CLINICAL ALERTS BEYOND SIMPLE DETECTION.
ELECTRONIC SURVEILLANCE OF FAILURE TO RESCUE IN SEPTIC SHOCK.

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MOTIVATION

Severe sepsis and septic shock account for about 10% of ICU admissions and 2.9% of hospital admissions in the US (1) and worldwide (2). Sepsis is the 10th leading cause of death in the United States (1, 3) and the most common reason for admission to ICU. Shock in general, or septic shock in particular, is an example of a major public health problem for which an effective treatment exists but is commonly instituted late or not at all. Early goal directed therapy applied within 6 hours of the development of sepsis syndrome can dramatically decrease mortality (4).

Failure to recognize and then treat sepsis appropriately remains a significant cause of patient morbidity and mortality. The principle reason for this error is still “failure to recognize” the syndrome on the side of the healthcare providers.

CURRENT STATUS OF HOSPITAL EMR SURVEILLANCE

Problems with clinical alerts.

In recent years, clinical alerting has become an important feature in hospital EMRs. Alerts have been shown to improve the quality [7,8] and reduce the cost [9] of medical care. But bedside ICU monitors are not designed for early recognition of complex physiologic syndromes. While current monitoring systems effectively monitor the extremes in heart rate and blood pressure, they lack the ability to recognize complex physiologic syndromes. Timely detection of syndromes requires cognizance of multiple factors including relationships between changing vital signs and specific laboratory or radiologic findings and patient comorbidities contained within a comprehensive EMR. The majority of alarms (over 90%) generated by bedside monitors are clinically insignificant and only distract the bedside providers (5). In one study done in the ICU, only eight out of 1455 alerts (0.05%) indicated potential life threatening problems (6). Most humans (about 90%) do not respond to all alarms, but instead they match their response rates to the expected probability of the true alarms (probability matching) (7).

Sepsis and septic shock detection.

As clinical detection of sepsis became a recognized problem, a number of attempts were made to develop electronic surveillance. A prospective computerized screening tool (sepsis sniffer) based on ACCP/ SCCM definition criteria had shown sensitivity of 48% and specificity of 86% with positive predictive value of 32% (5). This is similar to another study for real-time identification of SIRS patients using EMR surveillance that had shown sensitivity of 34% and specificity of 78% when compared to final hospital diagnosis (6). In a recent report, Philips bedside monitors using embedded Surviving Sepsis Campaign guidelines (Protocol Watch) were associated with significant improvements in compliance with the resuscitation bundle and decreased time to administer antibiotics. However, Protocol Watch was not associated with improvements in length of stay or reductions in patient mortality. Accuracy and tool perception by providers were not reported (7).
Problems with sepsis surveillance.
The importance of early recognition and treatment of sepsis is obvious, and systems such as septic shock sniffers can have even more benefits outside of the ICU. However, there are significant limitations in screening for sepsis in part because of the clinical definition. One study reported that 95% of patients admitted to a general medical service met the clinical criteria for SIRS (8). The established definition of SIRS criteria compared with final diagnosis of infection in patients admitted to the emergency rooms of two university based hospitals had a sensitivity of 69%, specificity of 35%, PPV of 90%, NPV of 12% (9). We have done a study assessing the availability of data necessary for detection of septic shock outside the ICU environment (13). Almost 30% of patients admitted to the medical ICU for septic shock did not have the necessary data in the EMR to detect their condition based on sepsis definition criteria (14). Another study conducted in the ICU of a healthcare facility with stage 7 EMR adoption found an average delay of 126 minutes from the time of meeting criteria for severe sepsis/septic shock as determined by physician review and the first appearance of a diagnosis in the EMR (15). This could support the usefulness of automatic sepsis detection in the ICU and using sniffers for determination of patients’ eligibility for enrollment in time-sensitive clinical studies. In a prospective trial using a severe sepsis/septic shock sniffer for enrollment into a clinical study, the sniffer performed with a positive predictive value of 34%. Even with the limitation of study coordinator availability (not available nights and weekends) implementation of electronic screening helped double enrollment (10).

Potential solutions for effective septic shock surveillance.
The availability of a comprehensive Electronic Medical Record (EMR) offers health care institutions the opportunity to develop surveillance algorithms (digital signatures) which identify patients with sepsis syndrome and notify appropriate frontline providers. More advanced smart algorithms in addition to simple detection can dramatically change accuracy of sniffers. For example, a three-step screening tool for early identification of sepsis in the Surgical ICU yielded a sensitivity and specificity of 97% with positive predictive value of 80% (11). To eliminate “alert fatigue” and increase adoption of the advanced electronic environment, it is important to develop electronic decision support systems which can detect provider actions or inactions (“failure to rescue”). Recently our group published results from the prospective implementation of a ventilator induced lung injury sniffer (VILI sniffer). By identifying some meaningful combinations of laboratory data, ventilator settings and combining them with the detection of expected provider actions, we were able to influence bedside practice at moderate cost. Implementation of the VILI sniffer was associated with decreased patient exposure to potentially injurious mechanical ventilation settings. The alert itself had a positive predictive value of 59% and a post implementation survey showed good perception of the alert by healthcare providers (18).
Based on previous experience, the present study was aimed to evaluate the performance of a computerized surveillance system (sepsis sniffer) for delayed resuscitation of patients with severe sepsis/septic shock in the intensive care unit (ICU).

**RESEARCH METHODOLOGY**

The study setting was a tertiary care academic medical center. The present study was done using a historical cohort of consecutive patients (>18 years of age) admitted to a medical ICU during a 2 month period.

To facilitate rapid development of clinical alert systems we previously have designed and tested a Simulation Sniffer Engine (SSE) that allows rapid cycle preliminary testing of new sniffer algorithms in a short period of time with a good level of agreement (12).

**Data source.**

The main data source for this project was the ICU data warehouse (METRIC data mart), a MS SQL based database, which integrates a near-real time copy of clinical and administrative data from the heterogeneous and distributed Mayo Clinic EMR. Replicated EMR data are available in near real time, with a delay ranging from 15 minutes for monitored data and laboratory results to 4 hours for chest radiograph reports and clinical notes (13). The ICU datamart continues to grow, and is now extended to the OR and PACU environments (14). A schematic representation of some of the data feeds in the ICU datamart is presented in Figure 1.

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**Figure 1. Data supplied from METRIC datamart**
Definition/algorithm

We used sepsis definitions improved during iterative process and sensitivity analysis - “digital signature of septic shock” based on ACCP/SCCM Consensus Conference criteria (15) (respiratory rate >20/ min, heart rate >90/ min, body temperature >38.6 C, < 35 C, leukocyte count >12k, < 4k, mean arterial blood pressure <65 mmHg, anion gap >12, base deficit < -5 and lactate >2.5 mmol/ l. Presence of a CVP (Central Venous Pressure) measurement was used as evidence for sepsis treatment initiation.

Figure 2. Basic digital signature of septic shock

All patients’ charts were evaluated by two independent reviewers to determine if sepsis syndrome criteria were met. Disagreements were resolved by a third (senior) reviewer. When the patient met sepsis rules criteria, alerts were generated and recorded. The diagnostic performance markers of the sepsis sniffer such as sensitivity, specificity, positive and negative predictive values were calculated.

RESULTS

A total 401 ICU admissions were analyzed. Thirty five patients with delayed resuscitation of severe sepsis/ septic shock (no central line during the disease course or no CVP at the time of alert) were identified manually. A total of 71 alerts were issued by the sepsis sniffer. Alerts in 28 patients were found to be true positives. Seven patients with sepsis were missed by the sniffer. The “failure to rescue” sepsis sniffer demonstrated a sensitivity of 80% (95% CI: 63-91) and specificity of 88% (95% CI: 84-91) with a positive predictive value of 39% (95% CI: 28-52) and a negative predictive value of 98% (95% CI: 96-99).
DISCUSSION

A real time computerized surveillance system (sepsis sniffer) can identify patients with severe sepsis or septic shock, whose initiation of early goal directed therapy has been delayed.

Delayed recognition of specific critical care syndromes is an error in action involving a temporary or permanent omission which contributes to morbidity, mortality and high costs of care. Our preliminary studies suggest that a “sniffer” approach can be helpful for syndromic surveillance in the ICU and may detect adverse events with good sensitivity and specificity. The severe sepsis / septic shock sniffer could prompt development of more electronic screening tools for early recognition of other major problems in critical care. The potential of this application is currently limited by the technical and administrative abilities of most EMRs which integrate disparate data feeds. Early recognition and treatment of these patients is still a considerable problem in the emergency department, ICU, and hospital wards (22, 23).

Our technology and methodology, when implemented, could potentially:

- Improve patient-safety
- Improve the effectiveness of practice in the ICU
- Improve the effectiveness of observational and experimental clinical research in the ICU

The key factor in development of clinically relevant sniffers is not only detection of condition, it is detection with context of action or inaction.

CONCLUSIONS. FUTURE DIRECTIONS

We have demonstrated a feasible approach that allows us to recognize “failure to rescue” in septic shock patients with high sensitivity and specificity. Integrated near-real time data warehouses such as the METRIC Datamart can be used as interim solutions for sniffers implementations. Established approaches to the development and validation of digital signatures and sniffers will be useful for early recognition of more complex, time-sensitive critical care syndromes.

REFERENCES


The work originated from Multidisciplinary Epidemiology and Translational Research in Intensive Care, Emergency and Perioperative Medicine (METRIC) Clinical Informatics in Intensive Care laboratory.

The biographies of authors and information about other projects can be obtained from laboratory web page (http://mayoresearch.mayo.edu/mayo/research/clinical-informatics-in-intensive-care/)

Authors, Ognjen Gajic, and Vitaly Herasevich have filled United States Patent Application #20110137852 - Sepsis Monitoring and Control