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ORIGINAL RESEARCH

General Medicine

Assessing lactate concentration as a predictor of 28-day in-hospital mortality in the presence of ethanol: A retrospective study of emergency department patients

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Abstract

Background: Presence of ethanol (EtOH) may alter the relationship between blood lactate concentrations and mortality. This study compares lactate-associated mortality risk in the presence and absence of EtOH.

Methods: We performed a retrospective cohort study including all patients, age >17 years, presenting from January 2012–December 2018, to an urban, academic emergency department, with a clinically measured lactate. Data were electronically abstracted from the medical record. The primary outcome was 28-day in-hospital mortality. Patients were grouped by EtOH test results as follows: 1) present (any EtOH detected), 2) absent (EtOH concentration measured and not detected), or 3) not ordered. Marginal analysis was used to calculated probability of mortality for fixed values of lactate and model covariates.

Results: Of 40,956 adult emergency department patients with measured lactate, we excluded 768 (1.89%) for lactate >10.0 mmol/L, leaving 40,240 for analysis: 4,066 (10.1%) EtOH present, 10,819 (26.9%) EtOH absent, 25,355 (63%) EtOH not ordered. Of these, 1790 (4.4%) had 28-day in-hospital mortality. Marginal probability of mortality calculated for specific lactate values found less risk for EtOH Present patients versus EtOH absent patients at lactate 0.0 mmol/L (0.8% [95%CI: 0.5–1.2%] vs 3.2% [2.8–3.6%]), 2.0 mmol/L (1.5% [1.1–1.9%] vs 4.0% [3.7–4.3%]), 4.0 mmol/L (2.6% [2.2–3.1%] vs 5.0% [4.6–5.4%]), until 6.0 mmol/L (4.5% [3.7–5.4%] vs 6.2% [5.4–7.0%]).

Conclusion: EtOH presence significantly alters lactate-associated mortality risk when lactate <6.0 mmol/L. Emergency department clinicians should interpret these lactate values with caution and consider other data for risk stratification when EtOH is present.

KEYWORDS
alcohol, emergency department, ethanol, lactate, mortality

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1 | INTRODUCTION

1.1 | Background

Serum lactate concentrations are associated with mortality in patients presenting to the emergency department.[1] Studies in sepsis,[2,3] trauma,[4,5] and acute cardiac disease[6] have demonstrated an independent association between lactate and mortality. Furthermore, serum lactate elevation appears to better predict mortality than vital sign abnormalities in elderly trauma patients[7] and indicates a poor prognosis in all patients admitted to the hospital.[8] The value of lactate as a prognostic indicator has made it a vital component of recent sepsis guidelines.[9] However, serum lactate concentrations are affected by many factors unrelated to severity of illness, potentially confounding physician interpretation of this prognostic test.

1.2 | Importance

Ethanol (EtOH) use is common in emergency department (ED) patients[10] and known to affect lactate concentrations.[11,12] Prior investigations have explored the degree to which EtOH confounds the association between lactate concentration and mortality, but results are conflicting; some demonstrate that lactate maintains its prognostic utility in the presence of EtOH;[13,14] whereas, others find lactate predicts mortality poorly in EtOH-intoxicated patients.[15] One study suggests that the threshold in which lactate predicts mortality is higher in the presence of EtOH.[16] Notably, these studies have been limited to trauma patients. Additionally, there is a commonly held perception that falsely elevated lactate concentrations exist because of EtOH, but the degree to which this interaction may occur and should affect clinical decisions is unclear.

1.3 | Goals of this investigation

Given the prevalence of EtOH use among ED patients and increasing use of lactate for ED risk stratification, data to inform lactate interpretation in the context of EtOH intoxication are needed. Our study aims to (1) compare lactate-associated mortality risk in patients with and without concomitant EtOH and (2) investigate whether these mortality rates are subject to a dose response with respect to EtOH concentrations.

2 | METHODS

2.1 | Study design and setting

We performed a retrospective cohort study including all patients presenting to an urban, academic ED with 65,000 annual visits, from January 2012–December 2018. The Human Subjects Division of our institutional review board provided approval for the study. Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) guidelines for reporting observational studies guided this research.[17]

The Bottom Line

Lactate is a critical indicator of shock severity during the initial assessment of patients. In this paper, Akhavan et al demonstrate that alcohol decreases the probability of mortality for lactate levels <6.0 mmol/L, suggesting that physicians should also consider other markers of critical illness when alcohol is present.

2.2 | Selection of participants

We included all ED patient encounters during the study period with a lactate measurement. We excluded minors (age <18 years), patients where ED EtOH concentrations were ordered but no results were available, and any patients missing data to be used for multivariate modeling. We also excluded patients with initial lactate ≥10.0 mmol/L (encompassing recorded concentrations as high as 29 mmol/L), as these concentrations occurred in <2% of patients and may have represented extremes of severe illness or tissue malperfusion, spurious values, or otherwise rare scenarios that would otherwise have an outsized influence on the models (Figure S1).

2.3 | Data collection

Data were electronically abstracted from the hospital's electronic medical record. Abstracted variables included patient demographics, initial ED lactate concentration, initial ED blood and urine EtOH concentrations, in-hospital mortality, ED administration of antibiotics, trauma registry inclusion, ED vital signs, vasopressor use, mechanical ventilation, and triage acuity (based on emergency severity index).

2.4 | Outcomes

The primary outcome for our study was in-hospital mortality within 28 days. Patients discharged from the ED were presumed to have survived.

2.5 | Definition of covariates

Arterial and venous lactate measurements were included and used interchangeably.[18] To determine the presence and concentration of serum EtOH, we preferentially used blood EtOH results but substituted urine EtOH concentrations if blood was unavailable. In dose response models, only blood EtOH concentrations were used. All EtOH concentrations were reported as quantitative. For the primary analysis, we grouped EtOH concentrations as Present (any EtOH detected), Absent (EtOH concentration measured and negative), and Not Ordered (EtOH concentrations not ordered). We separately

evaluated 2 major subgroups of patient pathology within our cohort: trauma and suspected infection. We used inclusion in the institutional trauma registry to identify patients who presented primarily for a traumatic mechanism. Patients who were administered antibiotics in the ED, but were not included in the trauma registry, were identified as having a suspected infection.

2.6 | Analysis

We used descriptive statistics to compare unadjusted demographics, clinical characteristics, commonly used lactate strata, and in-hospital mortality within 28 days between EtOH groups. Variables reported were identified a priori as possible ED predictors of mortality and used to determine a baseline risk of mortality for the entire population. Multivariate logistic regression was used to assess the relationship between lactate, ethanol, established predictors of ED mortality, and 28-day in-hospital mortality. Marginal probabilities of mortality were also calculated for fixed lactate values, from 0 to 10.0 mmol/L, in intervals of 2.0 mmol/L. In the marginal model, non-lactate model covariates were held at their means in order to isolate and measure discrete differences in 28-day mortality owing to lactate values alone.[19] These analyses also were performed for the trauma and suspected infection subgroups.

To evaluate whether EtOH concentration modified the relationship between lactate and mortality, we explored an EtOH dose-response. We developed a multivariate logistic regression model where an EtOH factor variable was used to represent quartile concentration, in lieu of a continuous variable. Marginal probability of mortality was again estimated for fixed lactate values in intervals of 2.0 mmol/L, with non-lactate covariates held at means.

All statistical analyses were performed in Stata 15.1 (College Station, TX).

3 | RESULTS

Of 457,426 patient encounters during the study period, we excluded 15,539 (3.4%) pediatric patients, 274 (0.1%) patients with EtOH ordered but not resulted, 393,472 (86.0%) patients without a lactate ordered, 768 (0.2%) patients with lactate values >10.0 mmol/L, and 7133 (1.6%) patients missing data for model covariates, leaving 40,240 (8.8%) patients for analysis (Figure 1). Of these patients, 1790 (4.4%) had 28-day in-hospital mortality.

Table 1 shows patient demographics and *a priori* covariates used for predicting baseline mortality before lactate evaluation. The study population was predominantly male (63.1%), with 6,765 (16.8%) encounters meeting institutional trauma activation criteria, and 17,971 (44.7%) patients suspected to have infection. Compared with EtOH Absent patients, EtOH Positive patients were more likely male gender and American Indian/Alaskan native, and they had higher mean initial lactate concentration. EtOH Absent patients were more likely to have suspected infection and had higher rates of mortality.

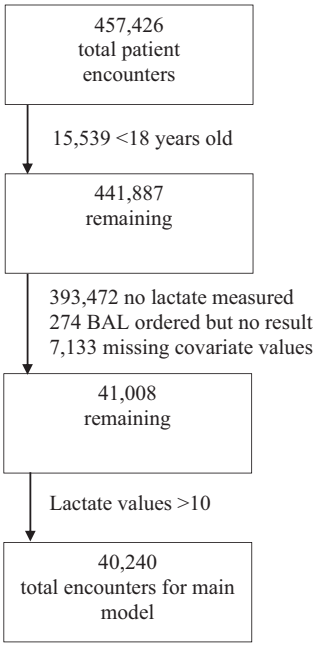

FIGURE 1 Patient encounter enrollment and exclusions. BAL, blood EtOH concentration

Table 2 shows the risk-adjusted odds ratios (aOR) for 28-day in-hospital mortality in the context of EtOH and lactate. Overall, EtOH presence alone resulted in an aOR of 0.24 (95% confidence interval = 0.15–0.40); whereas, EtOH absence alone resulted in an aOR of 1.10 (0.89–1.35), compared to a baseline of EtOH concentration not ordered. The interaction of EtOH Present and increased serum lactate resulted in an aOR of 1.07 (0.98–1.18); whereas, EtOH absent and increased serum lactate resulted in an aOR of 0.89 (0.85–0.94). Subgroup analyses for trauma patients and patients treated for infection showed similar results.

Marginal analysis examined probability of 28-day mortality at fixed lactate 2.0 mmol/L intervals for each EtOH group, with ED-based mortality covariate values held at their means in order to isolate and visualize the interactions at specific lactate concentrations (Figure 2A). Overall, the mortality risk associated with each lactate concentration was lower in EtOH present compared to absent patients, for lactate concentrations between 0.0 and 6.0 mmol/L. At 8.0 and 10.0 mmol, the risk between EtOH present and EtOH absent patients are not statistically different. The same marginal analyses were performed for subgroups restricted to suspected infection and trauma (Figure 2B and C). When limited to these high frequency etiologies, the risk of mortality is lower among patients with EtOH present than those with negative serum EtOH, for lactate concentrations between 0.0 and 4.0 mmol/L. In the overall cohort, as well as both subgroups, the mortality risk was similar when comparing EtOH present patients with lactate concentrations of 4.0 mmol/L to EtOH absent and not ordered patients with lactate concentrations of 0.0 mmol/L.

To determine whether serum EtOH concentration might influence the relationship between risk-adjusted probability of mortality and lactate concentrations, we modeled positive EtOH values by

TABLE 1 Demographics, clinical characteristics, etiology, and in-hospital 28-day mortality, all variables included in baseline models, except serum lactate, which was not included in baseline model construction

	Not Ordered	Negative	Positive	Total
N	25,355	10,819	4066	40,240
Female, n (%)	9355 (36.9)	3258 (30.1)	948 (23.3)	13561 (33.7)
Age, mean (SD)	52.98(16.9)	49.8 (17.5)	45.0 (14.2)	51.3 (17.0)
Race, n (%)				
White	14886 (58.7)	7462 (69)	2579 (63.4)	24927 (61.9)
Asian	2625 (10.4)	644 (6.0)	116 (2.9)	3385 (8.4)
Black/African American	5127 (20.2)	1688 (15.6)	589 (14.5)	7404 (18.4)
Hispanic/Latino	1025 (4.0)	265 (2.4)	155 (3.8)	1445 (3.6)
Native Hawaiian/Pacific Islander	263 (1.0)	72 (0.7)	30 (0.7)	365 (0.9)
Unknown/Other	552 (2.2)	257 (2.4)	125 (3.1)	934 (2.3)
American Indian/Alaskan Native	877 (3.5)	431 (4.0)	472 (11.6)	1780 (4.4)
ED vital signs, mean (SD)				
Minimum systolic blood pressure (mmHg)	118.3 (24.4)	112.9 (25.3)	110.4 (23.4)	116.0 (24.7)
Maximum heart rate (beats/min)	101.2 (21.0)	104.7 (23.4)	107.2 (22.3)	102.8 (21.9)
Maximum respiratory rate (breaths/min)	20.2 (5.4)	20.3 (5.5)	19.7 (4.9)	20.2 (5.4)
Minimum oxygen saturation (%)	95.7 (4.7)	95.5 (5.5)	95.4 (5.8)	95.6 (5.1)
Triage acuity, n (%)				
Unknown	60 (0.2)	34 (0.3)	10 (0.2)	104 (0.3)
1	1171 (4.6)	2153 (19.9)	889 (21.9)	4213 (10.5)
2	6075 (24.0)	4046 (37.4)	1417 (34.8)	11538 (28.7)
3	17284 (68.2)	4381 (40.5)	1633 (40.2)	23298 (57.9)
4	740 (2.9)	192 (1.8)	112 (2.8)	1044 (2.6)
5	25 (0.1)	13 (0.1)	5 (0.1)	43 (0.1)
Vasopressors in emergency department, n (%)	1094 (4.3)	830 (7.7)	209 (5.1)	2133 (5.3)
Suspected infection, n (%)	13194 (52.0)	3716 (34.3)	1061 (26.1)	17971 (44.7)
Trauma registration, n (%)	968 (3.8)	4147 (38.3)	1650 (40.6)	6765 (16.8)
Initial serum lactate, mean (SD)	1.8 (1.2)	2.3 (1.7)	3.4 (1.7)	2.1 (1.5)
In-hospital 28-d mortality, n (%)	953 (3.8)	714 (6.6)	123 (3.0)	1790 (4.4)

quartile, again applying marginal analysis for fixed lactate concentrations (Table 3, Figure 3). Although the lowest quartile of EtOH concentration tended toward higher probability of mortality at each lactate concentration examined, differences when compared to higher quartiles of serum EtOH were not statistically significant.

3.1 | Limitations

Our study should be interpreted in the context of several limitations. First, electronic data abstraction includes inherent constraints, potentially introducing erroneous data. We mitigated this risk by performing manual abstraction to create a gold standard to calibrate the electronic data abstraction process.[20] In addition, our primary covariates, EtOH concentration and lactate measurements, are discrete values less subject to charting variability. Second, variation exists in practice patterns regarding ordering of laboratory studies such as lactate and EtOH, potentially introducing confounding through indication. Similarly, unmeasured confounders may exist that were not available through the electronic medical record. Such confounders could relate to medical history (for example, liver failure), malnutrition, recent seizure, or substance abuse separate from current EtOH intoxication. Related to this, the causes of missing covariate data were unknown and were potentially missing not-at-random and related to severity of illness because of the emergency setting. Thus, missing data were not imputed or otherwise replaced; however, our decision to exclude patients missing covariate data likely introduced biases in another form. Finally, our study was performed at a large, urban academic center. Although this setting includes a broad spectrum of pathology and disease severity, this population may not generalize well to other clinical settings.

Additionally, our process for identifying infection (or other diagnoses outside of the trauma registry) was limited by the

TABLE 2 Model results from overall and subgroup logistic regression models predicting in-hospital 28-day mortality

Variable	Overall (n = 40,240)	Suspected infection (n = 16,303)	Trauma (n = 6704)
Ethanol result (baseline = not ordered)			
Negative	1.09 (0.89–1.35)	1.63 (1.13–2.35)	0.80 (0.52–1.21)
Positive	0.24 (0.14–0.39)	0.39 (0.09–1.55)	0.19 (0.09–0.37)
First serum lactate	1.28 (1.23–1.33)	1.31 (1.24–1.38)	1.22 (1.09–1.36)
Interaction between ethanol and serum lactate			
Negative ethanol and 1 unit increase in serum lactate	0.89 (0.84–0.94)	0.87 (0.80–0.96)	0.93 (0.82–1.05)
Positive ethanol and 1 unit increase in serum lactate	1.07 (0.97–1.18)	0.97 (0.76–1.25)	1.14 (0.97–1.33)
Vasopressors in emergency department	4.87 (4.29–5.54)	5.16 (4.19–6.36)	3.65 (2.97–4.48)
Age	1.04 (1.04–1.04)	1.04 (1.03–1.04)	1.04 (1.04–1.05)
Minimum systolic blood pressure	0.99 (0.99–0.99)	0.98 (0.98–0.99)	0.99 (0.99–0.99)
Minimum oxygen saturation	0.99 (0.98–1.00)	1.00 (0.98–1.01)	0.98 (0.97–1.00)
Maximum heart rate	1.00 (1.00–1.00)	1.00 (0.99–1.00)	1.00 (0.99–1.00)
Maximum respiratory rate	1.01 (1.00–1.02)	1.01 (1.00–1.03)	1.00 (0.98–1.01)
Female	1.19 (1.07–1.33)	1.10 (0.91–1.32)	1.16 (0.95–1.41)
Race (baseline = white)			
Asian	0.66 (0.55–0.80)	0.64 (0.48–0.86)	0.86 (0.57–1.30)
Black/African American	0.68 (0.57–0.82)	0.74 (0.57–0.97)	0.92 (0.62–1.38)
Hispanic/Latino	1.13 (0.81–1.59)	0.81 (0.45–1.48)	1.32 (0.69–2.52)
Native Hawaiian/Pacific Islander	0.42 (0.18–0.97)	0.76 (0.29–1.95)	n/a
Unknown/Other	1.46 (1.08–1.97)	1.40 (0.77–2.56)	1.69 (1.11–2.58)
American Indian/Alaskan Native	1.09 (0.81–1.48)	1.15 (0.73–1.79)	0.78 (0.40–1.51)
Acuity level	0.34 (0.31–0.36)	0.42 (0.37–0.48)	0.32 (0.27–0.38)
Suspected infection	0.86 (0.76–0.96)	n/a	n/a
Trauma registry	1.45 (1.25–1.67)	n/a	n/a
Model constant term	0.02 (0.00–0.06)	0.01 (0.00–0.08)	0.12 (0.02–0.66)

Results shown as adjusted odds ratios with 95% confidence interval.

retrospective nature of the analysis. For example, some patients in our suspected infection cohort may have been given antibiotics as a result of elevated lactate concentrations as opposed to other clinical indications.

4 | DISCUSSION

In this study, we evaluated whether the presence of EtOH, detected in either blood or urine, significantly modified the relationship between lactate concentrations and mortality. In multivariate logistic regression, the interaction between EtOH group and lactate concentration did not demonstrate a significant influence of EtOH on lactate-associated mortality risk. This ambiguous result is likely because of the convergence of mortality risk between EtOH negative and positive patients seen at very high lactate concentrations (8.0–10.0 mmol/L). However, the marginal analysis revealed that the EtOH present group had lower probabilities of mortality compared to EtOH present patients for lactate concentrations ≤6.0 mmol/L. In fact, the estimated mortality risk associated with lactate concentration of 4.0 mmol/L in EtOH present patients was similar to the risk of mortality when lactate was fixed at 0.0 mmol/L in EtOH negative patients. The discordance in estimated mortality risk between EtOH present and absent patients across the spectrum of common lactate values calls into question the reliability of this test when performing early risk stratification when EtOH is present.

Decreased estimated mortality risk among EtOH present patients persisted in both trauma and suspected infection subgroups, until lactate concentrations reached 6.0 mmol/L. As in the overall cohort, the estimated mortality risk in each subgroup associated with lactate concentration of 4.0 mmol/L in EtOH present patients was similar to the risk of mortality when lactate was fixed at 0.0 mmol/L in EtOH negative patients. Confidence intervals were wide at the higher lactate strata in the subgroup analysis, reflecting lower numbers of patients with these high lactate values. These results suggest that the effect of EtOH on the prognostic value of lactate persists within 2 of the most common ED disease states where lactate concentrations are ordered.

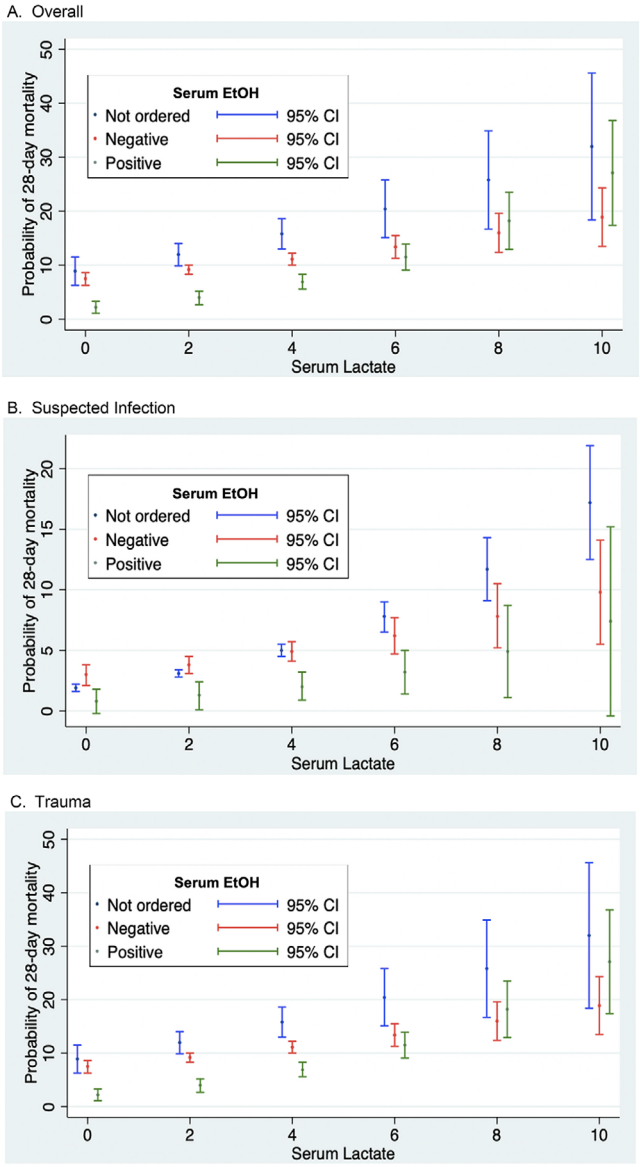

FIGURE 2 Risk-adjusted probability of 28-day in-hospital mortality (%) at fixed lactate (mmol/L) intervals, with model covariates held at means. Panel A shows the overall cohort. Panels B and C show populations limited to suspected infection and trauma, respectively. CI, confidence interval; EtOH, ethanol

Despite a broad range of EtOH concentrations observed in this population, the effect of EtOH on the relationship between lactate and mortality did not increase with increasing EtOH concentration. EtOH quartiles demonstrated similar probabilities of mortality at each lactate concentration examined, and these probabilities remained consistently lower than the probability of mortality among patients with negative serum EtOH. This finding suggests that presence or absence of EtOH may serve as a binary, not dose-dependent, modifier of the lactate-mortality relationship.

Some prior investigations suggested that lactate remains a significant predictor of mortality in the presence of EtOH,[13,14] whereas others have found that the presence of EtOH confounds or changes the prognostic value of lactate.[15,16] These studies were limited to trauma patients with smaller sample sizes. Our study did not limit the cohort to specific etiologies, instead investigating the relationship between lactate and mortality in the setting of EtOH in a broad cohort. Our study supports previous findings that EtOH modifies estimated mortality risk based on lactate concentrations.

Multiple mechanisms likely contribute to the modifying effect of EtOH on serum lactate concentration interpretation. Lactate clearance may slow owing to decreased liver function in alcoholic patients or to competitive metabolism in acute EtOH intoxication. Poor lactate metabolism may also result from vitamin deficiency, particularly the lack of thiamine, which is required to metabolize pyruvate to acetyl coenzyme A instead of lactate. In addition, the generation of NADH through EtOH metabolism leads to the formation of lactate from pyruvate, raising serum lactate concentrations.[11,12]

Patients with EtOH intoxication represent a significant proportion of ED visits,[10] and identifying patients with critical illness remains challenging in this population. Even though unsuspected critical illness appears in a notable proportion of the intoxicated ED population,[21] perceptions and behavioral challenges make objective evaluation of intoxicated patients difficult.[22] Therefore, objective tools for appropriate risk stratification in these patients are important to ED care. However, EtOH appears to modify the relationship between lactate and mortality and may dampen its utility in risk-assessment, until very high lactate concentrations are reached. Specifically, EtOH appears to shift lactate concentrations into ranges that would suggest a higher risk of mortality than is actually observed. Although our data do not preclude a relationship between lactate estimated mortality when EtOH is present, the association is significantly different than that seen in EtOH negative patient population. Therefore, using lactate thresholds to trigger protocolized care in sepsis, trauma, or other disease states may lead to overdiagnosis, inefficient resource use, or overtreatment when EtOH is present.

In practice, clinicians should use these data to support the de-escalation of compulsory care driven by lactate concentrations alone when lactate is <6.0 mmol/L in the presence of EtOH. Although associated mortality in the overall cohort was significantly different between EtOH groups at 6.0 mmol/L, the lack of difference at 6.0 mmol/L in patients with suspected infection and trauma suggests a more conservative threshold <6.0 mmol/L may be more appropriate. Likewise, we recommend that care decisions should be guided by alternative methods of risk stratification, across etiologies, when EtOH is present at any concentration. We also remind clinicians that a lactate level ≥6.0 mmol/L should be assumed to have a significant association with mortality, with or without concomitant EtOH, and should not be dismissed as an artifact of EtOH consumption.

Mortality risk associated with typically encountered serum lactate concentrations are significantly lower for patients who have positive circulating EtOH concentrations compared to those that do not, until lactate concentrations reach 6.0 mmol/L. This relationship persists when the cohort is restricted to patients with trauma and suspected infection. The presence or absence of EtOH serves as a binary, not dose-dependent, modifier of the lactate-mortality relationship.

TABLE 3 EtOH dose-response analysis: Risk-adjusted probability of mortality and 95% CI

	First Serum Lactate = 0			Lactate = 2		
BAL	Probability	Lower CI	Upper CI	Probability	Lower CI	Upper CI
Negative	4.2%	3.7%	4.8%	5.7%	5.3%	6.2%
Q1	3.1%	2.1%	4.1%	4.2%	3.0%	5.4%
Q2	2.0%	1.2%	2.7%	2.7%	1.8%	3.6%
Q3	2.0%	1.2%	2.8%	2.8%	1.8%	3.7%
Q4	1.7%	0.9%	2.5%	2.3%	1.3%	3.4%
	Lactate = 4			Lactate = 6		
BAL	Probability	Lower CI	Upper CI	Probability	Lower CI	Upper CI
Negative	7.6%	7.0%	8.2%	9.9%	8.8%	11.1%
Q1	5.6%	4.1%	7.1%	7.5%	5.6%	9.4%
Q2	3.7%	2.5%	4.9%	5.0%	3.4%	6.6%
Q3	3.8%	2.5%	5.1%	5.1%	3.4%	6.8%
Q4	3.2%	1.8%	4.6%	4.3%	2.5%	6.2%
	Lactate = 8			Lactate = 10		
BAL	Probability	Lower CI	Upper CI	Probability	Lower CI	Upper CI
Negative	12.8%	10.8%	14.9%	16.3%	13.1%	19.6%
Q1	9.8%	7.2%	12.4%	12.7%	9.1%	16.3%
Q2	6.7%	4.6%	8.9%	8.9%	5.9%	11.8%
Q3	6.8%	4.6%	9.1%	9.0%	5.9%	12.1%
Q4	5.8%	3.4%	8.3%	7.7%	4.4%	11.1%

BAL, blood EtOH concentration; CI, confidence interval; EtOH, ethanol.

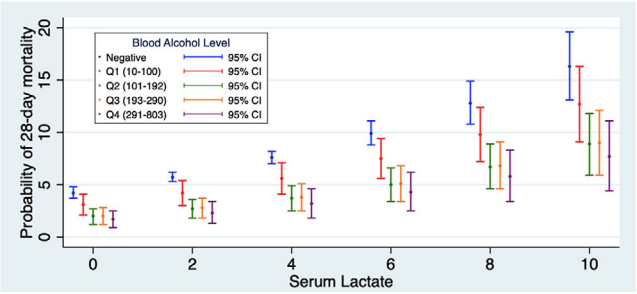

FIGURE 3 Ethanol (EtOH) dose-response analysis: Blood EtOH concentration modeled as quartiles versus negative EtOH. Risk-adjusted probability of 28-day mortality with 95% confidence interval (CI). Serum lactate concentration in mmol/L

Future research should continue to investigate how the prognostic value of lactate is affected by other patient characteristics, such as malnutrition, medication administration, liver disease, or seizure. In addition, further stratifying mortality risk in the setting of EtOH intoxication by other factors, such as trauma injury severity score, may add context to these data. Given the increasing use of lactate to identify high-risk patients and initiate treatment protocols, understanding how patient characteristics modify the relationship between lactate and mortality will allow for a more nuanced application of these values in assessing illness severity.

CONFLICT OF INTEREST

ARA, NJJ, BF, JH, KJ, and MKH report no conflicts of interest. DJH reports research funding from Baxter and provides research consulting to Cytoval.

AUTHOR CONTRIBUTIONS

ARA, NJJ, MKH, and DJH conceived and designed the study. ARA, NJJ, BF, KJ, MKH, and DJH were instrumental in the acquisition of the data. ARA, NJJ, JH, MKH, and DJH analyzed and interpreted the data. ARA, JH, and DJH drafted the manuscript. NJJ, MKH, and DJH critically revised the manuscript for intellectual content. JH and DJH provided statistical expertise. ARA and DJH acquired funding for the project. ARA and DJH takes final responsibility of the article.

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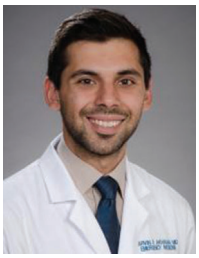
AUTHOR BIOGRAPHY



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SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section at the end of the article.

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