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Developing the Surveillance Algorithm for Detection of Failure to Recognize and Treat Severe Sepsis

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Abstract

Objective: To develop and test an automated surveillance algorithm (sepsis "sniffer") for the detection of severe sepsis and monitoring failure to recognize and treat severe sepsis in a timely manner.

Patients and Methods: We conducted an observational diagnostic performance study using independent derivation and validation cohorts from an electronic medical record database of the medical intensive care unit (ICU) of a tertiary referral center. All patients aged 18 years and older who were admitted to the medical ICU from January 1 through March 31, 2013 (N=587), were included. The criterion standard for severe sepsis/septic shock was manual review by 2 trained reviewers with a third superreviewer for cases of interobserver disagreement. Critical appraisal of false-positive and false-negative alerts, along with recursive data partitioning, was performed for algorithm optimization.

Results: An algorithm based on criteria for suspicion of infection, systemic inflammatory response syndrome, organ hypoperfusion and dysfunction, and shock had a sensitivity of 80% and a specificity of 96% when applied to the validation cohort. In order, low systolic blood pressure, systemic inflammatory response syndrome positivity, and suspicion of infection were determined through recursive data partitioning to be of greatest predictive value. Lastly, 117 alert-positive patients (68% of the 171 patients with severe sepsis) had a delay in recognition and treatment, defined as no lactate and central venous pressure measurement within 2 hours of the alert.

Conclusion: The optimized sniffer accurately identified patients with severe sepsis that bedside clinicians failed to recognize and treat in a timely manner.

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Sepsis is common and lethal in the United States and around the world.[1-3] Septicemia was also ranked as the most expensive in-hospital condition in the United States by the US Agency for Healthcare Quality and Research, based on 2011 data.[4] Current processes for sepsis management (including early goal-directed therapy [EGDT] and the data from the recent ProCESS [Protocolized Care for Early Septic Shock] and ARISE [Australasian Resuscitation in Sepsis Evaluation] trials) have been established.[5-7] The Surviving Sepsis Campaign (SSC) guidelines have refined the exact criteria for advanced disease, including organ dysfunction.[8] However, the fundamental process of sepsis management in these guidelines has not changed substantially, suggesting a barrier in implementation as the source of the continued sepsis problem. There is much room for improvement and optimization of existing computerized sepsis detection and alert systems. Although recent sepsis detection and alert systems have focused on clinical outcomes, these systems have failed to document improvement in clinically meaningful end points.[9-12] Thus, an improved approach is necessary to develop and validate a clinically useful sepsis alert system, especially for implementation in the critical care setting.

The aim of this study was to improve on previous studies in several ways. The first was by specifically targeting severe sepsis/septic shock (referred to as *severe sepsis* throughout the remainder of this article for brevity) to reduce the number of false-positive alerts from isolated or nonseptic systemic inflammatory response

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syndrome (SIRS).[13] The second was to target severe sepsis in the specific context of delay in recognition and treatment. This approach is derived from the concept of "failure to rescue" from the surgical literature, which suggests that hospital characteristics, as opposed to patient characteristics, are the primary determinant of adverse occurrences.[14,15] In this context, one example of delay in recognition and treatment would be progression to severe sepsis due to failure to adhere to established sepsis response and management protocols.[16] The third and final improvement was to target information overload, human error, interruption, and alert fatigue.[17,18] Combined, the objective of this study was to advance, test, and refine a delay in recognition and treatment of severe sepsis detection and alert system ("sniffer") for use in the critical care setting.

PATIENTS AND METHODS

Study Design and Setting

We conducted an observational diagnostic performance study that used independent derivation and validation cohorts for development and testing of the delay in recognition and treatment of severe sepsis sniffer. This study was performed at Mayo Clinic in Rochester, Minnesota, with Mayo Clinic Institutional Review Board approval.

Study Population and Data Collection

All patients aged 18 years and older who were admitted to the medical intensive care unit (ICU) at Mayo Clinic in Rochester, Minnesota, from January 1 through March 31, 2013, and provided research authorization were included in this study. This ICU setting has been described previously.[19] The purpose of this retrospective study was development of the sepsis sniffer algorithm. Thus, no patients admitted to the ICU with research consent were excluded from this study, including those patients with goal-limiting care preferences, such as do-not-resuscitate/do-not-intubate (DNR/DNI) orders. Patients with ICU-acquired sepsis, which typically occurs several days after ICU admission, were effectively excluded from this study.[20,21] It is unlikely that patient/proxy preferences, such as DNR/DNI status, would dramatically alter provisions of care, such as those related to transfer from the emergency department (ED) and/or hospital wards, in a way that would substantially confound the results of this study. At our institution, unless otherwise stated, patients with DNR/DNI orders receive central line placement when clinically indicated.

Patient data were collected using manual chart review and the METRIC (Multidisciplinary Epidemiology and Translational Research in Intensive Care) Data Mart, which has been described previously.[22] The data for the output response of severe sepsis was collected through manual review and scoring of all patient records by 2 trained reviewers (A.M.H., C.T.). Interobserver variability was solved by a third superreviewer (R.K.). This data set served as the criterion standard for the cohort. The data set for the full cohort (587 patients) was then randomly divided in half into derivation (293 patients) and validation (294 patients) cohorts. The derivation cohort was used for algorithm development and testing, while the validation cohort was reserved for final algorithm validation.

Algorithm Development

Sepsis Detection Component. For both manual review and scoring of patient records, as well as the first iteration of the severe sepsis sniffer (Algorithm 1), a standardized protocol for severe sepsis was used (Table 1). For the severe sepsis portion of this algorithm, this definition was divided into 3 components: suspicion of infection, SIRS, and organ hypoperfusion and dysfunction. A positive entry for all 3 of these components within a 6-hour window between ICU admission and ICU discharge (up to 72 hours) was required for classification as severe sepsis positive. Because of the high frequency of microbial culture orders before ICU admission, particularly in patients admitted from the ED, the suspicion of infection domain was permitted to include 72 hours before ICU admission.

Delay in Recognition and Treatment Detection Component. The 2012 international guidelines for management of severe sepsis and septic shock from the SSC were used as the basis for development of the delay in recognition and treatment portion of the severe sepsis sniffer.[8] Specifically, the protocol portion of