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Automated electronic medical record sepsis detection in the Emergency Department

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Background: While often first treated in the Emergency Department (ED), identification of sepsis is difficult. Electronic medical record (EMR) clinical decision tools offer a novel strategy for identifying patients with sepsis. The objective of this study was to test the accuracy of an EMR-based, automated sepsis identification system. Methods : We tested an EMR-based sepsis identification tool at a major academic, urban ED with 64,000 annual visits. The EMR system collected vital sign and laboratory test information on all ED patients, triggering a “sepsis alert” for those with ≥ 2 SIRS (systemic inflammatory response syndrome) criteria (fever, tachycardia, tachypnea, leukocytosis) plus ≥ 1 major organ dysfunction (SBP ≤ 90 mm Hg, lactic acid ≥ 2.0 mg/dL). We confirmed the presence of sepsis through manual review of physician, nursing, and laboratory records. We also reviewed a random selection of non-sepsis alert records. We evaluated the diagnostic accuracy of the sepsis identification tool. Results : From January 1 through March 31, 2012, we analyzed 795 automated sepsis alerts and 300 non-alerts. The true prevalence of sepsis was 293/795 (37%) among alerts and 0/300 (0%) among non-alerts. The positive predictive value was 36.9% (41.7-49.6). Respiratory infections (36.5%) and urinary tract infection (35.5%) were the most common infections among the 293 patients with true sepsis (true positives). Among false-positive sepsis alerts, the most common medical conditions were gastrointestinal (22.9%), traumatic (22.3%), and cardiovascular (17.5%). Conclusion : This ED EMR-based automated sepsis identification system was able to detect sepsis patients. Automated EMR-based detection may provide a viable strategy for identifying sepsis.

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3 **Automated electronic medical record sepsis detection in the Emergency Department**

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INTRODUCTION

Sepsis is the syndrome of microbial infection complicated by systematic inflammation. Sepsis may subsequently lead to organ dysfunction, shock, and death.(Levy et al. 2003) Sepsis is a major public health problem, accounting for more than 750,000 hospital admissions, 500,000 emergency department (ED) visits and 200,000 deaths annually.(Angus et al. 2001; Annane et al. 2005; Jones 2006) Early aggressive therapy is essential for optimizing outcomes from sepsis.(Rivers et al. 2001)

In recent years, physicians have increasingly utilized electronic medical records (EMR) systems to aid clinical decision making.(Levy & Heyes 2012) By collecting and organizing clinical data, EMR systems have strong potential to improve the detection of conditions where symptoms or laboratory findings are difficult to discern. Diagnosis of sepsis is difficult because clinicians may not recognize the constellation of clinical, physiologic and laboratory abnormalities that comprise the syndrome. Several efforts have attempted to use EMR systems for sepsis detection, albeit with marginal results.(Jaimes et al. 2003; Nelson et al. 2011) A prominent limitation of these prior efforts was the absence of data for hypotension or lactic acidosis, which are often prominent features of sepsis and may indicate the need for aggressive protocolized resuscitation.(Rivers et al. 2001)

In this study we sought to determine the accuracy of an automated EMR sepsis detection system in the ED.

METHODS

Study Design

We conducted a retrospective analysis of automated clinical data collected by an ED EMR system. The study was approved via a written application by the Institutional Review Board of the University of Alabama at Birmingham (approval #X120409014).

Study Setting

This study utilized ED data from the University of Alabama at Birmingham (UAB) Hospital, an urban academic tertiary care referral medical center in Birmingham, Alabama, United States. The ED treats over 64,000 patients annually and is the only Level I trauma center in Alabama. While the ED does not restrict the age of treated patients, the ED population is predominantly adult. UAB Hospital has over 900 inpatient beds, including more than 180 critical care beds.

Selection of Subjects - EMR Sepsis Detection System

This study included all ED patients identified with possible sepsis, according to the automated ED EMR sepsis detection system. The Cerner FirstNet® (Kansas City, Missouri) EMR system was utilized in the ED. An automated sepsis detection system was developed for the FirstNet interface, utilizing electronic clinical data. Applied to all ED patients, a “sepsis alert” was triggered if the EMR identified two or more Systemic Inflammatory Response Syndrome (SIRS) criteria and at least one sign of shock. SIRS criteria included 1) (temperature $\leq 36^{\circ}\text{C}$ (96.8°F) or

80 $\geq 38^{\circ}\text{C}$ (100.4°F), 2) respiratory rate ≥ 20 breaths/min, 3) heart rate ≥ 90 beats/min, and 4) total
81 WBC count $\leq 4,000$ or $\geq 12,000$ cells/mm³, or $>10\%$ bands. Signs of shock included 1) systolic
82 blood pressure ≤ 90 mm Hg, or lactic acid >2.0 mg/dL. Nursing staff entered vital signs manually
83 into the EMR system. Laboratory values were populated in an automatic fashion from the
84 hospital laboratory computer system (HealthQuest Data Systems, Highland, California).

85 The EMR system generated alerts in real time as soon as combinations of findings fulfilled
86 defined criteria. All patients treated in the ED were included in the study. The data for this study
87 originated from a 3-month period January 3, 2012 to March 31, 2012, where automated alerts
88 were generated and evaluated *post hoc*, but were not communicated to clinicians.

89 Determination of the true diagnostic accuracy would require manual review of ED records for all
90 patients that did not activate the sepsis detection system. However, this would require manually
91 reviewing over 18,000 medical records, which was not logistically feasible. Therefore, to provide
92 some level of comparison, we randomly selected 300 patients treated in the ED during the study
93 period but who did not activate the EMR sepsis detection system.

94 ***Outcomes and Methods of Measurement***

95 Confirmed sepsis was defined as the presence of 1) a serious infection related to the ED
96 presentation, 2) ≥ 2 SIRS criteria, and 3) systolic blood pressure ≤ 90 mm Hg or lactic acid level
97 ≥ 2.0 mg/dL. Although clinicians usually use a lactic acid cutoff of 4.0 mg/dL to define septic
98 shock, we chose a lower level because our goal was to identify a range of patients, including

those with lower sepsis acuity levels. Two investigators manually reviewed the ED medical records for all sepsis alert activations as well as for the randomly selected non-alert controls. The reviewers resolved all discrepancies by consensus. Inter-rater agreement based upon initial review was kappa=0.78.

Data Analysis

We determined the diagnostic accuracy of the automated EMR sepsis detection system by calculating positive predictive value (PPV) of the sepsis alerts. Because of the sampled nature of the non-alerts, it was not possible to calculate negative predictive value (NPV), sensitivity, specificity and area under the ROC curve. We determined the infection category for true-positive sepsis alerts, We also determined the chief reason for ED visit for false-positive sepsis alerts and true-negative non-sepsis alerts. We conducted all analyses using Excel (Microsoft, Inc., Redmond, Washington) and Stata v.12.2 (Stata, Inc., College Station, Texas).

RESULTS

During the three-month study period, there were 795 activations of the EMR sepsis alert system. Sepsis alert were older than non-alert patients, but this difference was not statistically significant (55 vs. 40 years, $p=1.00$). The gender distribution was similar between the sepsis alert and non-alert patients (50.9% vs. 46.7% male, $p=0.2$).

Of the 795 EMR sepsis alerts, manual record review confirmed the presence of sepsis in 293 cases. (Table 1) The PPV of the sepsis alert system was 36.9% (95% CI: 33.5- 40.3%). Of the 300 randomly selected non-sepsis alert patients, none exhibited sepsis on manual chart review. While not encompassing all ED visits, based upon the sepsis alert and randomly selected non-alert patients, the NPV for the sepsis alert was high (100%; 95% CI: 98.8-100.0%), the sensitivity for sepsis was high (100.0%, 95% CI: 98.7-100.0%), and specificity was low (37.4%, 95% CI: 34.0-40.9%).

Among true positive sepsis alerts, the most common infections were those of the respiratory and urinary tract. (Table 2) Among the false positive sepsis alerts, trauma, non-infectious gastrointestinal disorders and cardiovascular disorders were the most common conditions. (Table 3) The true negative non-sepsis alerts included a range of patients with infections that did not fulfill SIRS criteria. (Table 4)

DISCUSSION

Over the three-month study period, this novel ED sepsis alert system was activated 795 times, identifying nearly 300 confirmed sepsis cases. Our results suggest that an EMR-based sepsis alert system could be used to identify sepsis patients in the ED.

The number of false positive sepsis alerts in this series is not clinically excessive. The clinical identification of sepsis is extremely difficult, requiring assimilation of clinical, physiologic and laboratory data.(Jaimes et al. 2003) Anecdotal data suggest that clinicians often under-detect sepsis cases. Jones et al. found that in a survey of emergency medicine physicians at 30 academic tertiary care hospitals, only 7% reported implementing early goal-directed therapy for sepsis, and the primary reason for this low rate was due to the poor identification of sepsis.(Jones & Kline 2005) Other studies have shown that automated detection of medical conditions like abdominal aortic aneurysm and central line-associated blood stream infections is more effective than by manual surveillance alone.(Padberg et al. 2009; Woeltje et al. 2011) Our observations indicate that one in three sepsis alerts will be associated with a true sepsis case. Thus, the system offers aid in the identification of sepsis cases but with only a modest number of false positives. While we could not formally calculate the sensitivity of the system, the random sample of non-alert patients resulted in no sepsis cases, assuring that the prevalence of false-negatives (undetected sepsis) is relatively low.

The number of false-positive sepsis alerts is not surprising given that many non-infectious medical conditions can present with vital signs and laboratory abnormalities that fulfill SIRS

criteria. For example, patients with cardiovascular, respiratory and even toxicologic conditions may present with tachycardia, tachypnea, or leukocytosis. Patients with trauma may exhibit tachypnea and tachycardia secondary to pain. Elevated lactic acid may be present in a range of conditions due to tissue hypoxia and subsequent anaerobic metabolism.(Bakker et al. 1996)

Prior studies have evaluated the use of EMR clinical decision tools to identify sepsis. Nelson, et al. evaluated the use of an automated surveillance algorithm at the University of Michigan Hospital, classifying sepsis as individuals with ≥ 2 SIRS criteria plus systolic blood pressure of ≤ 90 . The system demonstrated a sensitivity of 64%, PPV of 54%, and NPV of 99% for detecting severe sepsis with signs of organ dysfunction.(Nelson et al. 2011) Our study enhanced the Nelson, et al. criteria by adding elevated lactate (≥ 2.0 mg/dL) as an additional inclusion criteria. As expected, this strategy increased the number of detected sepsis cases but at the cost of additional false positives (decreased PPV). Also, the Nelson study was based upon only 1 week of ED visits. Our study included a broader range of ED patients from a 3-month time frame.

While it would be possible to enhance the system by adding additional laboratory or diagnostic results, we believe that the most important strategy for improving the system's accuracy is to incorporate methods for identifying infections. For example, with clinician input, the system might exclude patients presenting with major trauma where vital signs may mimic those of sepsis. Biomarkers such as procalcitonin may complement sepsis detection efforts; a recent study demonstrated that procalcitonin had an excellent NPV (96%) and good sensitivity (75%) and specificity (71%) for identifying bacteremia and pneumonia.(Albrich & Mueller 2011; Torres et al. 2012) Future studies must evaluate these and other strategies.

LIMITATIONS

Due to logistical limitations, we were not able to examine all non-alert ED patients; as discussed previously, this would have required manual review of 18,000 records. However, our comparison with randomly selected controls offered important insights, including the low rates of false negatives. Examination of a larger series would likely have affirmed a higher NPV. The EMR system depended on manual input of vital signs by ED personnel. Delayed or erroneous entries may have altered alert activation patterns. This study also examined the accuracy of automated sepsis detection but not its clinical implementation. ED personnel reaction to sepsis alert data was not an *a priori* objective of this study but is clearly an extremely important factor that merits additional study. An important future study is to determine how activated prompts from the decision support system to the clinician may increase the number of recognized sepsis cases in clinical practice.

191 **CONCLUSION**

192 This ED EMR clinical support system identified patients presenting to the ED with sepsis.

193 Automated EMR sepsis detection may provide a viable strategy for ED sepsis identification.

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TABLE 1

Emergency Department (ED) automated sepsis alerts, January 1, 2012 – March 31, 2012.
Includes 795 ED visits with triggered sepsis alert. Table includes comparison with 300 randomly selected ED patients that did not trigger a sepsis alert.

Confirmed Sepsis			
Sepsis Alert	Sepsis	No Sepsis	Total
Yes	293	502	795
No	0	300	300
Total	293	802	1095

TABLE 2

Infection types of Emergency Department visits with triggered sepsis alert and confirmed sepsis (true positive alert). A patient may have had more than one infection.

Infection Type	n (%)
Pneumonia or Other Respiratory	107 (36.5)
Urinary Tract	104 (35.5)
Bacteremia	44 (15.01)
Gastrointestinal	43 (14.7)
Soft Tissue Infection	25 (8.5)
Gynecologic	5 (1.7)
Central Nervous System	2 (0.7)
Other Infection	10 (3.4)

TABLE 3

Medical conditions of Emergency Department visits with triggered sepsis alert but not confirmed sepsis (false positive alert). A patient may have had more than one medical condition.

Medical Condition	N (%)
Gastrointestinal	115 (22.9)
Trauma	112 (22.3)
Cardiovascular	88 (17.5)
Respiratory	43 (8.6)
Overdose/Intoxication	42 (8.4)
Central Nervous System	39 (7.8)
Renal	34 (6.8)
Hematologic-Oncologic	15 (3.0)
Miscellaneous	120 (23.9)

TABLE 4

Medical conditions of Emergency Department visits without triggered sepsis alert and without confirmed sepsis (true negative alerts). A patient may have had more than one medical condition.

Medical Condition	N (%)
Trauma	43 (14.3)
Non-infection Gastrointestinal Conditions	30 (10)
Urinary Tract Infections	27 (9.0)
Respiratory Infections	25 (8.3)
Other Infections	20 (6.7)
Non-Infection CNS	16 (5.3)
Soft Tissue Infections	5 (1.7)
Drug Overdose	11 (3.7)
Cardiovascular Conditions	8 (2.7)
Non-Infection Respiratory	3 (1.0)
Gastrointestinal Infections	4 (1.3)
Gynecologic Infections	4 (1.3)
Non-infection Renal	4 (1.3)
Hematologic-Oncologic	1 (0.3)
Non-Infection Other	135 (45.0)