Design of an Electronic Medical Record (EMR)-Based Clinical Decision Support System to Alert Clinicians to the Onset of Severe Sepsis

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Abstract

Background: The aim of our study was to design an electronic medical record -based alert system to detect the onset of severe sepsis with sensitivity and positive predictive value (PPV) above 50%.

Methods: The PPV for each of seven potential criteria for suspected infection (white blood cell count (WBCC) >12 or <4 x 10^9 /L, immature granulocyte count >0.1 K/uL or immature granulocyte % >1%, temperature >38 C. or <36 C. or the initiation of broad-spectrum antibiotics) was determined by chart review of 160 consecutive patients who had evidence of organ system failure (as defined by standard criteria)plus at least one of the proposed criteria. Then, using only criteria with calculated PPV >50%, the charts of sixty consecutive patients who met CMS criteria for severe sepsis were reviewed to calculate the sensitivity of organ dysfunction plus any one of the suspected infection criteria.

Results: Four proposed criteria for suspected infection had PPV >50%: WBCC >12 x 10 9 /L (69%; 95%CI:53-84%), Temperature >38C. (84%; 95%CI:68-100%), Temperature <36C. (57% 95%CI:36-78%), and initiation of antibiotics (70% 95%CI:56-84%). These four criteria were present in 53/60 of the patients with severe sepsis by CMS criteria, yielding a sensitivity of 88.3% (95%CI: 80.2-96.4%). Alert criteria were satisfied before the onset of severe sepsis in 25/53 cases, and within 90 minutes afterwards in 28/53 cases.

Conclusions: Our criteria for suspected infection plus organ dysfunction yields reasonable sensitivity and PPV for the detection of severe sepsis in real-time.

Introduction

The American College of Chest Physicians and the Society for Critical Care Medicine define sepsis as a systemic inflammatory syndrome in response to infection and defined sepsis as “severe” when associated with acute organ dysfunction (1,2). The incidence of severe sepsis varies depending on the method of data abstraction from 300 to >1,000 per 100,000 person-years with an in-hospital mortality of 14.7% to 29.9% (3). Severe sepsis was estimated to cost

U.S. healthcare system more than $24 billion in 2007 (4). The incidence and mortality of severe sepsis is expected to continue to rise (3-6).

Early recognition of severe sepsis and rapid implementation of standardized treatment bundles is associated with improved patient outcomes (7-12), but compliance rates with standardized time-sensitive treatment bundles for severe sepsis are generally in the 30% range (13). One reason may be that clinicians do not always recognize the onset of severe sepsis and therefore don't have the opportunity to initiate all the elements required for bundle compliance in time. Therefore, a system that could alert providers to the onset of severe sepsis could help them achieve bundle compliance.

Clinical Decision Support Systems (CDSSs) use innovative software incorporated into electronic medical records (EMRs) to augment the awareness and expert knowledge of clinicians by providing pertinent and timely information at the point of care. CDSSs are adept at performing surveillance of electronic data to identify patients with vital signs and laboratory findings consistent with clinical deterioration. Several researchers have previously attempted to identify patients with severe sepsis in real-time with EMR-based CDSSs, but these systems suffered poor positive predictive value (PPV) and uncertain sensitivity (14,15). The PPV of a CDSS surveillance alert is important because it is inversely related to the proportion of false alerts. False alerts lead to clinician alert fatigue and subsequent disregard of alert recommendations (16,17). High sensitivity is another important operating characteristic, but sensitivity is typically only achievable at the cost of reducing PPV.

The goal of this pilot study was to develop criteria that could be used in a CDSS to identify patients at the onset of severe sepsis in real-time in order to alert clinicians. We chose to operationalize severe sepsis as organ system dysfunction due to infection, *without* requiring systemic inflammatory response syndrome, since a recent study that showed that the requirement of SIRS in the definition of severe sepsis excludes 1-in-8 patients suffering organ system dysfunction due to infection (18). Organ dysfunction already has a standard definition based on laboratory results and vital signs (2) that are discrete and easily extracted from the EMR by CDSS logic, but *suspected infection* does not. Thus, a specific aim of this study is to determine optimal EMR-based criteria to define *suspected infection* in relation to the diagnosis of severe sepsis. Our hypothesis was that we could identify a set of criteria for *suspected infection* which would have acceptable sensitivity and PPV for severe sepsis when combined with standard organ system dysfunction criteria.

Methods

We chose seven potential criteria to identify suspected infection: the presence of a white blood cell count (WBCC) >12 x 10^9/L or <4 x 10^9/L, immature granulocyte count >0.1 K/uL or immature granulocyte % >1%, temperature >38 C. or <36 C.

or the initiation of broad-spectrum antibiotics (piperacillin/tazobactam, third or fourth-generation cephalosporin, aminoglycoside, carbapenem, or vancomycin). Organ system dysfunction was identified in the EMR as previously described and delineated in Table 1. Our study occurred in two phases. In the first, we tested individual criteria related to suspected infection in order to determine which had PPV >50% and were therefore incorporated into the second phase of the study. In the second phase, we combined those accepted criteria for suspected infection with organ system dysfunction criteria and calculated the sensitivity for the diagnosis of severe sepsis as defined by Centers for Medicare and Medicaid (CMS).

Phase 1. We used Cerner Discern® to access clinical data in our Cerner Millennium® EMR (Cerner Corporation, North Kansas City MO, USA) in order to identify a retrospective cohort of 160 Banner Health inpatients who satisfied any one of the seven potential suspected infection criteria *plus* one organ system dysfunction criteria (see Table 1 below) within an eight-hour window. The cohort consisted of four groups of forty patients each based on the type of suspected infection criteria present: abnormal WBCC, abnormal temperature, elevated immature granulocytes and initiation of antibiotics. Patients were also selected so that half met criteria in the emergency department and half on the hospital wards. Patient selection was otherwise consecutive. Chart reviews were performed by physician research staff to determine whether each patient was suffering the onset of severe sepsis at the time suspected infection and organ dysfunction criteria were satisfied. Such patients were considered to be true positive for the purposes of calculating PPVs. We decided *a-priori* that individual criteria that did not achieve at least 50% PPV would not be used in our final list of accepted criteria for suspected infection to be used in phase 2 of our study. We also compared PPV for each criteria between emergency department patients and inpatients.

Phase 2. The charts of sixty consecutive patients who met CMS criteria for severe sepsis in Banner Health were reviewed to calculate sensitivity of the combination of any *one* of the suspected infection criteria accepted in phase 1, plus one organ system dysfunction criteria (see table 1 below) occurring together within a six-hour window. The gold standard for the diagnosis of severe sepsis, and the time of onset of severe sepsis, were determined using CMS criteria by trained Banner Health data extraction staff for the primary purpose of regulatory reporting to CMS. The chart of each patient identified with severe sepsis by CMS methodology was reviewed to determine how many exhibited criteria for suspected infection and organ system dysfunction within 8 hours *before*, or 90 minutes *after* the onset of severe sepsis determined by CMS methodology. [The rationale for this time window was that a hypothetical alert triggered by these criteria would only be valuable if it identified patients before, or shortly after the onset of severe sepsis]. We considered these to be *true positive* for the purposes of calculating sensitivity.

Table 1. Suspected infection and organ dysfunction criteria.

Suspected infection plus organ system dysfunction Both occurring within any eight-hour window.	
Suspected infection criteria: Any one of the following:	**Organ system dysfunction:** Any one of the following
•Temperature >38 °C •Temperature <36 °C •White blood cell count >12x10^9/L •White blood cell count <4x10^9/L •Immature granulocyte count > 0.1 K/uL • Immature granulocyte % > 1% •Initiation of broad spectrum antibiotics	•Systolic blood pressure <90 mmHg or mean blood pressure <65 mmHg, or plasma lactate >1.7 mmol/L •Plasma creatinine >2.0 mg/dL and 50% increase from prior plasma creatinine •Plasma bilirubin >2.0 mg/dL and 50% increase from prior plasma bilirubin •Platelet count <100x10^9/L •Activated partial thromboplastin time >60 seconds (disregarded if receiving antithrombotic medication) •INR >1.5 (disregarded if patient receiving warfarin) •Confusion Assessment Method for the ICU (CAM-ICU) positive •Oxygen saturation <90%

Results

Phase 1: PPVs with 95% confidence intervals for each of the potential criteria for suspected infection are listed in Table 2 below. Only WBCC had a significantly different PPV when used in the emergency department vs the inpatient wards: 84% vs 50% (p=0.03).

Immature granulocytes and WBCC <4 x 10^9/L had PPV <50% and could be excluded from the set of accepted criteria with no loss of sensitivity. The set of *accepted* criteria include: WBCC >12 x 10^9/L. temperature >38 or <36 and initiation of antibiotics. Finding any one of these accepted criteria in association with organ system dysfunction yielded a PPV of 70% (95%CI: 61-78%) for the diagnosis of severe sepsis.

In 35/115 cases in which patients with one of these accepted criteria for suspected infection were *not* suffering an infection (false positive) the actual diagnoses included: cardiovascular diseases (s/p coronary artery bypass, myocardial infarction, cardiogenic shock), post-operative state, endocrinological disorders (hypothyroidism, diabetic ketoacidosis, adrenal failure), central nervous system pathology (intracranial hemorrhage, subarachnoid hemorrhage, seizure),

obstetrical complications (placenta previa, spontaneous hemorrhage), and gastrointestinal hemorrhage.

Table 2. PPV and 95% CI for individual suspected infection criteria (when found in temporal association with organ system dysfunction) for the clinical diagnosis of severe sepsis.

Potential criteria for suspected infection	Positive predictive value	95% confidence interval
WBCC >12 x 10^9/L	69%	53-84%
WBCC <4 x 10^9/L	20%	0-55%
Temperature >38 C.	84%	68-100%
Temperature <36 C.	57%	36-78%
Immature granulocyte % > 1%	20%	0-40%
Immature granulocyte count > 0.1 K/uL	39%	21-57%
Initiation of antibiotics	70%	56-84%

Conclusions

Our data suggests that the best criteria set for suspected infection are likely to be: WBCC >12 x 10^9/L, temperature >38 or <36 C. or initiation of broad spectrum antibiotics. The PPV of this set of criteria is likely to be >60%. Leukopenia, and elevated immature granulocyte counts each had poor PPV and their exclusion would not significantly diminish the sensitivity of the set of criteria.

Compared to other alert systems, this logic is novel for its abandonment of the use of SIRS criteria and the inclusion of antibiotic initiation. It could be argued that initiation of antibiotics should not be used to identify suspected infection because the clinician starting antibiotics is obviously *already* aware of infection. However, unpublished analysis of 323 Banner health patients who qualified for severe sepsis by CMS criteria showed that 76% of those who failed bundle compliance received appropriate and timely antibiotics, but failed other important aspects of care, such as getting blood cultures before starting antibiotics and assessing lactate concentration. This suggests that a severe sepsis alert, triggering when a clinician enters an order for antibiotics could potentially assist the clinician in ordering *other* bundle elements. Exclusion of antibiotic initiation from our accepted criteria would have reduced the sensitivity of our alert logic to 75%.

The operating characteristics of our CDSS compares favorably to four previously published severe sepsis surveillance CDSSs which utilized SIRS criteria (see table 3 below).

Table 3. Operating characteristics of CDSSs designed to provide surveillance for severe sepsis.

Reference	Sensitivity	Positive Predictive Value
Herasevich et al. (19)	48%	32%
Nelson et al (20)	Not reported	54%
Amland et al (21)	72%	73%
Alsolamy (22)	98%	21%
Our CDSS:	*89%*	*70%*

One of the strengths of this alert logic is that is it widely generalizable. It only includes data that is collected on most, if not all, hospitalized patients. It does not require additional tests or measurements that may limit its utility to a smaller patient population. It does not require physicians or ancillary staff to perform additional tasks or deviate from their standard workflow. Another strength of this logic is that it was created within the software program Cerner Discern® in our Cerner Millennium® EMR, one of the most widely used EMRs across the country. This would potentially allow seamless integration into any hospital system using this software, improving patient care and fulfilling "meaningful use" mandate of the Affordable Care Act. However, our study is only a small pilot study. These results will need further validation using a larger data set. Further studies are needed to show whether a CDSS using these criteria can improve clinical outcomes of patients with severe sepsis.

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