Repeating Lactate Concentrations in Ward Patients Admitted with a Diagnosis of Possible Sepsis Lacks Utility for Prediction of Escalation of Care or Mortality

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Introduction

- ✓Sepsis and septic shock remains a leading cause of morbidity and mortality in the United States, with a 28-day mortality of 25%, despite significant progress in its management (e.g. source control, intensive care, early recognition).
- ✓Sequential Organ Failure Assessment (qSOFA) was proposed as a simple tool aid in such early detection and to predict in-patient mortality. However, the discriminatory value of the qSOFA score was found to be poor in subsequent studies.
- ✓Lactate concentrations were excluded from qSOFA, as this measurement was originally thought to have minimal impact to improve the discriminatory power of the score; however, further research revealed that lactate may enhance qSOFA predictive potential.
- ✓There is limited guidance for patients who have elevated lactate ≥2.0 mmol/L, but who are not hypotensive on presentation or after initial fluid bolus in ED ("cryptic shock").
- ✓The latest edition of the Surviving Sepsis Campaign recommends to re-measure lactate level in intermediate group to assess lactate clearance aiming to identify patients at risk of deterioration.
- ✓The objective of this study was to evaluate the potential utility of following lactate concentrations for the premonitory detection of deterioration in patients admitted to the ward who have blood cultures ordered in emergency department for the work up of suspected sepsis.

Methods

- ✓ The study was approved by the Institutional Review Board of the University of Miami (IRB#20190845).
- ✓ Inclusion criteria encompassed adult, non-hospice patients (≥18 years old), admitted from the ED to the U-Health Tower regular ward (the main hospital of the University of Miami) in whom blood cultures were ordered, between October 1, 2017 and November 12, 2019.
- ✓ A diagnosis of possible sepsis was inferred from a blood culture sample obtained in the ED. An order for a blood culture was used in previous studies as a reliable surrogate of provider documentation for suspected infection in the work-up of patients with suspected sepsis
- ✓ We tested 4 hypotheses related to serum clearance of lactate within 6 hours of the admission value, in patients admitted to the floor from the ED with a diagnosis of possible sepsis:

- An increase in the lactate concentration would be associated with an increased incidence of ICU transfer (Hypothesis 1a) and an increase in in-hospital mortality (Hypothesis 1b).
- No change in the lactate concentration would be associated with an increased incidence of ICU transfer (Hypothesis 2a) and in increase in in-hospital mortality (Hypothesis 2b).
- Each of the hypotheses were evaluated based on whether the initial lactate from arrival in the emergency department was in the normal, intermediate, or high range.

Results

Highlights

- Compared to patients with normal admission lactate concentrations, there was a clinically relevant increased risk of in-hospital mortality in patients with intermediate (RR = 2.66, P < 0.001) and high (RR = 6.67, P < 0.001) lactate concentrations, but no increased risk in patients in whom a lactate was not drawn.

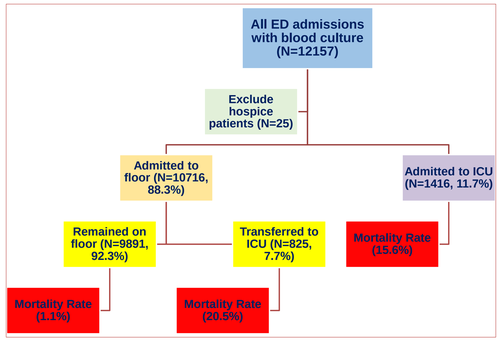
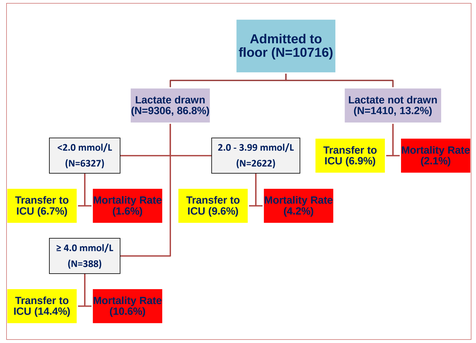


Figure 1. Flow diagram of population analyzed with in-hospital disposition and mortality rate.



- Compared to patients with normal admission lactate concentrations, there was a clinically important increased risk of ICU transfer in patients with intermediate (RR = 1.43, P < 0.001) and high (RR = 2.15, P < 0.001) lactate concentrations, but no increased risk in patients in whom a lactate was not drawn.
- Repeat lactate determinations were performed in 10.7%, 77.1% and 90.2% of patients with normal, intermediate, and high admission lactate concentrations, respectively.

Figure 2. Hospital survival and intensive care unit transfer rates by admission lactate determination in non-hospice patients admitted to the floor.

	In Hospital Mortality				ICU Transfer		
Admission Lactate Concentration[a]	Total	Death	RR vs. Normal Lactate (95% CI)	P-value	Transfer	RR vs. Normal Lactate (95% CI)	P-value
Normal	6327	1.58%			6.75%		
Not Measured	1422	2.11%	1.33 (0.89 to 2.00)	0.16	6.96%	1.03 (0.84 to 2.00)	0.77
Intermediate	2622	4.20%	2.65 (2.03 to 3.47)	<0.001	9.50%	1.41 (1.21 to 3.47)	<0.001
High	388	10.57%	6.69 (4.72 to 9.48)	<0.001	14.43%	2.14 (1.65 to 9.48)	<0.001

Table 1. Relative risk of in hospital mortality or intensive care unit transfer based on admission lactate concentration.
[a]Normal: < 2.0 mmol/L; Intermediate: 2.0 to 3.99 mmol/L; High: ≥ 2.0 mmol/L

Discussion

- ✓ Repeat lactate determinations were performed in 10.7%, 77.1% and 90.2% of patients with normal, intermediate, and high admission lactate concentrations, respectively.
- ✓ The follow-up test was performed in 80% of patients within 8 hours of the initial value.
- ✓ There was no increase in the relative risk of intensive care transfer among patients with either an increase in the lactate concentration of >10% or no change (within 10% of the initial value) compared to those in whom the lactate decreased by >10%.***Thus, hypotheses 1a and 2a were rejected in all initial lactate concentration groups.***
- ✓ There was no increase in the relative risk of hospital mortality among patients with either an increase in the lactate concentration of >10% or no change (within 10% of the initial value) compared to those in whom the lactate decreased by >10% (Table 3). ***Thus, hypotheses 2a and 2b were rejected in all initial lactate concentration groups.***
- ✓ The data presented suggests that following lactate levels in ward patients admitted with possible sepsis is not useful to preemptively identify patients who might benefit from an earlier escalation of care.
- ✓ We emphasize that our findings of lack of utility of repeating the lactate are restricted to patients who were sufficiently stable to be admitted to the floor.
- ✓ The findings should not be generalized to patients admitted from the ED directly to an ICU, as those patients often are in septic shock (e.g., requiring vasopressor or ventilator support) or are judged as of high risk of deterioration.
- ✓ **Limitations:** First, this was a non-randomized, single-center, retrospective trial, that in despite of having an adequate sample size, the application of the results from this study would require further confirmation in large multicenter trials. Second, our hospital well established sepsis care protocol with high adherence, which are based on surviving sepsis campaign guidelines. Consequently, sepsis related mortality is lower than estimated in most resent epidemiologic data. Therefore, findings may not be generalizable to other practice settings.
- ✓ **Conclusions:** Re-measuring lactate level in patients with intermediate initial of lactate (2 mmol/L -3.99 mmol/L) is not of value in predicting the need for care escalation of care or death. Further studies are needed to investigate if serial lactate measurements should be ubiquitously mandated for intermediate lactate group.

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