[Original Research]

CHEST

Implications of Centers for Medicare & Medicaid Services Severe Sepsis and Septic Shock Early Management Bundle and Initial Lactate Measurement on the Management of Sepsis

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BACKGROUND: Sepsis remains a significant cause of morbidity and mortality in the United States, leading to the implementation of the Severe Sepsis and Septic Shock Early Management Bundle (SEP-1). SEP-1 identifies patients with "severe sepsis" via clinical and laboratory criteria and mandates interventions, including lactate draws and antibiotics, within a specific time window. We sought to characterize the patients affected and to study the implications of SEP-1 on patient care and outcomes.

METHODS: All adults admitted to the University of Chicago from November 2008 to January 2016 were eligible. Modified SEP-1 criteria were used to identify appropriate patients. Time to lactate draw and antibiotic and IV fluid administration were calculated. In-hospital mortality was examined.

RESULTS: Lactates were measured within the mandated window 32% of the time on the ward (n = 505) compared with 55% (n = 818) in the ICU and 79% (n = 2,144) in the ED. Patients with delayed lactate measurements demonstrated the highest in-hospital mortality at 29%, with increased time to antibiotic administration (median time, 3.9 vs 2.0 h). Patients with initial lactates > 2.0 mmol/L demonstrated an increase in the odds of death with hourly delay in lactate measurement (OR, 1.02; 95% CI, 1.0003-1.05; $P = .04$).

CONCLUSIONS: Delays in lactate measurement are associated with delayed antibiotics and increased mortality in patients with initial intermediate or elevated lactate levels. Systematic early lactate measurement for all patients with sepsis will lead to a significant increase in lactate draws that may prompt more rapid physician intervention for patients with abnormal initial values.

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KEY WORDS: critical care; lactic acid; sepsis; septic shock

ABBREVIATIONS: CMS = Centers for Medicare & Medicaid Services; eCART = Electronic Cardiac Arrest Risk Triage; ICD = International Statistical Classification of Diseases; IQR = interquartile ratio; IVF = intravenous fluids; SEP-1 = Severe Sepsis and Septic Shock Early Management Bundle; SIRS = systemic inflammatory response syndrome

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Sepsis is a leading cause of in-hospital death, and its incidence continues to rise, creating an ever-growing economic and health care burden.[1-3] Recognition of this issue has led to the development of initiatives aimed at promoting recognition and treatment of sepsis through care bundles.[4] On October 1, 2015, the Centers for Medicare & Medicaid Services (CMS) introduced the Severe Sepsis and Septic Shock Early Management Bundle (SEP-1). SEP-1 selects patients who meet two of four systemic inflammatory response syndrome (SIRS) criteria, display at least one new organ dysfunction, and have documentation of suspicion of infection. Patients who meet all three of these criteria within a 6-h period are identified as having "severe sepsis." To meet bundle compliance, providers need to measure serum lactate, obtain blood cultures, and initiate antibiotics within a time window specified by the bundle.[5] An initial serum lactate level must be drawn between 6 h before and 3 h after severe sepsis presentation, followed by a repeat within 6 h of presentation if the initial value is elevated. Given prior work suggesting lactate clearance as a goal of sepsis management, it is likely that patients with elevated values would likely receive more aggressive resuscitation.

The SEP-1 measures are intended to improve timely diagnosis and management of sepsis and are made on the basis of prior studies demonstrating the efficacy of bundles on reducing in-hospital mortality.[6] It is unclear, however, whether SEP-1 captures the appropriate population or what the characteristics of this population are.[7,8] Prior evidence exists to support early antibiotic administration[9]; however, the evidence for early serum lactate measurement is more complex. Studies demonstrate clear correlations between elevated lactate, time to lactate clearance, and mortality in the ED and ICU.[10-12] Whether measuring lactate leads to improved outcomes is unknown. Furthermore, the relationship between delays in initial lactate measurement and mortality has not been examined.

In this study, we aimed to retrospectively apply the SEP-1 definitions to a large inpatient population to identify and characterize patients who met SEP-1 criteria for severe sepsis. We assessed how frequently serum lactate levels were drawn and whether these lactate levels were associated with increased rates of interventions. Last, we aimed to characterize the relationship between delay in lactate measurement and mortality to better understand the utility of lactate measurements in sepsis management.

Materials and Methods

Study Population

Adult patients admitted to the University of Chicago, an urban tertiary care medical with approximately 500 beds, from November 2008 until January 2016 who met one of the International Classification of Diseases, 9th revision (ICD-9), codes specified by SEP-1 (e-Table 1) were included in the study. The protocol was approved by the University of Chicago institutional review board (#15-1705), and a waiver of consent was granted on the basis of general impracticability and minimal harm.

Data Collection

Vital signs, laboratory, orders, ICD-9 codes, and demographic data were collected by the University of Chicago's Clinical Research Data Warehouse, deidentified, and then made available on a secure SQL server for analysis. Nonphysiologic data points were changed to missing as per prior work.[13] ICD-10 to ICD-9 cross-walking was performed to identify SEP-1 ICD-9 codes (e-Table 1). The Electronic Cardiac Arrest Risk Triage (eCART) score, a previously developed model used to predict the risk of cardiac arrest, ICU transfer, and death on wards, was used to adjust for severity of illness.[14]

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Identifying Patients Meeting SEP-1 Criteria

In the SEP-1 measure, patients who meet the following three criteria within a 6-h time frame are identified as demonstrating severe sepsis: (1) at least one organ dysfunction, (2) two or more SIRS criteria, and (3) documentation of suspected source of infection. Because we did not have access to provider documentation, the time of blood culture order was used as a proxy for suspicion of infection. SIRS criteria were defined per the consensus conference definition[15] and organ dysfunction was defined per SEP-1 (e-Table 2), with the exceptions that urine output and drop in systolic BP $>$ 40 mm Hg from baseline were not included as organ dysfunction criteria. Furthermore, to exclude patients with persistent organ dysfunction resulting from chronic comorbidities, we included the additional requirement that if a patient met these criteria for organ dysfunction, it must also be a change of at least 10% from that patient's most normal value during the admission. Finally, patients with an ICD-9 code for end-stage renal disease were excluded from meeting renal organ dysfunction criteria.

Lactate Measurements

All serum lactate samples drawn for admissions meeting the SEP-1 criteria for severe sepsis were analyzed. The time difference between the time a patient met all SEP-1 criteria for severe sepsis and the time of lactate draw was calculated. Serum lactate samples that were drawn within 6 h before and 3 h after the initial time meeting severe sepsis criteria were identified as having met SEP-1 requirements for lactate measurement, as described in the CMS guidelines. Serum lactate samples drawn after 3 h were considered delayed lactate draws.

Statistical Analysis

Patient characteristics were compared between patients of different groups using t tests, Wilcoxon rank sums, and $\chi 2$ tests as