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Original Contribution

A prehospital screening tool utilizing end-tidal carbon dioxide predicts sepsis and severe sepsis



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ABSTRACT

Objective: To determine the utility of a prehospital sepsis screening protocol utilizing systemic inflammatory response syndrome (SIRS) criteria and end-tidal carbon dioxide (ETCO₂).

Methods: We conducted a prospective cohort study among sepsis alerts activated by emergency medical services during a 12 month period after the initiation of a new sepsis screening protocol utilizing ≥2 SIRS criteria and ETCO₂ levels of ≤25 mmHg in patients with suspected infection. The outcomes of those that met all criteria of the protocol were compared to those that did not. The main outcome was the diagnosis of sepsis and severe sepsis. Secondary outcomes included mortality and in-hospital lactate levels.

Results: Of 330 sepsis alerts activated, 183 met all protocol criteria and 147 did not. Sepsis alerts that followed the protocol were more frequently diagnosed with sepsis (78% vs 43%, P < .001) and severe sepsis (47% vs 7%, P < .001), and had a higher mortality (11% vs 5%, P = .036). Low ETCO $_2$ levels were the strongest predictor of sepsis (area under the ROC curve (AUC) of 0.99, 95% CI 0.99-1.00; P < .001), severe sepsis (AUC 0.80, 95% CI 0.73-0.86; P < .001), and mortality (AUC 0.70, 95% CI 0.57-0.83; P = .005) among all prehospital variables. Sepsis alerts that followed the protocol had a sensitivity of 90% (95% CI 81-95%), a specificity of 58% (95% CI 52-65%), and a negative predictive value of 93% (95% CI 87-97%) for severe sepsis. There were significant associations between prehospital ETCO $_2$ and serum bicarbonate levels (r = 0.415, P < .001), anion gap (r = -0.322, P < .001), and lactate (r = -0.394, P < .001).

Conclusion: A prehospital screening protocol utilizing SIRS criteria and ETCO₂ predicts sepsis and severe sepsis, which could potentially decrease time to therapeutic intervention.

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1. Introduction

Severe sepsis caused by overwhelming infection is responsible for significant morbidity and mortality among hospitalized patients [1]. Early identification and aggressive treatment of this disorder has been shown to improve survival [2,3]. Clinical identification of sepsis includes 2 or more of the systemic inflammatory response syndrome (SIRS) criteria in the presence of a suspected infection [1–3]. A hallmark of severe sepsis is hypoperfusion leading to end-organ damage and cardiovascular collapse (septic shock) [1–3]. Objective measures for hypoperfusion allow for risk stratification along the continuum of this disease process.

Lactic acidosis is a well-accepted marker for hypoperfusion and disease severity in this population [2,4] and has been shown to predict mortality in emergency department (ED) patients with infection [5]. Additionally, low end-tidal carbon dioxide (ETCO₂) levels have been

associated with lactic acidosis, organ dysfunction, and mortality in ED patients with suspected sepsis [6,7].

Prehospital identification and initiation of therapy for severe sepsis may expedite resuscitative efforts. Prior studies have shown that sepsis is common among patients transported by emergency medical services (EMS) [8–11], and that outcomes improve with appropriate prehospital care [8,12–14]. It is feasible to obtain serum lactate levels in the prehospital environment [15], and a recent study demonstrated that utilizing this marker of hypoperfusion might allow for recognition of severe sepsis and decrease in-hospital mortality [16].

While early identification and resuscitative efforts may improve outcomes in severe sepsis, obtaining lactate levels in the field can be difficult and expensive. However, prior studies have shown that prehospital providers can accurately obtain ETCO₂ levels simultaneously with traditional vital signs [17]. In the current study, we examined a prospective cohort of patients after initiating a new prehospital "sepsis alert" screening protocol utilizing ETCO₂ as an objective measure for hypoperfusion. We hypothesized that patients meeting all of the protocol criteria would be more likely to have a hospital diagnosis of sepsis and severe sepsis.

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The purpose of a **Sepsis Alert** is to provide pre-arrival Emergency Department notification in order to facilitate rapid assessment and treatment of a suspected severe sepsis patient. A **Sepsis Alert** will be instituted for patients meeting the following **3** criteria:

- 1. Suspected infection
- 2. Two or more of the following:
 - Temperature > 38° C (100.4° F) OR < 36° C (96.8° F)
 - Respiratory Rate > 20 breaths/min
 - Heart Rate > 90 beats/min
- 3. ETCO2≤25 mmHg

Fig. 1. Sepsis alert protocol.

2. Methods

2.1. Design and Setting

We conducted a prospective cohort study among patients transported by a single EMS system to several regional hospitals during a one-year period from July 2014 through June 2015 in Orange County, Florida. The institutional review board at the participating hospitals approved the study protocol.

Inclusion criteria consisted of any case where prehospital personnel activated a "sepsis alert". Per the Orange County EMS system protocols, a sepsis alert is called when an adult patient (≥18 years) has a suspected infection, two or more of the following SIRS criteria (temperature > 38°C or <36°C, heart rate > 90 beats/min, or respiratory rate > 20 breaths/ min) and an ETCO₂ level ≤25 mmHg (see Fig. 1). The protocol was established immediately prior to the study period, and during the rollout time education was provided in the form of a short, on-line training module. Despite this, there were variations in protocol compliance. This was the basis for our comparison groups. Those patients whereby EMS personnel followed all diagnostic criteria of the protocol formed our "protocol compliant" cohort. In one hundred percent of these patients, EMS personnel suspected infection, patients had ≥ 2 of the above SIRS criteria, and initial ETCO₂ values were ≤25 mmHg. This was strictly a protocol driven process - EMS personnel activated sepsis alert notifications based on their determination that patients met all criteria (see Fig. 1). Those patients whereby EMS personnel activated a sepsis alert but did not follow all diagnostic criteria of the protocol defined our control or "protocol noncompliant" group. In the protocol noncompliant group, EMS personnel suspected infection in all patients, but they either did not have ≥2 SIRS criteria (5% of the cases), or ETCO₂ values were >25 mmHg (95% of the cases). This was a paramedic discretionary process, where sepsis alert notifications were activated despite the fact that not all protocol criteria were met.

Exclusion criteria included pediatric patients (< 18 years old), and patients without available hospital records. Orange County, Florida is an urban/suburban region with a population of approximately 1.2 million individuals. The Orange County EMS system consists of 8 Advanced Life Support EMS agencies utilizing the same medical protocols, providing over 100, 000 transports annually.

2.2. Data Collection

Initial out-of-hospital vital signs documented by first arriving EMS personnel including respiratory rate (RR), systolic blood pressure (SBP), diastolic blood pressure (DBP), pulse (P), oxygen saturation (Spo₂), and ETCO₂ were obtained utilizing LIFEPAK ® 15 multiparameter defibrillator/monitors. Prehospital measurement of ETCO₂ is a standard practice performed by paramedics in the Orange County EMS System. ETCO₂ was measured via Microstream capnography using LIFEPAK 15 devices (PhysioControl, Redmond, WA). Microstream capnography is an ETCO₂ sampling method using molecular correlation spectroscopy applicable to both intubated and non-intubated patients. ETCO₂ was recorded when capnographic wave peaks were at a constant

end-tidal for 3 to 5 respirations as directed by protocol. All included patients were spontaneously breathing at the time of evaluation.

Patient age, gender, race, ETCO₂, RR, SBP, DBP, P, Spo₂, were obtained from prehospital run reports. Patient mortality, admission to hospital or intensive care unit (ICU), initial ED vital signs, pertinent past medical history, principle and admitting diagnoses defined by *International Classes of Disease*, *Ninth Edition (ICD-9)* codes, as well as serum bicarbonate (HCO₃), lactate, and calculated anion gap (when available) were obtained from the hospital chart. Records were linked by manual archiving of EMS and hospital data.

The primary outcome was diagnosis of sepsis and severe sepsis upon hospital admission. We also measured mortality, patient disposition described as discharge, hospital admission, or ICU admission, ICD-9 codes, and the relationship between ETCO₂ and HCO₃, anion gap, and lactate levels.

2.3. Analysis

Data were described using means and proportions with 95% confidence intervals. Data were assessed for variance and distribution and comparisons between groups were performed using Fisher exact test and independent sample t tests with pooled or separate variance as appropriate. Receiver operating characteristic (ROC) curves were constructed to assess the performance of $ETCO_2$, and traditional vital signs for predicting sepsis, severe sepsis, and mortality. The correlation between levels of $ETCO_2$ and HCO_3 , anion gap, and lactate were conducted using Spearman's correlation. Significance was set at .05. Data were analyzed using STATA (StataCorp, College Station, TX).

3. Results

There were 330 prehospital sepsis alerts activated over a one-year period. Of the 330 sepsis alerts, 183 (55%) were protocol compliant and 147 (45%) were protocol noncompliant. Complete hospital records were available for 298 patients. The mean age was 70 years (SD17), 169 (51%) were male, 286 (97%) were admitted to the hospital, 100 (34%) were admitted to the ICU, and 25 (8%) died during hospital admission (see Table 1). Among the patients with complete hospital records, 187 (63%) were diagnosed with sepsis and 87 (29%) were diagnosed with severe sepsis (see Table 2). The protocol compliant sepsis alerts were significantly older (72 vs 67 years old, P = .014) and more likely to be admitted to the hospital (99% vs 93%, P = .014) and to the ICU (41% vs 25%, P = .006, see Table 1). A significantly higher percentage of the protocol compliant sepsis alerts were diagnosed with sepsis (78% vs 43%, P < .001) and severe sepsis (47% vs 7%, P < .001), and these patients also had a higher mortality rate (11% vs 5%, P = .036, see Table 1).

In all patients, average temperature was $101.4^{\circ}F$ (95% CI 101.1-101.6°F), P was 118 bpm (95% CI 115-120 bpm), RR was 30 bpm (95% CI 29-31 bpm), SBP was 128 mmHg (95% CI 125-131 mmHg), DBP was 78 mmHg (95% CI 72-85 mmHg), Spo₂ was 93% (95% CI 92%-93%) and ETCO₂ was 25 mmHg (95% CI 25-26 mmHg, see Table 2). There was no significant difference in mean DBP between the group that followed the protocol and those that did not. The overall mean level of ETCO₂ in protocol compliant sepsis alerts was 20 mmHg

Table 1 Demographics

	Protocol noncompliant $N = 147$	Protocol compliant $N = 183$	Total N = 330	P
Age	67 (SD18) [range 16-96]	72 (SD16) [range 24-99]	70 (SD17) [range 16-99]	.014
Gender (% male)	79 (54%)	90 (49%)	169 (51%)	.439
Admitted to hospital $(n = 295)$	124 (93%)	162 (99%)	286 (97%)	.014
Admitted to ICU $(n = 295)$	33 (25%)	67 (41%)	100 (34%)	.006
Diagnostic category ($n = 297$)				
Abdominal/GI	9 (7%)	8 (5%)	17 (6%)	
Altered mental status	13 (10%)	13 (8%)	26 (9%)	
Cardiac	4(3)	1 (1%)	5 (2%)	
Respiratory	20 (15%)	24 (15%)	44 (15%)	
Infectious	58 (44%)	90 (55%)	148 (50%)	.352
Neurological	2 (2%)	1 (1%)	3 (1%)	
Metabolic/endocrine	3 (2%)	8 (5%)	11 (4%)	
Trauma	0 (0)	0 (0)	0 (0)	
Alcohol/drugs	0 (0)	0 (0)	0 (0)	
Urinary/renal	15 (11%)	15 (9%)	30 (10%)	
Other	8 (6%)	5 (3%)	13 (4%)	
Mortality $(n = 298)$	6 (5%)	19 (11%)	25 (8%)	.036
Developed sepsis ($n = 298$)	58 (43%)	129 (78%)	187 (63%)	<.001
Developed severe sepsis	9 (7%)	78 (47%)	87 (29%)	<.001

(95% CI 19-20 mmHg) and in protocol noncompliant it was 33 mmHg (95% CI 32-34 mmHg; P < .001, see Table 2). Sepsis alerts that were protocol compliant also had higher P (120 bpm, 95% CI 117-124 bpm vs 115 bpm, 95% CI 111-119 bpm, P = .043) and RR (31 bpm, 95% CI 30-32 bpm vs 28 bpm, 95% CI 27-30 bpm, P = .007), and lower SBP (125 mmHg, 95% CI 121-129 mmHg vs 132 mmHg, 95% CI 127-137 mmHg, P = .031) and Spo₂ (92%, 95% CI 92-93% vs 94%, 95% CI 92-95%, P = .043, see Table 2). Interestingly, protocol noncompliant sepsis alerts had significantly higher mean temperatures (101.9°F, 95% CI 101.7-102.2°F) vs 100.9°F, 95% CI 100.6-101.3°F, P < .001).

ROC curves were constructed to determine the accuracy of prehospital ETCO₂ and conventional vital signs for predicting outcomes when a sepsis alert was activated. By comparison of ROC curves, ETCO₂ had a higher discriminatory power to predict sepsis, severe sepsis, and mortality than the other collected variables. When all patients were considered, the area under the ROC curve predicting sepsis was 0.99 for ETCO₂ (95% CI 0.99-1.00; *P* < .001) and 0.64 for temperature (95% CI 0.64-0.71; P < .001, see Fig. 2A). The area under the ROC curve predicting severe sepsis was 0.80 for ETCO₂ (95% CI 0.73-0.86; P < .001), 0.41 for temperature (95% CI 0.33-0.49; P = .029), 0.65 for SBP (95% CI 0.57-0.73; P < .001), 0.64 for DBP (95% CI 0.55-0.72; P = .001),and 0.59 for Spo₂ (95% CI 0.52-0.68; P = .024, see Fig. 2B). The area under the ROC curve predicting mortality was 0.70 for ETCO₂ (95% CI 0.57-0.83; P = .005), 0.31 for temperature (95% CI 0.18-0.48; P = .005) .018), 0.62 for SBP (95% CI 0.48-0.76; P = .089), and 0.55 for Spo₂ (95% CI 0.40-0.70; P = .497, see Fig. 2C).

In the 259 subjects that had a metabolic blood panel drawn, ETCO₂ was associated with metabolic acidosis. There was a significant correlation between ETCO₂ and HCO₃ levels with a correlation coefficient of 0.415 (P < .001), and a negative correlation between ETCO₂ and anion gap with a correlation coefficient of -0.322 (P < .001, see Fig. 3A and B). Lower ETCO₂ levels also correlated with elevated serum lactate

levels. There was a negative relationship between ETCO₂ and lactate in the 89 subjects where serum lactate was measured, with a correlation coefficient of -0.394 (P < .001, Fig. 3C).

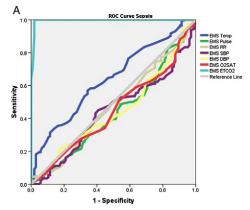
To better establish the effectiveness of the sepsis alert protocol, comparisons were performed between the protocol compliant and protocol noncompliant groups. For those sepsis alerts that followed the protocol, the sensitivity for predicting sepsis was 69% (95% CI 62%-75%), the specificity was 67% (95% CI 57%-75%), the positive predictive value was 78% (95% CI 70%-84%), and the negative predictive value was 99% (95% CI 92%-100%). The sensitivity for predicting severe sepsis was 90% (95% CI 81%-95%), the specificity was 58% (95% CI 52%-65%), the positive predictive value was 47% (95% CI 39%-97%), and the negative predictive value was 93% (95% CI 87%-97%). The sensitivity for predicting mortality was 76% (95% CI 54%-90%), the specificity was 46% (95% CI 40%-52%), the positive predictive value was 11% (95% CI 7%-18%), and the negative predictive value was 95% (95% CI 90%-98%). The sensitivity for predicting ICU admission was 67% (95% CI 57%-76%), the specificity was 50% (95% CI 43%-57%), the positive predictive value was 41% (95% CI 33%-49%), and the negative predictive value was 75% (95% CI 66%-

4. Discussion

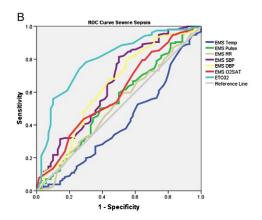
This study demonstrates that it is feasible for prehospital providers to utilize a sepsis screening tool that incorporates $ETCO_2$ as an objective measure for hypoperfusion, and suggests that severe sepsis can be identified in this manner. Appropriate use of a sepsis alert protocol incorporating ≥ 2 SIRS criteria and an $ETCO_2 \leq 25$ mmHg in adult patients with suspected infection identified patients that were more likely to be diagnosed with sepsis or severe sepsis, require ICU admission, and had a higher mortality rate. Regardless of whether the protocol was appropriately followed, decreased prehospital $ETCO_2$ levels correlated with metabolic acidosis and increased inhospital lactate levels. Furthermore,

Table 2 Prehospital vital signs

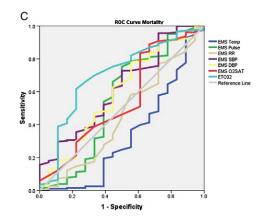
	Protocol noncompliant N $= 147 (95\% CI)$	Protocol compliant $N=183\ (95\%\ CI)$	Total N = 330 (95% CI)	P
Temperature ($n = 264$)	101.9 (101.7-102.2)	100.9 (100.6-101.3)	101.4 (101.1-101.6)	<.001
Range	[96.6-106.3]	[91.5-104.3]	[91.5-106.3]	
Pulse	115 (111-119)	120 (117-124)	118 (115-120)	.043
Respiratory rate	28 (27-30)	31 (30-32)	30 (29-31)	.007
Systolic BP	132 (127-137)	125 (121-129)	128 (125-131)	.031
Diastolic BP	77 (74-81)	79 (68-91)	78 (72-85)	.784
Oxygen Saturation ($n = 318$)	94 (92-95)	92 (91-93)	93 (92-93)	.043
$ETCO_2 (n = 320)$	33 (32-34)	20 (19-20)	25 (25-26)	<.001



EMS VITAL SIGNS	AUC (95% CI)	P-Value
ETCO2	0.99 (0.99-1.00)	< 0.001
Temperature	0.64 (0.57-0.71)	< 0.001
Pulse	0.44 (0.36-0.51)	0.081
Respiratory Rate	0.47 (0.40-0.54)	0.417
Systolic BP	0.44 (0.37-0.51)	0.114
Diastolic BP	0.45 (0.38-0.52)	0.163
Oxygen Saturation	0.45 (0.38-0.52)	0.165

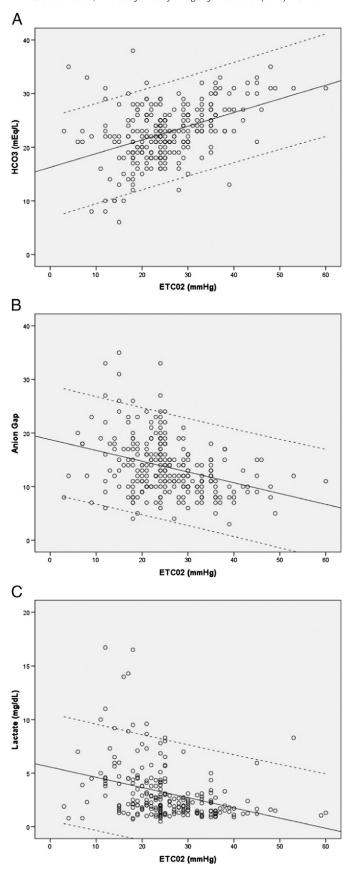


EMS VITAL SIGNS	AUC (95% CI)	P-Value
ETCO2	0.80 (0.73-0.86)	< 0.001
Temperature	0.41 (0.33-0.49)	0.029
Pulse	0.54 (0.46-0.63)	0.309
Respiratory Rate	0.52 (0.43-0.60)	0.690
Systolic BP	0.65 (0.57-0.73)	< 0.001
Diastolic BP	0.64 (0.55-0.72)	0.001
Oxygen Saturation	0.59 (0.52-0.68)	0.024



EMS VITAL SIGNS	AUC (95% CI)	P-Value
ETCO2	0.70 (0.57-0.83)	0.005
Temperature	0.31 (0.18-0.48)	0.018
Pulse	0.55 (0.38-0.72)	0.478
Respiratory Rate	0.45 (0.30-0.60)	0.490
Systolic BP	0.62 (0.48-0.76)	0.089
Diastolic BP	0.59 (0.44-0.74)	0.217
Oxygen Saturation	0.55 (0.40-0.70)	0.497

Fig. 2. A, ROC predicting sepsis. B, ROC predicting severe sepsis. C, ROC curve predicting mortality.



 $\label{eq:Fig. 3.} \textbf{A.} \text{ A. Correlation between ETCO}_2 \text{ and HCO}_3 \ (n=259); \text{ correlation coefficient} = 0.415 \ (P < .001). \ \textbf{B.} \text{ Correlation between ETCO}_2 \text{ and anion gap } \ (n=253); \text{ correlation coefficient} = -0.322 \ (P < .001). \ \textbf{C.} \text{ Correlation between ETCO}_2 \text{ and lactate } \ (n=89); \text{ correlation coefficient} = -0.394 \ (P < .001).$

among all collected prehospital vital signs, low ETCO₂ concentration had the best predictive value for sepsis, severe sepsis, and mortality.

Exhaled ETCO₂ is a function of basal metabolic rate, cardiac output, and ventilation [18]. A recent study suggested that abnormal prehospital ETCO₂ levels are associated with in-hospital mortality, lactate levels, and metabolic acidosis across a wide cohort of patients [17]. Others have reported a relationship between ETCO₂ and disease severity or mortality in adult patients with shock [19], sepsis [6,7], and metabolic disturbances [20], as well as pediatric patients with diabetic ketoacidosis [21] and dehydration [22]. Additionally, low ETCO₂ levels are associated with lactate levels [23], odds of operative intervention [23], and mortality [24,25] in trauma patients. The current report suggests that ETCO₂ may be utilized as part of a prehospital screening process for severe sepsis. The advantage of ETCO₂ relative to lactate is that it can be measured immediately and noninvasively, making it a simple, clinically useful outcome predictor for prehospital providers. Capnography is easily and frequently used in prehospital care [16], and the detection equipment is standard for many advanced life support units. Previous reports have demonstrated that ETCO₂ predicts mortality and is inversely proportional to serum lactate levels in ED patients with suspected sepsis [7]. This study suggests a similar performance as an outcome predictor in prehospital patients with suspected sepsis.

An analysis of sepsis incidence and outcomes in prehospital emergency care demonstrated that septic patients are commonly transported by EMS and have a high mortality rate [10,11]. Several studies have shown that a large percentage of septic patients arrive to the ED by ambulance, including those that require critical care [10–12]. Characteristics of septic patients transported by EMS included elevated heart and respiratory rates [10], and a small study showed that time to antibiotics was decreased when sepsis was identified by prehospital providers [8]. An observational study showed that prehospital placement of an intravenous catheter and administration of intravenous fluids decreased mortality in patients with severe sepsis [14], and Guerra et al. [16] reported that the activation of a sepsis alert protocol utilizing point-of-care lactate levels may decrease mortality. Here, we show that a prehospital sepsis alert protocol utilizing ETCO₂ successfully screens for severe sepsis without the need for point-of-care lactate. The combination of factors that produce ETCO₂ may make it difficult to interpret in critically ill patients, as levels can be altered with a change in respiratory rate or administration of certain medications. Since it is measured in real time, ETCO₂ levels may also change relatively quickly as compared with serum lactate levels, and it is unknown how these levels change in association with lactate clearance. Further studies will be necessary to determine if this protocol will decrease inpatient

Several large trials have demonstrated that early identification and aggressive therapy reduce mortality in sepsis and severe sepsis [2,3]. Despite questions regarding appropriate physiological targets, it is well accepted that minimizing delay to antibiotics therapy is paramount [26]. Mortality increases with delayed administration of antibiotics [27], and empirical antimicrobial treatment has shown to improve outcomes [26]. The appropriate delivery of antibiotics typically requires several administrative and clinical tasks to be performed, such as the registration and initial evaluation of the patient, and the drawing of blood cultures. Pre-arrival notification from EMS may allow hospitals to better utilize resources such as beds, staffing, pharmaceuticals, and lab equipment to expedite this process, thus promote better outcomes.

The most common cause for noncompliance with the protocol was the criteria for $ETCO_2$ (139 or 95% of the group met all criteria except for $ETCO_2 \le 25$ mmHg). In fact, the average $ETCO_2$ was significantly higher in the protocol noncompliant group. Across all patients, low $ETCO_2$ correlated with elevated lactate levels and predicted sepsis, severe sepsis, and mortality, suggesting that it serves as an objective measure for hypoperfusion. Since the average temperatures were higher in the non-compliant group, it is possible that the EMS providers felt more confident that patients in this group had an infection, and

proceeded with the sepsis alert despite not meeting the ETCO₂ criteria. While the diagnosis of sepsis was not uncommon in this group, the incidence of severe sepsis was significantly lower when compared to the protocol compliant group. This suggests using ETCO₂ as an objective marker for hypoperfusion may help discriminate between potentially septic and severely septic patients.

There are several limitations to this study. The comparison groups were due to poor adherence to the initial criteria for sepsis alerts. Although protocol compliance improved over the course of the study, there was still a large number of protocol noncompliant sepsis alerts. Another limitation to this study is that patients enrolled were all sepsis alert activations, and we are unaware how many potentially septic patients were not recognized by the providers. Ideally, all patients diagnosed with severe sepsis in the hospital would be linked back to EMS transport to determine the actual incidence of appropriate protocol usage. Sepsis alerts that followed the protocol were significantly older, so it is possible that the increase in disease severity and mortality were biased by advanced age or comorbid conditions. However, the predictive value to ETCO₂ for sepsis, severe sepsis, and mortality was constant across groups. The data collected for this study represent only a single-point assessment for both ETCO₂ and lactate levels. A continuous assessment of lactate clearance and concomitant ETCO₂ concentration may better reflect the severity of illness.

Further studies are necessary to evaluate if this sepsis alert protocol reduces hospital mortality, and whether any improvement in care is due to pre-arrival notification, specific interventions, or both. Also of interest is the trending of $ETCO_2$ during resuscitation, and how it may relate to lactate clearance as a prognostic indicator.

5. Conclusion

In conclusion, prehospital patients may be screened for severe sepsis with a protocol utilizing ETCO₂. When appropriately followed, a sepsis alert protocol incorporating ≥ 2 SIRS criteria and an ETCO₂ ≤ 25 mmHg in adult patients with suspected infection predicted sepsis (69% sensitivity, 67% specificity), severe sepsis (90% sensitivity, 58% specificity), ICU admission (67% sensitivity, 50% specificity) and mortality (76% sensitivity, 46% specificity). Furthermore, prehospital ETCO₂ is correlated with elevated lactate levels in patients with suspected sepsis. Further studies are necessary to determine if this protocol can be used to decrease time to antibiotics and improve outcomes in septic patients.

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