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Clinical value of triage lactate in risk stratifying trauma patients using interval likelihood ratios

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ABSTRACT

Emergency physicians face the challenge of rapidly identifying high-risk trauma patients. Lactate (LAC) is widely used as a surrogate of tissue hypoperfusion. However, clinically important values for LAC as a predictor of mortality are not well defined. Objectives: 1. To assess the value of triage LAC in predicting mortality after trauma. 2. To compute interval likelihood ratios (LR) for LAC.

Methods: Retrospective chart review of trauma patients with a significant injury mechanism that warranted labs at an urban trauma center. Outcome: In-hospital mortality. Data are presented as median and quartiles or percentages with 95% confidence intervals. Groups (lived vs. died) were compared with Man-Whitney-U or Fisher's-exact test. Multivariate analysis was used to measure the association of the independent variables and mortality. The interval likelihood ratios were calculated for all LAC observed values.

Results: 10,575 patients; median age: 38 [25–57]; 69% male; 76% blunt; 1.1% [$n = 119$] mortality. LAC was statistically different between groups in univariate (2.3 [1.6,3.0] vs 2.8 [1.6,4.8], $p = 0.008$) and multivariate analyses (odds ratio: 1.14 [1.08–1.21], $p = 0.0001$). Interval ratios for LR- ranged from 0.6–1.0. Increasing LAC increased LR+. However, LR+ for LAC reached 5 with LAC > 9 mmol/L and passed 10 (moderate and conclusive increase in disease probability, respectively) with LAC > 18 mmol/L.

Conclusions: In a cohort of trauma patients with a wide spectrum of characteristics triage LAC was statistically able to identify patients at high risk of mortality. However, clinically meaningful contribution to decision-making occurred only at LAC > 9. LAC was not useful at excluding those with a low risk of mortality.

1. Introduction

Trauma is the leading cause of death in the United States for ages 1–46 years and the third leading cause across all age groups [1]. A major proportion of acute deaths (≤48 h) are attributed to exsanguination with global organ failure [2]. Early detection and reversal of tissue hypoperfusion is crucial for improved outcome. Patients presenting to the emergency department (ED) after their injury may appear clinically stable despite significant ongoing occult hemorrhage. Optimal care of injured patients is dependent on early strategies to assess risk.

Uncontrolled hemorrhage results in failure of oxygen delivery, increasing oxygen debt, anaerobic metabolism and acid/base dysregulation [3]. Serum lactate (LAC) and base deficit (BD), have long been used as surrogates for tissue hypoperfusion. They supplement physical exam and predictor injury severity and prognosis, more reliably than abnormal vital signs [4,5]. Numerous studies have evaluated the association of LAC, BD, and LAC clearance with mortality. Most have concluded that elevated LAC, from either a venous or arterial sample, and failure to clear LAC, are highly predictive of in-hospital mortality [3,6,7,8,9,10]. However, review of the trauma literature highlights challenges in generalizing existing data and limitations of available studies. Summation of data is difficult given patient variability. Existing studies are largely retrospective and registry-based. Registry sourcing imparts limitations on validity and variability of data, as inclusion criteria is significantly different between institutions and there are no universal methods for cleaning or verification of trauma registry data. There is minimal information about hospital course and interventions included in trauma registries [11]. Additionally, most prior studies have small sample sizes and are conducted in single trauma centers, potentially limiting their generalizability.

Another challenge is identifying the clinical application of specific LAC values. If LAC is associated with mortality, what does a normal value mean for the patient? How elevated must the LAC be for the risk of death to be significant?

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The objective of our study was twofold: 1. To assess the value of triage LAC in predicting mortality after trauma. 2. To determine if there is greater clinical applicability in a continuous model by computing interval likelihood ratios (LR) for LAC.

2. Methods

2.1. Study design, population, and setting

This retrospective cohort study was carried out at a large, urban trauma center. The Institutional Review Board (IRB) approved the study. The hospital's ED has an annual census of approximately 135,000 patient encounters, with over 1200 annual trauma admissions.

All trauma patients (all ages) who presented to the ED during the study period (January 1st, 2011 to June 30th, 2016) with any injury mechanism of significance to warrant laboratory work up (including venous LAC) were included in the study. Patients with renal or liver failure and those with suspicion of severe infection/sepsis at time of triage were excluded from the study.

2.2. Study protocol

We followed the recommendations proposed by Gilbert et al. to reduce risk of bias in retrospective studies [12]. Electronic medical records (Quadramed, Quadramed Corporation, Reston, USA) were queried for all patients who had venous LAC measured upon admission to the ED. Trained research assistants reviewed electronic medical records using a pre-determined study protocol and excluded patients who presented with non-trauma related complaints. Patients were selected for the study based on a multi-tiered system of manually checking the following electronic documents: triage information, ED disposition diagnosis and hospital discharge diagnosis to confirm the traumatic nature of the ED visit. Crosschecks were performed on 10% of entries.

Information pertaining to patient demographics, the index trauma mechanism (blunt versus penetrating), vital signs, presence or absence of intracranial hemorrhage, venous LAC and BD, hospital admission and mortality were documented. If patients had additional LAC measurements beyond the initial, LAC clearance was also calculated.

2.2.1. Primary outcome

In-hospital mortality. The electronic medical record was queried for mortality data and the information was matched to the enrolled patients.

2.2.2. Method of measurement of LAC and outcomes

Venous LAC concentration (ABL 800 FLEX Blood Gas Analyzer, Radiometer Medical, Bronshoj, Denmark) was measured at time of initial evaluation. Triage BD was simultaneously measured with the same blood gas analyzer. LAC clearance was defined by the difference between the first LAC measurement and a subsequent LAC level (at least 60 min apart, but not >24 h from ED presentation).

2.3. Statistical analysis

Continuous variables are presented as median and quartiles and categorical variables are presented as percentages with 95% confidence intervals. Study subjects were categorized into two groups (survived vs. died). Groups were compared with Man-Whitney-*U* test or Fisher's exact test, when appropriate. Multiple logistic regression models were used to determine predictors significantly associated with mortality. We considered the following predictors: age, gender, mechanism of injury, intracranial hemorrhage, triage blood pressure and heart rate, venous LAC and BD. Pearson correlation coefficient was used to determine the association between triage LAC and BD.

The interval likelihood ratios for positive (LR+) and negative (LR-) tests were measured by first calculating the sensitivity and specificity of every observed value of LAC in predicting mortality. Subsequently, likelihood ratios for positive and negative tests for all observed LAC levels were calculated using the standard likelihood ratio formula (LR+ = sensitivity/1- specificity & LR- = 1- sensitivity/specificity).

We planned a subgroup analysis a priori to repeat the same multivariate analysis only for admitted patients to examine whether the predictive value of LAC was stronger in patients who had more severe injuries that warranted admission.

As a rule of thumb, a study is required to have at least 10 positive outcomes per number of variables included in the multivariate analysis [13]. We expect to have 10 variables in this multivariate model (Age, gender, mechanism of injury, presence or absence of intracranial hemorrhage, hospital admission, systolic blood pressure, diastolic blood pressure, heart rate, BD and LAC). Therefore, 100 deaths are required in order for the analysis to have adequate power. The lowest reported mortality rate among the reviewed literature is 3% (range: 3% to 24%) [1,2,3,4,6,8,10]. Therefore, we would need at least 3000 subjects for the study to achieve its objective with adequate power. P value <0.05 was considered statistically significant. Statistical analyses were performed with SAS version 9.4 (SAS Institute Inc., Cary, NC, USA).

3. Results

A total of 11,800 patients presented to the ED with injury during the study period. After applying the inclusion/exclusion criteria, 10,575 patients were included in the final analysis (median age: 38 [25–57]; age range 1–105 years; 69% male; 76% blunt trauma). The in-hospital mortality rate was 1.1% [n = 119]. The baseline characteristics of the study cohort are listed in Table 1.

In univariate analysis (Table 2) age, BD, LAC and hospital admission were statistically different between the groups. In multivariate analysis (Table 3), older age, higher LAC, larger BD and hospital admission were associated with increased mortality.

The results were not changed when only admitted patients were included in the multivariate analysis (Table 4).

We calculated the LR (for positive and negative tests) for all the observed LAC levels (157 observations, LAC ranging from 0.4 to 30 mmol/L). The interval LR- for the observed LAC values ranged from 0.6 to 1. This range represents test results that do not substantially decrease the post-test probability and therefore are not helpful in clinical decision making [14]. The interval LR+ and the corresponding LAC levels are presented in Table 5. Increasing LAC increased LR+. However, LR+ for LAC reached 5 (moderate increase in disease probability) with LAC >9 mmol/L and LR+ passed 10 (conclusive increase in disease probability) with LAC >18 mmol/L (Table 5) [14]. The mortality rates

Table 1
Baseline characteristics of the study population

Variable	Median and quartiles
Age	38 (25, 57)
Systolic blood pressure	136 (122, 151)
Diastolic blood pressure	83 (72, 94)
Heart rate	87 (74, 99)
Lactate	2.3 (1.6, 3.3)
Base deficit	1.3 (−0.80, 3.0)
Variables	**n/N % (95% confidence interval)**
Gender (male)	7266/10575 69%(66–71%)
Mechanism (blunt)	7993/10575 76% (73–78%)
Intracranial hemorrhage	237/10575 2% (1–3%)
Overall admission rate	5298/10575 50% (47–53%)
In-hospital mortality	119/10575 1.1% (0.6–2%)

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