism of injury and Injury Severity Scores (ISSs), provide inconsistent and sometimes inaccurate information. In addition, this information is often calculated in a delayed fashion and is not immediately available to help guide resuscitation decisions.2 Serum assays that evaluate the broader physiologic milieu and the hemodynamic response to injury have been proposed as tools for outcome prediction. Serum venous lactate (LAC) is one of the most commonly used ED markers of hemorrhage, shock, and outcome prediction.3–5 While an elevated LAC (>2 mmol/L)
is concerning, previous research has shown that a critical serum LAC level $\geq 4.0$ mmol/L is associated with increased transfusion requirements and higher mortality.\(^{[4,6–8]}\) In addition, serum venous LAC levels obtained early in the trauma patients’ hospital course are helpful in discriminating between survivors and nonsurvivors.\(^{[29]}\)

Serum venous LAC is a rapid and low-cost test. It is a marker of end-organ perfusion and helps guide resuscitation of severely injured patients. However, the utility of abnormal ED serum LAC in risk stratifying patients in relation to in-hospital mortality is unclear.\(^{[10,11]}\) There is even less clarity in the utility of noncritical serum venous LAC (serum LAC <4.0 mmol/L) in high-risk ED patients who eventually die from their injuries. Our null hypothesis was that noncritical LAC (NCLAC) is not associated with death after trauma within 24 h of injury. The objective of this study is to describe the characteristics of trauma patients with NCLAC levels ($< 4.0$ mmol/L) who died during their hospitalization. We will also assess the association between serum venous LAC levels and in-hospital survival time in injured patients.

**METHODS**

**Study design, population, and setting**

This retrospective cohort study was carried out at a large urban, teaching, Level 1 trauma center. The Institutional Review Board approved the study and consent requirement was waived. The hospital’s ED has an annual census of approximately 135,000 patients encounters with over 1200 annual admissions to the trauma service. Inclusion criteria: All trauma patients (all ages) who presented to the ED with any injury and who met the following inclusion criteria were enrolled in the study. (1) Had a venous LAC drawn at the time of arrival that resulted in an NCLAC (serum venous LAC <4 mmol/L); (2) were admitted to the hospital; (3) died during their hospitalization.

**Study protocol**

Study personnel reviewed admissions between September 1, 2010 and August 31, 2014. The hospital’s electronic medical record (Quadramed, Quadramed Corporation, Reston, USA) was queried for patients meeting inclusion criteria. Data were extracted by trained research personnel using a structured data acquisition protocol. Cross-checks were performed on 10% of entries showing an error rate of $<5%$. Information pertaining to patient demographics, medical history, the index trauma, presentation vital signs, anatomical regions of injuries, initial laboratory results, treatments, the cause of death, date and time of ED arrival, and date and time of death were obtained. ISS were calculated at the time of data abstraction by board certified trauma and acute care surgeons through review of the electronic medical record for all included patients using the standardized methodologies.\(^{[12,13]}\)

**Outcomes**

(1) Characteristics of trauma patients with NCLAC levels that died during their hospitalization. (2) Survival time (time from ED arrival to in-patient death) in trauma patients with noncritical triage LAC levels.

The method of measurement of LAC and outcomes: Serum venous LAC concentration (Radiometer ABL800 Flex, Denmark) was measured at the time of initial patient evaluation. The time of death was calculated as the difference between initial triage time (time-stamped in the electronic medical record) and the time of death (documented time the patient was pronounced dead or time of expiration disposition note in the patient’s medical record). The survival time was calculated in hours. In patients with mortality that occurred in <24 h, fractional days were calculated based on survival hours and minutes.

**Statistical analysis**

Data were analyzed using descriptive statistics with frequencies and corresponding percentages with 95% confidence intervals (CIs) for categorical variables and medians with interquartile ranges (25%–75%) for continuous variables. Statistical associations between comparison variables were performed using Mann–Whitney U-tests for continuous variables and Fisher’s exact tests for categorical variables. Kaplan–Meier curves were used to define survival estimates with median values and corresponding 95% CIs calculated. We also planned an “a priori” subgroup analyses of subjects expiring within 24 h of presentation and those $\geq 65$ years of age. This age cut-off has been used in the literature previously to define older populations in trauma cohorts.\(^{[14]}\) All analyses were performed using STATA version 11.0 (College Station, TX, USA). Significance levels were set at 0.05 (two-tailed).

**RESULTS**

During the study, a total of 440 patients died during their hospitalization. Patient characteristics in this study are generally consistent with national averages for blunt versus penetrating trauma.\(^{[15]}\) Sixty patients (14%) met inclusion criteria and were included in the analysis. The characteristics of the study cohort are presented in Table 1.

The Kaplan–Meier survival curve for the overall cohort is illustrated in Figure 1. The median survival time is demarcated on the curve by the vertical hashed line corresponding to 5.6 days (134.4 h) (95% CI, 2.3–12.6). The survival time range was 1–240 days. Tables 2 and 3 demonstrate the comparison of serum LAC levels, the cause of death and ISS among the overall cohort, patients who died within the first 24 h and those who died after 24 h. Of the 16 patients that had cause of death listed as hemorrhage, all but two received blood products, and a single patient received blood products >24 h after presentation. For the two patients that were not treated with blood products, their in-hospital survival times were 2 and 5 h.

Almost one-third (27%, 95% CI, 17%–39%) of the cohort died within the first 24 h. If we exclude patients who died from intracranial injuries (for expected early death), this number is slightly higher (11/27, 41%, 95% CI, 25%–59%).
The characteristics of older (age ≥65) versus younger patients (age <65) is compared in Table 4.

**Table 1: Baseline characteristics of study patients**

| Characteristic                          | n (%)       |
|----------------------------------------|-------------|
| Sex                                    |             |
| Male                                   | 44 (73)     |
| Female                                 | 16 (27)     |
| Prior comorbidities                    | 18 (30)     |
| Triage emergency severity index        |             |
| 1                                      | 34 (57)     |
| 2                                      | 20 (33)     |
| 3                                      | 6 (10)      |
| Trauma injury type                     |             |
| Blunt                                  | 44 (73)     |
| Penetrating                            | 16 (27)     |
| Isolated head trauma on presentation   | 14 (23)     |
| ED antibiotics administered            | 39 (65)     |
| Required endotracheal intubation       | 51 (85)     |
| Required red blood cell transfusion    | 47 (78)     |
| Admitted to intensive care unit        | 50 (83)     |

**Table 2: Initial serum venous lactate level and injury severity scores in the overall cohort compared to two subgroups of patients who did and did not survive beyond 24 h**

| Characteristic                  | Overall cohort (n=60) | Death by <24 h (n=16) | Death >24 h (n=44) |
|---------------------------------|-----------------------|------------------------|--------------------|
| Lactate (mmol/L)                | 1.9 (1.5, 2.1)        | 2.0 (1.6, 2.2)         | 1.9 (1.5, 2.1)     |
| Injury severity score           | 26 (22, 34)           | 26 (9, 41)             | 25 (29, 29)        |

All values are reported as median with corresponding 25% and 75% quartiles.

**DISCUSSION**

In this study, we found that almost one-third of trauma patients with noncritical ED serum venous LAC levels and in-hospital mortality died within the first 24 h. Furthermore, excluding patients that died as a result of intracranial injuries increased this proportion to 41%. These findings indicate that a single, noncritical serum venous LAC alone may not be an adequate marker of injury severity and should not be relied on as the sole prognostic indicator for outcome in trauma patients.

Characteristics of trauma patients with noncritical triage serum venous LAC levels and subsequent death have not been described in the literature.15 Many studies describe the importance of elevated LAC and LAC clearance as predictors of injury severity and survival.16 Odom et al.7 reported a 5.4% mortality rate in trauma patients with initial serum venous LAC level <2.5 mg/dL, 6.4% when LAC was 2.5–4 mg/dL, and 19% in those with LAC above 4 mg/dL group. Régnier et al.17 studied 586 trauma patients and described the value of initial serum LAC versus LAC clearance in patients who died within the first 48 h (9%). In this cohort, initial LAC was not a reliable predictor of early mortality (odds ratio 1.11, 95% CI, 0.98–1.27, not statistically significant) while LAC clearance (10%/h increase in LAC) was a statistically significant predictor of early mortality (odds ratio 1.24, 95% CI, 1.06–1.43). These findings indicate that initial serum venous LAC, especially when at a noncritical level, should be interpreted with caution and refrain from early placation. Other prognostic markers such as vital signs, mechanism of injury, ISS, and clinical gestalt should be taken into account too. There is a need for a large prospective study to further delineate the characteristics of trauma patients who died despite noncritical triage serum venous LAC levels.

There were notable characteristics that increased the likelihood of death in our study patients with noncritical serum venous LAC levels. According to our results, patients who required endotracheal intubation, red blood cell transfusions or were admitted to the intensive care unit, were more likely to die, despite a normal resuscitation marker. However, due to the small sample size, we were unable to perform a multivariate analysis. These results should, therefore, be interpreted with caution.

Approximately half of the deaths in our cohort were attributed to intracranial injury. When compared to patients with elevated LAC, nonsurvival was associated with an irreversible process such as intracranial hemorrhage, which is not unexpected.18-20

**Figure 1: Kaplan–Meier survival curve for in-hospital mortality. The hashed line demarcates the median survival time among the overall cohort of 5.6 days (95% confidence interval 2.3–12.6)**
While early mortality after trauma can most often be attributed to hemorrhage or intracranial injuries, delayed trauma deaths (beyond the first 24 h) generally result from sepsis and multi-system organ failure.

Advanced age has consistently been reported as a significant risk factor for morbidity and mortality in trauma patients. This is particularly important because serum LAC levels are less reliable predictors of severe injury in the elderly due to their decreased muscle mass and other factors that contribute to their inability to produce LAC to the same degree as younger patients. In our subgroup analysis, 35% of patients who died with NCLAC levels were over the age of 65. The most common cause of death in these elderly patients was infection. Our findings support the concept that the elderly are more vulnerable to morbidity and mortality from both their primary injury insult (e.g., hemorrhage), as well as from secondary insults, such as infection. To justify outcome prediction, this study suggests that more resources may need to be allocated when treating severely injured elderly patients, perhaps consider a higher level of care despite an NCLAC.

**Limitations**

This was a retrospective review and therefore subject to limitations inherent to such a study design. However, we implemented steps recommended by Gilbert et al. to reduce the risk of such biases as much as possible. The study was also conducted in one urban academic center, and therefore, the findings may not be generalizable to other populations. The study cohort might not adequately represent all patients who died after trauma. All patients with death in the hospital were included and not limited to the first 24 h, so as to characterize this patient population. It was only after the data were analyzed that the <24 h subgroup results became significant. Patients with early ED deaths (arrived in traumatic arrest and pronounced dead on arrival or those who died shortly after initial ED evaluation) were excluded from data analysis because laboratory testing was not performed. The study cohort was limited to patients with an electronic medical record, which was initiated in 2010, thereby limiting the study size.

**Conclusion**

Although the median survival time for trauma patients with a noncritical serum venous LAC level who died during their hospitalization was 5.6 days, approximately one-third of patients died within the first 24 h. These findings indicate that relying on a triage NCLAC level alone may result in underestimating injury severity and subsequent morbidity and mortality. Other markers of physiologic and anatomic
derangement should be considered in addition to serum LAC to more effectively risk stratify trauma patients.

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**Conflicts of interest**
There are no conflicts of interest.

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