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Validation of sepsis screening tool using StO₂ in emergency department patients



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ABSTRACT

Background: Sepsis is a deleterious systemic response to an infection with a high incidence of morbidity and mortality, affecting more than a million patients a year in the US. The purpose of this study was to develop a screening tool for the early identification of sepsis in emergency department patients using readily available information at triage.

Materials and methods: This prospective, observational study took place at an academic tertiary referral hospital. Over a period of 10 wk, all patients who were seen at triage were screened for study enrollment. Inclusion criteria were adult (age ≥ 18 y) nontrauma patients and exclusion criteria were prisoners and pregnant women. Using a Spot Check StO₂ device to measure StO₂ value, heart rate, respiratory rate, and temperature, these values were used to generate a cumulative screening score indicating whether a patient may have sepsis.

Results: A total of 500 patients were screened. The incidence of sepsis in the present study population was 8.4%. The screening tool yielded a sensitivity of 85.7%, a specificity of 78.4%, a positive predictive value of 26.7%, and a negative predictive value of 98.4%.

Conclusions: Heart rate, respiratory rate, and temperature have good diagnostic potential for the early identification of sepsis among emergency department triage personnel. Additionally, early evidence suggests StO₂ may play a complementary and synergistic role in the early identification of sepsis by triage personnel.

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1. Introduction

Sepsis is a deleterious systemic response to an infection with a high incidence of morbidity and mortality, affecting more than a million patients a year. Sepsis accounts for more than 1,141,000 cases, 193,970 deaths, and \$16.4 billion dollars in

healthcare costs annually and is the leading cause of multiple organ failure and mortality in noncoronary intensive care units (ICUs) in the US [1–3]. It is estimated that there are 260,000 explicit sepsis cases presenting to the emergency department (ED) every year with an ICU admission rate of 31% and an ICU mortality rate of 40% [4]. In a landmark study, it was shown that

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patients presenting with sepsis in the ED randomly assigned to early goal-directed therapy before admission to the ICU resulted in a 34.4% relative risk reduction of in-hospital mortality, compared with patients assigned to standard therapy [5].

Despite significant clinical and research achievements in improving evidence-based treatment of sepsis, the early identification of sepsis remains difficult because of the ambiguous nature of its manifestation. In a previous study, we developed a sepsis screening tool for general surgery patients that incorporates the American College of Chest Physicians and the Society for Critical Care Medicine systemic inflammatory response syndrome (SIRS) criteria: heart rate, respiratory rate, white blood cell (WBC) count, and temperature, generating a graded, cumulative score indicating patients' severity of SIRS derangement. Use of this screening tool in a surgical ICU decreased mortality rates of severe sepsis and septic shock from 35.1% to 24.2% [6]. In light of these advances and others, the 2012 Surviving Sepsis Campaign recommends screening of critically ill patients for sepsis, as early identification and the subsequent treatment according to the Surviving Sepsis Campaign evidence-based guidelines have been shown to reduce morbidity and mortality [5,7,8].

The purpose of this study was to develop a sepsis screening tool that quantifies readily available SIRS criteria in conjunction with an InSpectra StO₂ Spot Check device (Hutchinson Technologies, Hutchinson, MN) for the early identification of sepsis in ED patients at triage. We hypothesized that this screening tool would aid in the early recognition of sepsis in ED patients.

2. Methods

This prospective, observational study took place at Memorial Hermann Hospital, an academic tertiary referral hospital in Houston, TX. Over a period of 10 wk, all patients who were seen at triage were screened for study enrollment, in accordance with the Institutional Review Board–approved protocol. Inclusion criteria were adult (age ≥ 18 y) nontrauma patients and exclusion criteria were prisoners and pregnant women. Additionally, patients were excluded if they bypassed the typical hospital triage station and received intervention in a location other than the ED (e.g., ST elevation myocardial infarction or tissue plasminogen activator protocol patients). All patients enrolled in the present study were screened for sepsis by obtaining their heart rate, respiratory rate, temperature, and StO₂ value at triage. These values were then used to generate a cumulative screening score indicating whether a patient may have sepsis. An InSpectra Near Infrared Spectroscopy StO₂ Spot Check device (Model 300) was used to obtain StO₂ measurements on the thenar eminence of patients' hands in a relaxed position on their lap. Vital signs were obtained by triage staff and recorded by research staff.

The screening tool in this study was developed based on a previously validated inpatient sepsis screening tool [6]. The previous tool incorporated common vital signs and laboratory values readily available to healthcare providers, that is, heart rate, respiratory rate, WBC count, and temperature, and generating a cumulative score that indicates whether a patient may have sepsis [9]. For this current ED population, patients' StO₂ value from an InSpectra Spot Check device was

Table 1 – Patient population descriptive statistics.

Variable	Not septic	Septic (all)	P value
n	458	42	NA
Age	47.2 $\pm$ 18.0	52.4 $\pm$ 18.6	0.076
Triage HR	84.7 $\pm$ 16.9	106.9 $\pm$ 20.5	<0.001
Triage RR	18.9 $\pm$ 2.1	20.3 $\pm$ 3.9	0.043
Triage temp (F)	98.4 $\pm$ 0.9	99.7 $\pm$ 2.0	<0.001
WBC	8.7 $\pm$ 3.7	12.8 $\pm$ 8.0	<0.001
StO ₂ (%)	77.8 $\pm$ 8.4	74.8 $\pm$ 12.6	0.189
Lactate level*	1.9 $\pm$ 1.0	2.4 $\pm$ 1.9	0.416
GCS	14.8 $\pm$ 1.1	14.0 $\pm$ 2.7	0.002
APACHE II*	17.6 $\pm$ 6.7	19.6 $\pm$ 8.6	0.549
SOFA*	5.0 $\pm$ 2.6	6.5 $\pm$ 4.7	0.455
LOS (d)	1.4 $\pm$ 2.8	6.4 $\pm$ 6.6	<0.001
Mortality	0.0%	4.8% (n = 2)	<0.001

APACHE II = Acute Physiology and Chronic Health Evaluation II score; GCS = Glasgow Coma Scale; HR = heart rate; LOS = hospital length of stay; RR = respiratory rate; SOFA = Sequential Organ Failure Assessment score; temp = temperature, in degrees Fahrenheit; WBC = white blood cell count, in 1000 cells/mm³.

Mean $\pm$ S.D.

* Only comparing those that are available.

incorporated into the screening tool instead of WBC count, because blood counts are not available at triage. Thus, heart rate, respiration rate, temperature, and triage StO₂ values were used to generate a cumulative screening score indicating whether a patient may have sepsis at triage. WBC count, lactate draw StO₂, lactate levels, Glasgow Coma Score (GCS), age, hospital length of stay, and mortality were also collected as ancillary data for this study (Tables 1 and 2).

The sepsis gold standard used in the sensitivity analysis was the 2001 American College of Chest Physicians/Society for Critical Care Medicine SIRS criteria plus a documented (or suspected) source of infection. Data were collected, entered, and recalled using a secure research database and all patient

Table 2 – Descriptive statistics: side-to-side comparison.

Variable	Not septic	Sepsis	Severe sepsis	Septic shock
n	458	33	4	5
Age	47.2 $\pm$ 18.0	49.4 $\pm$ 3.3	59.8 $\pm$ 3.1	66.2 $\pm$ 6.0
Triage HR	84.7 $\pm$ 16.9	105.2 $\pm$ 3.4	104.0 $\pm$ 4.9	112.0 $\pm$ 15.4
Triage RR	18.9 $\pm$ 2.1	20.1 $\pm$ 0.6	17.5 $\pm$ 1.7	24.0 $\pm$ 2.9
Triage temp (F)	98.4 $\pm$ 0.9	99.7 $\pm$ 0.3	101.3 $\pm$ 1.1	98.4 $\pm$ 1.1
WBC	8.7 $\pm$ 3.7	12.6 $\pm$ 1.4	17.9 $\pm$ 6.4	10.1 $\pm$ 1.2
StO ₂ (%)	77.8 $\pm$ 8.4	76.2 $\pm$ 1.7	70.3 $\pm$ 5.7	69.0 $\pm$ 11.7
Lactate level*	1.9 $\pm$ 1.0	1.9 $\pm$ 0.4	2.0 $\pm$ 0.6	4.8 $\pm$ 0.9
GCS	14.8 $\pm$ 1.1	14.8 $\pm$ 0.2	12.8 $\pm$ 2.3	10.0 $\pm$ 2.2
APACHE II*	17.6 $\pm$ 6.7	12.5 $\pm$ 2.6	17.7 $\pm$ 3.5	26.4 $\pm$ 3.3
SOFA*	5.0 $\pm$ 2.6	2.0 $\pm$ 1.1	6.3 $\pm$ 2.0	10.2 $\pm$ 1.6
LOS (d)	1.4 $\pm$ 2.8	5.5 $\pm$ 0.8	17.2 $\pm$ 6.6	3.2 $\pm$ 1.7
Mortality	0.0%	0.0%	0.0%	40.0%

APACHE II = Acute Physiology and Chronic Health Evaluation II score; GCS = Glasgow Coma Scale; HR = heart rate; LOS = hospital length of stay; RR = respiratory rate; SOFA = Sequential Organ Failure Assessment score; temp = temperature, in degrees Fahrenheit; WBC = white blood cell count, in 1000 cells/mm³.

Mean $\pm$ SD.

* Only comparing those that are available.

data were deidentified before it was entered. Acute Physiology and Chronic Health Evaluation II scores were calculated using ICU patients' worst blood pressure, temperature, heart rate, respiratory rate, PaO₂ (in millimeters of mercury) and FiO₂, arterial pH, serum HCO₃⁻ (in milliequivalents per liter), serum sodium (in milliequivalents per liter), serum potassium (in milliequivalents per liter), serum creatinine (in milligrams per deciliter), hematocrit (in percent), and WBC count within 24 h of admission according to established guidelines [10]. Sequential Organ Failure Assessment scores were calculated using patients' worst PaO₂ (in millimeters of mercury) and FiO₂, platelets (10³ per cubic millimeter), bilirubin (in milligrams per deciliter), GCS, mean arterial pressure (in millimeters of mercury), vasopressor status (type and dose), serum creatinine (in milligrams per deciliter), and urine output (milliliters per day) within 24 h of admission according to established guidelines [11].

3. Analysis

The sepsis screening tool was validated using a standard sensitivity analysis. A *post hoc* percentile analysis using the same database was done between the nonseptic and septic populations and a new cumulative scoring system for the screening criteria was determined. A follow-up sensitivity analysis was performed with the modified screening tool. A multivariate logistic regression analysis on all variables in Table 1 with a *P* value <0.200 between septic and nonseptic patients was entered into the model to predict the probability of having sepsis at triage. The model was reduced through a variable elimination technique in which the nonsignificant variables were removed in a serial fashion, and the analysis repeated until only statistically significant (*P* < 0.050) variables remained [12]. The sensitivity, logistic regression, and *post hoc* percentile analyses were done using STATA data analysis and statistical software, version 12.1, produced in College Station, TX.

4. Results

Over a period of 10 wk 500 patients were screened. The incidence of sepsis in the study population was 8.4%. There was a significant difference between mean heart rate, respiratory rate, temperature, WBC count, GCS, hospital length of stay, and mortality between septic and nonseptic populations (Table 1). Moreover, a comparison among sepsis, severe sepsis, and septic shock populations shows trends toward increasing severity (Table 2). A multivariate logistic regression analysis demonstrated that triage heart rate, triage temperature, and low triage StO₂ (<75%) were independent predictors of sepsis at triage.

Using a standard sensitivity analysis, the screening tool yielded an initial sensitivity of 31.0%, a specificity of 95.6%, a positive predictive value (PPV) of 39.4%, and a negative predictive value (NPV) of 93.8% (Table 3). A *post hoc* percentile analysis revealed a more optimal cumulative scoring system for the ED population and the tool was modified accordingly (Figs. 1 and 2). A follow-up sensitivity analysis with the new scoring system improved the sensitivity to 85.7% and the NPV

Table 3 – Initial validation, sensitivity analysis.

	Positive	Negative	Total
Sepsis	13	29	42
No sepsis	20	438	458
Total	33	467	500
Prevalence of sepsis	8.4%		
Sensitivity	31.0%	PPV	39.4%
Specificity	95.6%	NPV	93.8%

NPV = negative predictive value; PPV = positive predictive value.

to 98.4%, whereas decreasing the specificity to 78.4% and the PPV to 26.7% (Table 4).

There was a difference among nonseptic, sepsis, severe sepsis, and septic shock patients' mean StO₂ values at triage: 77.8 ± 8.4%, 76.2 ± 1.7%, 70.3 ± 5.7%, and 69.0 ± 11.7%, respectively (Table 2). Moreover, there was an increase in abnormal triage StO₂ values (<75% or ≥90%) among nonseptic, sepsis, severe sepsis, and septic shock patients at triage: 37.1%, 48.5%, 75.0%, and 80.0%, respectively.

Patient Label

ED Triage Sepsis Screening Form

Triage Date/Time: _____

Heart Rate: _____

Temperature: _____

Respiratory Rate: _____

StO₂ Reading: _____

	0	1
Heart Rate	65 - 94	≤ 64 or ≥ 95
Temp (°C)	36.5 - 37.3	≤ 36.4 or ≥ 37.4
Temp (°F)	97.6 - 99.3	≤ 97.5 or ≥ 99.4
Respiratory Rate	≤ 20	> 20
StO ₂ Reading	75 - 89	< 75 or ≥ 90
Total Score		

All Variables Collected at Triage. A Total Score ≥ 2 is a Positive Screen

Fig. 1 – ED sepsis screening tool, with a new cumulative scoring system.

New Cumulative Scoring System	
HR:	≤ 64 or ≥ 95
Temp (F):	≤ 97.5 or ≥ 99.4
RR:	> 20
StO ₂ :	< 75 or ≥ 90

Fig. 2 – New cumulative scoring system. For each variable, 1 point is given if it is within the range for a “positive” value; ≥ 2 points is deemed a positive screen for sepsis.

HR = heart rate, RR = respiratory rate,
Temp = temperature, in degrees Fahrenheit.

5. Discussion

Sepsis continues to present a significant challenge to health-care providers. Over the past 15 y, a great deal of attention has been focused on the development of evidence-based guidelines for the management of sepsis [7,13–15]. The purpose of these guidelines is to provide clinicians with a comprehensive set of evidence-based recommendations for the initial resuscitation of sepsis. Although there is no question that these guidelines have resulted in improvements in patient outcomes, the initiation of these therapies is incumbent on the clinician recognizing that a patient has sepsis. Unfortunately, the early recognition of sepsis remains challenging.

Failure of clinicians to recognize sepsis in its early stages is because of multiple factors. The early signs and symptoms of sepsis are nonspecific, especially in the early phases of sepsis. Although bedside nurses and other healthcare providers are often focused on multiple patients with multiple priorities, the early signs of sepsis are missed. Lack of awareness of the signs and symptoms of sepsis may also contribute to the problem. A national survey of 53 EDs reported that identifying sepsis in the ED was a significant and frequent barrier to initiating early goal-directed therapy [16]. Similar results were reported in a recent study by Burney *et al.* They reported that delay in the diagnosis of sepsis by ED physicians was the most common cause for delay in intervention [17]. In this same study, more than 40% of ED physicians reported that they “hardly ever” order serum lactate levels in patients with

suspected infection. Ultimately, this failure of the clinical team to recognize sepsis in its early phase results in delayed implementation of time sensitive interventions that have been shown to improve outcomes [5,18]. Fortunately, the implementation of a routine sepsis screening programs in the ED and inpatient setting has been shown to aid in the early identification of sepsis and improve patient outcomes. Sadly, routing sepsis screening remains underused.

StO₂ also presents its own challenges. Conceptually, StO₂ shows great promise in controlled perfusion models [19]. However, studies in septic patients show mixed results. StO₂ has been shown to be lower in severe septic patients compared with healthy volunteers, and correlates with SvO₂ and ScvO₂ after hemodynamic stabilization, but does not correlate with severity of illness (as measured by lactate levels and Acute Physiology and Chronic Health Evaluation II scores) [20,21]. On the other hand, in a recent study, low StO₂ was shown to be associated with admission to the ICU in patients that screened positive for sepsis in the ED and exhibited a slight correlation with lactate levels [22].

The discrepancies in the literature are possibly due in part by septic patients at various levels of compensation and disease states at the time of clinical presentation [23]. Some patients may present with active arteriovenous shunting and decreased peripheral microcirculation, whereas others may present shortly after shock and are adequately compensating with minimal peripheral circulatory compromise. Some may even present in a posthypoxic, reactive hyperemic state, possibly manifesting as an abnormally high StO₂. Discrepancies may also indicate that static StO₂ measurements may not adequately assess microcirculatory disturbances in septic patients.

Studies have shown that StO₂ measurements before, during, and after venous occlusion helps noninvasively measure compromise of microcirculation in these patients and may be a superior measurement technique than static StO₂. The rate of desaturation of the thenar eminence after venous occlusion (R_{des} , percent per second), the rate of reestablished saturation of the thenar eminence after blood flow restoration (R_{sat} , percent per second), and reactive hyperemia were compromised in septic shock patients *versus* healthy controls. R_{sat} values also correlated with morbidity and mortality [24–27]. Moreover, although static StO₂ measurements show considerable overlap between septic and healthy volunteers in all published studies, dynamic StO₂ measurements show little overlap [23].

In this study, static StO₂ measurements were obtained and categorized as either abnormal or normal. On the basis of the previous literature and clinical gestalt, abnormal StO₂ values were defined as $<75\%$ or $\geq 90\%$ [28]. This binomial categorization of StO₂ was found to have a better synergistic effect in predicting sepsis than as a continuous variable and helped detect seven septic patients (16.7%) that would have otherwise not been accounted for in a screening tool that did not incorporate StO₂. A logistic regression analysis showed that a low StO₂ value (along with triage heart rate and triage respiratory rate) was an independent predictor of sepsis at triage, supporting the finding that StO₂ plays a complementary role in screening sepsis at triage.

Although the screening tool in its current form (Fig. 1) shows good diagnostic potential for the early identification of

Table 4 – Sensitivity analysis of a new cumulative scoring system.

	Positive	Negative	Total
Sepsis	36	6	42
No sepsis	99	359	458
Total	135	365	500
Prevalence of sepsis	8.4%		
Sensitivity	85.7%	PPV	26.7%
Specificity	78.4%	NPV	98.4%
NPV = negative predictive value; PPV = positive predictive value.			

sepsis among ED triage personnel, careful examination of the sensitivity analysis reveals ways the tool can be further improved. Namely, future modifications of the tool should elucidate the possibility of a source of infection. Only 20% of false-positive patients (20 of 99) had a documented source of infection at discharge or admission and 67% (4 of 6) false-negative patients had an obvious infection source at triage. Thus, a modification of the screening tool that incorporates simple screening questions (analogous to a mini “review of systems” for tuberculosis screening) may aid in determining a potential source of infection and help limit false positives and false negatives [29].

There are also limitations of the screening tool for this population. Patients exhibiting limited SIRS criteria and leukocytosis are prone to being missed (all six false-negative patients had an elevated WBC count [12,000 cells/mm³]). Also, it should be noted that because the incidence of sepsis in this population is low (8.4%), the PPV is inherently limited, regardless of the modifications made to the tool. Moreover, this screening tool is designed to limit the amount of septic patients missed at triage (i.e., limit the number of false negatives). Thus, the sensitivity and NPV of this ED sepsis screening tool were maximized, conceding some level of specificity and PPV.

6. Conclusions

Heart rate, respiratory rate, and temperature have good diagnostic potential for the early identification of sepsis among ED triage personnel. Additionally, early evidence suggests that StO₂ may play a complementary and synergistic role in the early identification of sepsis by triage personnel. However, characterization of StO₂ in this population needs to be investigated further. Moreover, the screening tool's *post hoc* modifications must be validated in a separate prospective study, which is currently underway.

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Disclosure

The authors have no financial or nonfinancial interest in the subject matter or materials discussed in this article.

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