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# Original Contributions

# HELPFUL ONLY WHEN ELEVATED: INITIAL SERUM LACTATE IN STABLE EMERGENCY DEPARTMENT PATIENTS WITH SEPSIS IS SPECIFIC, BUT NOT SENSITIVE FOR FUTURE DETERIORATION

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☐ **Abstract—Background: Early emergency department (ED) identification of septic patients at risk of deterioration is critical. Lactate is associated with 28-day mortality in admitted patients, but little evidence exists on its use in predicting short-term deterioration. Objective: Our aim was to determine the role of initial serum lactate for prediction of short-term deterioration in stable ED patients with suspected sepsis. Methods: We conducted a prospective cohort study of adult ED sepsis patients. Venous lactate was obtained within 2 h of ED arrival. Main outcome was subsequent deterioration (defined as any of the following: death, intensive care admission > 24 h, intubation, vasoactive medications for > 1 h, or noninvasive positive pressure ventilation for > 1 h) within 72 h. Patients meeting any endpoint within 1 h of arrival were excluded. Results: Nine hundred and eighty-five patients were enrolled, of whom 84 (8.5%) met the primary outcome of deterioration. Initial lactate ≥ 4.0 mmol/L had a specificity of 97% (95% confidence interval [CI] 94–100%), but a sensitivity of 27% (95% CI 18–37%) for predicting deterioration, with positive and negative likelihood ratios of 10.7 (95% CI 6.3–18.3) and 0.8 (95% CI 0.7–0.9), respectively. A lower threshold of lactate (≥2.0 mmol/L) had a sensitivity of 67% (95% CI 55–76%) and specificity of 66% (95% CI 63–69%), with corresponding positive and negative likelihood ratios of 2.0 (95% CI 1.7–2.3) and 0.5 (95% CI 0.4–0.7). Conclusions: High ED lactate is predictive of subsequent deterioration from sepsis within 72 h, and may be useful in determining disposition, but low lactate is not effective in screening stable patients at risk of deterioration.** © **2018 Elsevier Inc. All rights reserved.**

☐ **Keywords—emergency department; sepsis; lactate; intensive care unit; critical care; risk-stratification**

## INTRODUCTION

In the emergency department (ED), identification of patients with sepsis is critical, as it allows for the prompt initiation of appropriate resuscitation, including fluids and antibiotics (1). Once diagnosis is made and treatment

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is initiated, risk stratification (i.e., determining risk of future deterioration) of this patient population is difficult and ultimately paramount in determining the disposition of the patient (2). While many patients with severe sepsis or septic shock will require critical care in the intensive care unit (ICU), some patients are stable enough for management on the wards. However, patients who subsequently deteriorate on the wards and then require ICU admission have worse outcomes than those who are admitted directly to the ICU from the ED (3–5). It is therefore important to identify patients at risk of short-term deterioration at an early stage (6). Recent work in this area has focused on the utility of early warnings scores, and decision tools, such as the quick Sequential Organ Failure Assessment (qSOFA) (7). Unfortunately, the early data show that such tools have variable accuracy when tested in the ED setting, both prospectively and retrospectively, and include variables that are already suggestive of deterioration, such as hypotension (8–11).

Serum biomarkers present an interesting avenue for investigation in risk stratification of ED patients with sepsis and, to date, > 180 different biomarkers have been linked with this disease process (12). Perhaps the biomarker of greatest interest to emergency physicians is serum lactate (13,14). In the septic ED patient, lactate elevation occurs for several reasons, but the most common is inadequate tissue oxygenation (15). Most of the evidence surrounding the utilization of lactate in ED septic patients comes from patients admitted to hospital, where a lactate level $\geq$ 4.0 mmol/L is highly specific for in-hospital mortality (16). Hyperlactatemia is also a poor prognostic sign in these admitted patients, independent of evidence of organ hypoperfusion or shock, and regardless of the presumed etiology (14,17–19). Furthermore, improved outcomes in patients with septic shock have been associated with clearance of lactate (20,21). However, little is known regarding the use of lactate in risk stratification of ED patients not admitted to hospital, or about the ability of this biomarker to predict short-term deterioration (an important decision for the ED clinician in determining disposition). Furthermore, there are few published data on low lactate levels (i.e., < 2.0 mmol/L) and the prognostic value of a low lactate level in ruling out deterioration in ED patients with sepsis. Several studies have espoused the idea of cryptic shock, suggesting that patients who are hemodynamically stable, yet with evidence of hyperlactatemia, may in fact be in true shock, despite what would appear to be blood pressure capable of providing adequate organ perfusion (22,23). Given this, we aimed to test the ability of initial ED serum lactate in predicting future deterioration among initially stable ED patients (defined as those not requiring endotracheal intubation, initiation of vasopressors or inotropes, or ICU admission, within the first hour following ED arrival). Additionally, with regard to patients with intermediate lactate levels (2.0–3.9 mmol/L), we sought to determine any differences between those who deteriorated and those who did not, as patients in this group are often the most difficult to prognosticate, and up to one-quarter may progress to septic shock (24).

## MATERIALS AND METHODS

This study was approved by the Albert Einstein College of Medicine Institutional Review Board.

## STUDY DESIGN

This was a prospective observational cohort study of adult ED patients satisfying the 1992 Society of Critical Care Medicine (SCCM)/American College of Chest Physicians (ACCP) criteria for diagnosis of sepsis, and performed in the EDs of the Montefiore Medical Center (Moses and Einstein campuses), both urban, academic EDs in Bronx, NY, with a combined annual adult census of > 190,000 visits per year (25). Salaried, trained, fluently bilingual (English and Spanish) ED research associates gathered data for the study. All participants, or their surrogates, provided informed consent in either English or Spanish, based on the patient's preferred language.

### *Selection of Participants*

The study population consisted of adult ED patients ($\geq$21 years of age) who satisfied the SCCM/ACCP criteria for sepsis, and were diagnosed with and treated for sepsis. These criteria require a presumptive or demonstrated focus of infection, combined with at least 2 of the following: temperature > 38° or < 36°C, heart rate > 90 beats/min, respiratory rate > 20 breaths/min or $PaCO_2$ < 32 mm Hg, white blood cells (WBCs) > 12,000 $mm^3$ or < 4000 $mm^3$ or at least 10% immature (band) polymorphonuclear WBCs.

Potential subjects were identified through clinician referral and an electronic sepsis order set (indicating physician suspicion of infection), and screened for enrollment by trained research assistants 24 h/day, 7 days/week from December 2014 to September 2015. Patients were enrolled within 2 h of triage.

### *Exclusion Criteria*

Patients requiring critical care interventions (defined as intubation, noninvasive positive pressure ventilation, or vasoactive medications), or who died within 1 h of arrival were excluded, as the importance of lactate in this population is well understood (16). Furthermore, risk stratification of this patient population is less difficult, as all will