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Original Contribution

Early recognition of sepsis through emergency medical services pre-hospital screening☆

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ABSTRACT

Background: The Surviving Sepsis Campaign implemented a 3-hour bundle including blood cultures, lactate, intravenous fluids, and antibiotics to improve mortality in sepsis. Though difficult to achieve, bundle compliance is associated with decreased hospital mortality. We predict that the implementation of an Emergency Medical Services (EMS) sepsis screening tool will improve 3-hour bundle compliance.
Objectives: To determine if pre-hospital sepsis screening improves 3-hour bundle compliance.
Methods: Prospective implementation of an EMS sepsis screening tool (June 2016–November 2016) was compared to a historical control (August 2015–March 2016). The protocol was facilitated via communication between nurses and EMS personnel. The primary outcome was 3-hour bundle compliance. Secondary outcomes included time to individual bundle components.
Results: Of 135 patients screened, 20 were positive and included in the study, and subsequently compared to 43 control patients. Baseline demographics were similar, except median Sequential Organ Failure Assessment (SOFA) score was higher for the pre-EMS tool group (5 [interquartile range (IQR) 2–8] vs. 2 [IQR 1–4], $p < 0.01$). Three-hour bundle compliance was significantly higher in the EMS tool group (80% vs. 44.2%, $p < 0.01$). The pre-EMS tool group had lower median time to lactate (15 [IQR 0–35] vs. 46 min [IQR 34–57], $p < 0.001$), 30 mL/kg IV fluids (6.5 [IQR 0–38] vs. 46 min [IQR 27.5–72], $p < 0.001$), and, although not significant, antibiotics (63.5 [IQR 44–92] vs. 72 min [IQR 59.5–112], $p = 0.26$).
Conclusion: Implementation of an EMS sepsis screening tool resulted in improved 3-hour bundle compliance compared to retrospective control.

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1. Introduction

Sepsis is a life-threatening response to infection that can lead to tissue ischemia, organ failure, and death [1]. Progression to the most severe form of sepsis, septic shock, can dramatically increase mortality [1]. Early intervention with antibiotics and fluid resuscitation is critical to patient outcomes. Septic shock mortality increases by 7.6% every hour the patient is left without appropriate antibiotics [2]. In 2012, The Surviving Sepsis Campaign (SSC) recommended that early intervention of sepsis patients is of vital importance for reducing mortality [3,4]. Early intervention includes a bundle to be completed within 3 h of recognition of severe sepsis or septic shock. The bundle is comprised of measurement of serum lactate concentration, fluid resuscitation of 30 mL/kg intravenous (IV) fluids for hypotension or lactate ≥4 mmol/L, blood cultures prior to antimicrobials, and the administration of broad spectrum antibiotics for suspected or documented infection [4].

The evidence for the need of early identification and medical intervention for septic patients is clear; however, global compliance of the bundle guidelines is lacking. One study showed that overall compliance of the SSC 3-hour bundle is 19% [5]. In addition, patients who received care with full compliance of the 3-hour bundle had a 40% decrease in hospital mortality [5]. The 3-hour bundle guidelines significantly reduce sepsis mortality with appropriate compliance; however, further evidence is needed to determine how complete bundle compliance can be achieved.

One study found that half of septic patients that present to the Emergency Department (ED) arrive via Emergency Medical Services (EMS)

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[6]. EMS provides great opportunity for early sepsis recognition and medical intervention. EMS early interventions have been shown to improve outcomes in time-sensitive cases of stroke, cardiac arrest, myocardial infarction, and trauma [7-9]. Evidence shows that vital sign based sepsis screening in the pre-hospital setting often leads to earlier initiation and completion of the resuscitation bundle protocol [10]. The impact of pre-hospital screening and initiation of treatment has been widely debated, with one study concluding that although the bundles were completed in less time, the overall mortality rate did not improve [11]. Another study showed that initiation of intravenous access and fluids in the field decreased the mortality rate [9]. There is further need to explore the pre-hospital setting to improve both the screening process of septic patients and 3-hour bundle compliance in order to improve sepsis patient outcomes.

2. Methods

This retrospective cohort study was conducted at a large, multispecialty, quaternary-care academic center Emergency Department in the United States in partnership with all EMS providers that transported to the ED. This study was approved by the academic center's Institutional Review Board. The Emergency Department has a yearly census of approximately 47,000 patients, with 21% of patients transferred via EMS. The study took place in a high acuity ED with an admission rate of 33%. During the 6-month period of the study, June 2016 to November 2016, there was a census of 22,476 patients with approximately 4800 patients arriving by ambulance. In 2017, the Emergency Department received 22,743 calls with 10,040 transported to the ED. An EMS pre-hospital sepsis screening tool was created and prospectively implemented (Fig. 1). The screening tool was compared to a retrospective cohort historical control of EMS patients who presented to the Emergency Department with an initial presentation of severe sepsis or septic shock between August 2015 and March 2016. Severe sepsis was defined as documented two out of four Systemic Inflammatory Response Syndrome (SIRS) criteria, a suspected infection, and evidence of organ dysfunction such as an elevated lactate (>2 mmol/L), acute mental status change, hypotension with a mean arterial pressure <65 mm Hg or systolic pressure <90 mm Hg, or an oxygen saturation <90%. Septic shock was defined as severe sepsis with persistent hypotension or end organ dysfunction despite fluid resuscitation or vasopressors. The protocol was carried out with the communication between Emergency Communications Registered Nurse (ECRN) and EMS personnel while the patient was en route to the ED. If the patient screened positive, EMS was directed by the ECRN to administer a 500 mL 0.9% NaCl fluid bolus, unless there was evidence of fluid overload. The ECRN then noted the time and notified the attending physician of a positive sepsis screen. SSC 3-hour bundle compliance and the time to SSC 3-hour bundle recommendations were recorded and compared between groups. The majority of providers in the study were ALS providers. Of all providers, only two were BLS providers. All providers participating in the study were educated on sepsis and the sepsis protocol prior to initiation of the protocol. Both ALS and BLS providers were able to identify sepsis and utilize the screening tool. Only ALS providers were able to initiate the fluid bolus. The screening tool consisted of the following seven possible criteria: Respiratory Rate >20 breaths per minute, Heart Rate >90 beats per minute, Systolic Blood Pressure <90 mm Hg, Documented Fever or History of Temperature >38.3 °C or <36 °C (>100.9 °F or <96.8 °F), New Onset of Mental Status Change, Oxygen Saturation <90%, and Suspected Infection. ECRN personnel directed the screening process by asking EMS responders if any of the seven criteria were present in the patient. The ECRN completed a screening tool form which was filed in a collection folder located in the radio room. The form was labeled with a sticker that included the name and Electronic Medical Record number of the patient. All patients over 18 years of age who presented to the ED via EMS between June 2016 and November 2016 were screened with the tool. The presence of three or more of the criteria was considered a positive screen and sepsis protocol was immediately initiated. Patients with the following conditions were excluded from both study groups: <18 years of age, trauma, cardiopulmonary arrest, pregnancy, ST-segment elevation myocardial infarction (STEMI), and stroke. All ECRN and EMS personnel received standardized education.

The primary outcome was 3-hour bundle compliance. Secondary outcomes included time to completion of the following bundle components: measurement of serum lactate concentration, fluid resuscitation of 30 mL/kg IV fluids for hypotension or lactate ≥4 mmol/L, and administration of broad spectrum antibiotics for suspected or documented infection. Other secondary outcome measures included the following: blood cultures prior to antimicrobials, hospital mortality, 30-day mortality, hospital length of stay (LOS), Intensive Care Unit (ICU) LOS, vasopressors, and hydrocortisone.

Retrospective chart review was conducted on a historic cohort of patients who presented to the Emergency Department via EMS with severe sepsis or septic shock between August 2015 and March 2016. Time zero for the pre-EMS screening tool group was defined as the time when two out of four SIRS criteria, a suspected infection, and organ dysfunction were documented. Signs of organ dysfunction

Respiratory Rate > 20 breaths per minute

Heart Rate > 90 beats per minute

Systolic Blood Pressure < 90 mmHg

Documented Fever or History of Temperature >38.3°C or <36°C (>100.9°F or <96.8°F)

New Onset of Mental Status Change

O_2 Saturation less than 90%

Suspected Infection

1. Stop if sepsis criteria not met
2. If 3 or more criteria are met, patient is positive

Fig. 1. Emergency Medical Services (EMS) pre-hospital sepsis screening tool. All patients arriving to the Emergency Department via EMS were screened.

include an elevated lactate (>2 mmol/L), acute mental status change, hypotension with a mean arterial pressure <65 mm Hg or systolic pressure <90 mm Hg, or an oxygen saturation <90%. Time zero for the post-EMS screening tool group was defined as the time of the first vital sign upon presenting to the ED via EMS. Vital signs at time zero, creatinine, albumin, white blood cell count, suspected source of infection, blood culture results, presence of chronic comorbid conditions such as chronic obstructive pulmonary disease and chronic kidney disease, time to antibiotics, amount and time to intravenous fluids, time to lactate and lactate level, hospital and ICU LOS, hospital and 30-day mortality, and use of vasopressors and hydrocortisone were recorded for both study groups. Median Sequential Organ Failure Assessment (SOFA) score was calculated for both study groups. Three-hour bundle compliance was assessed and recorded as a percentage. Prior to the implementation of the EMS pre-hospital sepsis screening tool, there was no sepsis screening program in place. Therefore, the study compared two groups. One pre-intervention historical control group with no existing sepsis screening program and a post-intervention group with the EMS pre-hospital sepsis screening tool implemented.

Descriptive statistics were used to characterize baseline demographics. Chi-square test or Fisher's exact test, as appropriate, were used to analyze categorical data. Comparisons of parametric continuous variables were conducted using a *t*-test. Non-parametric data was expressed as a median using the Mann-Whitney test. A *P*-value <0.05 was considered significant in the bivariate analysis. A multivariate logistic regression was used to account for confounding variables and to determine if the EMS pre-hospital sepsis screening tool was independently associated with improved 3-hour bundle compliance.

3. Results

Sixty-three adults were included in this study (pre-EMS tool group: $n = 43$; post-EMS tool group: $n = 20$). The electronic medical records of 126 patients were reviewed retrospectively; 43 of the patients were included in the pre-EMS tool group. Of the 135 patients screened with the screening tool, 22 were positive and 2 of the patients who screened positive were excluded due to age and study enrollment during a prior hospitalization (Fig. 2). Baseline characteristics and comorbidities were similar between the study groups, with the exception of the SOFA score (Table 1). The median SOFA score was significantly higher for the pre-EMS tool group (5 [interquartile range (IQR) 2–8] vs. 2 [IQR 1–4], $p < 0.01$). The primary outcome of 3-hour bundle compliance was significantly higher in the post-EMS tool group compared to the pre-EMS tool group (80% vs. 44.2%, $p < 0.01$). The pre-EMS tool group had a lower median time to serum lactate concentration measurement (15 min [IQR 0–35] vs. 46 min [IQR 34–57], $p < 0.001$) and a lower median time to 30 mL/kg IV fluids (6.5 min [IQR 0–38] vs. 46 min [IQR 27.5–72], $p < 0.001$). Median time to broad spectrum antibiotics was lower in the pre-EMS tool group (63.5 min [IQR 44–92] vs. 72 min [IQR 59.5–112], $p = 0.26$), however; not significant (Table 2).

Median hospital LOS was significantly shorter in the post-EMS tool group (8 days [IQR 5–12] vs. 5 days [IQR 3–6], $p = 0.01$). Median ICU LOS was also significantly shorter in the post-EMS tool group (3 days [IQR 0–6] vs. 0 days [IQR 0], $p = 0.001$). Hospital mortality was lower in the post-EMS tool group (11.6% vs. 0%, $p = 0.14$), however; not significant. A significantly larger percentage of patients in the pre-EMS tool group required vasopressors (46.5% vs. 10.5%, $p < 0.01$) and hydrocortisone (39.5% vs. 10%, $p = 0.02$) (Table 2). Suspected sources of infection were similar between groups ($p = 0.17$), with genitourinary, pneumonia, and unknown the most common (Table 1).

Variables included in the multivariate logistic regression were pre-screening tool group vs. post-screening tool group, baseline SOFA score, atrial fibrillation, and heart failure. After accounting for confounders, pre-screening tool group vs. post-screening tool group, baseline SOFA score, and atrial fibrillation were found to be independently predictive of 3-hour bundle compliance. Heart failure was found to be inversely predictive of 3-hour bundle compliance.

4. Discussion

We found that an EMS pre-hospital sepsis screening tool was associated with an increased 3-hour bundle compliance. This provides evidence that the EMS pre-hospital sepsis screening tool was effective at promoting completion of the 3-hour bundle for sepsis patients. Despite improvement in bundle compliance, we found that time to the individual bundle components of IV fluids, broad spectrum antibiotics, and

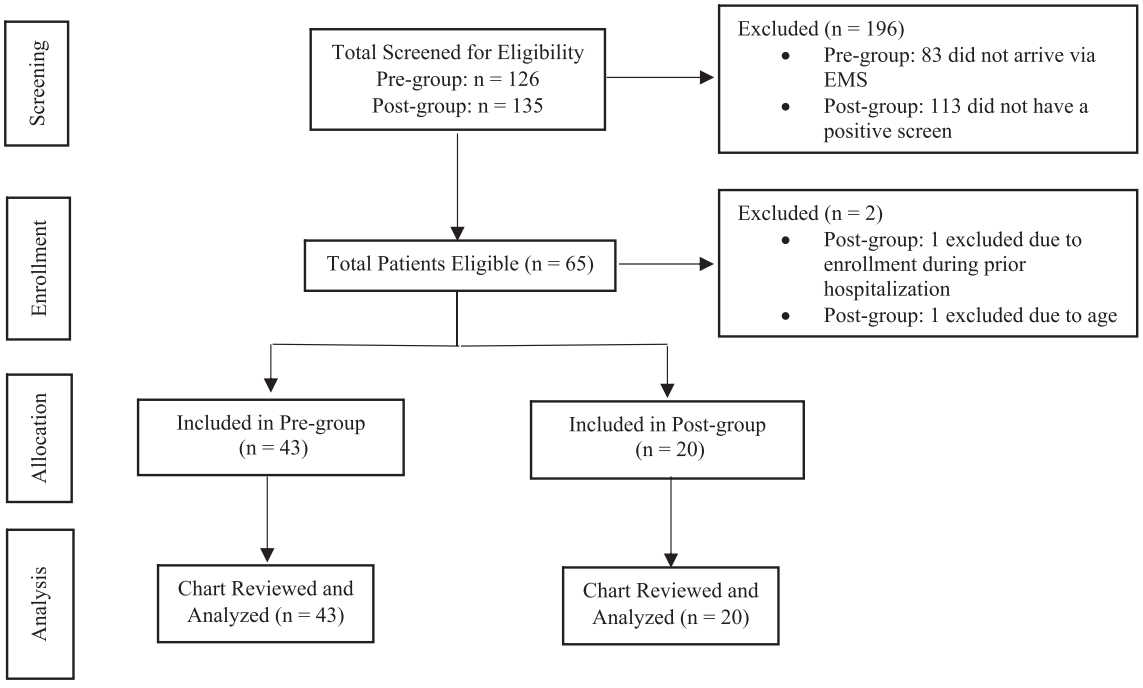

Fig. 2. Flowchart of included and excluded screens. EMS = Emergency Medical Services. Pre-group = Pre-screening tool group. Post-group = Post-screening tool group. Arriving to the Emergency Department via EMS is a requirement needed for patients to be included in the study for both the pre-screening tool group and the post-screening tool group.

Table 1
Baseline demographics. IQR = Interquartile Range. SOFA = Sequential Organ Failure Assessment. Significant difference between groups: $p < 0.05$.

Characteristic	Pre-screening tool ($n = 43$)	Post-screening tool ($n = 20$)	P-value
Age, mean (IQR)	63 (56–73)	70.5 (45.5–76)	0.86
Sex, male, n (%)	24 (55.8)	11 (55.8)	0.95
Race, white, n (%)	20 (46.5)	7 (35)	0.52
SOFA score, median (IQR)	5 (2–8)	2 (1–4)	0.003
Comorbidities, n (%)			
Atrial fibrillation	11 (26.2)	2 (10)	0.14
Coronary artery disease	10 (23.3)	2 (10)	0.21
Cancer	18 (41.9)	7 (35)	0.60
Stroke	11 (25.6)	3 (15)	0.35
Chronic obstructive pulmonary disease	5 (11.6)	1 (5)	0.40
Heart failure	13 (30.2)	3 (15)	0.20
Hypertension	27 (62.8)	15 (75)	0.34
Liver disease	7 (16.3)	1 (5)	0.21
Chronic kidney disease	13 (30.2)	5 (25)	0.67
Source of infection, n (%)			0.17
Pneumonia	11 (25.6)	3 (15)	
Abdominal	4 (9.3)	0 (0)	
Genitourinary	8 (18.6)	8 (40)	
Bloodstream	3 (6.98)	1 (5)	
Skin and soft tissue	3 (6.98)	1 (5)	
Other	1 (2.3)	3 (15)	
Unknown	13 (30.2)	4 (20)	

serum lactate measurements were higher in the post-EMS tool group. This is likely due to higher disease severity in the pre-EMS tool group, as evident in the higher median SOFA score in the pre-EMS tool group. A prospective, multicenter study consisting of 1449 patients in 40 intensive care units in 16 countries found that increased SOFA scores were associated with worsening organ failure and increased mortality [12]. Another prospective observational cohort study of 352 consecutive patients admitted to the ICU calculated a SOFA score for each patient every 48 h while admitted to the ICU. Their results demonstrated that higher average SOFA scores throughout the ICU stay and highest SOFA scores overall corresponded to an increased likelihood of organ failure and death [13]. Therefore, patients with higher SOFA scores would naturally be triaged to receive faster care in the Emergency Department upon arrival. Since our post-EMS tool group had a lower median SOFA score, it would likely mean that those patients had a higher probability of appearing more stable upon arrival and a less likelihood of death overall. This could explain why bundle completion took more time in the post-EMS tool group. However, the increase in bundle compliance in the post-EMS tool group, despite the lower SOFA scores, suggests that the screening tool performed its intended role. These patients may have appeared less critical, but they still received more comprehensive care.

Table 2
Primary and secondary outcomes. IQR = Interquartile Range. IVF = Intravenous Fluids. LOS = Length of Stay. ICU = Intensive Care Unit. Significant difference between groups: $p < 0.05$.

Primary outcome	Pre-screening tool ($n = 43$)	Post-screening tool ($n = 20$)	P-value
3-Hour bundle compliance, n (%)	19 (44.2)	16 (80)	<0.01
Secondary outcomes			
Time to Lactate, median (IQR)	15 (0–35)	46 (34–57)	<0.001
30 mL/kg IVF, n (%)	19 (46.3)	11 (73.3)	0.07
Time to IVF, median (IQR)	6.5 (0–38)	46 (27.5–72)	<0.001
Blood cultures prior to antibiotics, n (%)	42 (97.7)	20 (100)	0.49
Time to antibiotics, median (IQR)	63.5 (44–92)	72 (59.5–112)	0.26
Hospital LOS, median (IQR)	8 (5–12)	5 (3–6)	0.01
ICU LOS, median (IQR)	3 (0–6)	0 (0)	0.001
Hospital Mortality, n (%)	5 (11.6)	0 (0)	0.14
Vasopressors, n (%)	20 (46.5)	2 (10.5)	<0.01
Hydrocortisone, n (%)	17 (39.5)	2 (10)	0.02

Patients in the post-EMS tool group also had improved outcomes in terms of hospital and ICU LOS, vasopressor and hydrocortisone use, and a non-significant trend towards improved mortality. This is likely due to the difference in baseline severity of illness indicated by the difference in SOFA scores rather than to the screening tool. We attempted to control for this difference with a multivariate logistic regression analysis.

Previous studies have shown that sepsis screening tools can be implemented in the pre-hospital setting using a variety of variables for criteria. A retrospective cohort study examining 555 EMS encounters created the Pre-hospital Severe Sepsis (PRESS) score to be used by EMS to screen for severe sepsis with a sensitivity of 86% and specificity of 47% [14]. Chief complaint, age, nursing home status, temperature, and blood pressure were the variables found to most predict severe sepsis [14]. To our knowledge, no further validation of the PRESS score has been published. This study also did not seek to determine the impact of the PRESS score on patient care and outcomes upon arrival to the ED [14]. Hunter et al. also piloted a pre-hospital sepsis screening tool using suspected infection, temperature, heart rate, respiratory rate, and end tidal volume of CO_2 ($ETCO_2$) [15]. When sepsis was suspected, a sepsis alert was initiated to the incoming hospital. They found that sepsis alert patients were more likely to be diagnosed with sepsis or severe sepsis upon arrival [15]. They also determined that $ETCO_2$, which could be measured in the back of an ambulance, was a better predictor of severe sepsis and mortality than other variables such as vital signs [15]. This study demonstrated the feasibility of implementing a pre-hospital screening tool, but it did not examine the impacts of these tools on treatment quality measures. A prospective observational study of 160 patients transported by EMS showed that 33 patients who had a documented suspicion of sepsis received treatment and antibiotics faster than those 127 who had no documented suspicion [16]. The study did not analyze the effects of earlier treatment on ICU stay and overall survival. This study also relied on EMS documentation instead of using a standardized screening tool. Similar to our study, Guerra et al. used EMS education and application of a vital sign based severe sepsis screening tool to investigate the effect of pre-hospital screening on the detection of severe sepsis in 112 patients by EMS providers over 1 year. A Sepsis Alert Protocol was then initiated on all patients EMS deemed to have severe sepsis [17]. Retrospective analysis showed that the 32 of 67 severe sepsis patients correctly identified by EMS providers had a faster time to antibiotics, more fluids at 2 and 6 h, and a shorter hospital LOS compared to patients who were not identified by EMS [17].

Our use of education and a screening tool aimed to remove any variation in EMS provider knowledge and judgement. Therefore, our protocol is based on variables that are included in standardized measures such as the SIRS criteria and the qSOFA score. The protocol also has the ability to easily and quickly evaluate patients in the pre-hospital setting. Since no pre-hospital sepsis screening tools have been validated by multiple robust studies, we created our own screening tool to standardize the EMS assessment of patients with objective criteria. Therefore, our screening tool still requires external validation. Our primary aim was to investigate the effects of a pre-hospital sepsis screening tool on bundle compliance and time to treatment in the ED since studies are lacking. These previous studies have demonstrated the ability to implement a reliable screening tool, while our study aimed to measure the effects of these tools on care quality and patient survival. We were able to determine that a combined effort of the ED and EMS to implement and act on the screening tool led to increased SSC 3-hour bundle compliance.

5. Limitations

Data collection heavily depended on the ability of ECRN personnel to successfully communicate with EMS via radio and fill out the sepsis

screening tool forms. As a result, many potential patients were missed due to missing screening tools, especially on weekends and overnights when nursing staff and radio room coverage was limited. Inconsistent form filling, incorrect Electronic Medical Record number labeling of screening forms, and physical misplacement of the sepsis screening forms all led to data loss. This process led to a lower than anticipated sample size. Data collection has continued and will be analyzed at a later date to generate more robust results. Documentation was provided by different providers in each case, and there is no way to ensure accuracy and consistency after the fact. The objective nature of our screening tool lessened the likelihood of inaccurate data, but we still relied on ED personnel to accurately determine a time zero for notifying the emergency physician of possible sepsis. The screening tool created for the study still requires external validation. Due to the exact number not being saved in hospital records, the number of patients between June 2016 and November 2016 who arrived by ambulance, as noted in the methods section, is an estimation. Lastly, the number of patients transported by ALS versus BLS providers could not be obtained due to information not being saved in hospital records.

6. Conclusions

There is great potential in the pre-hospital setting for earlier recognition of sepsis in patients arriving to the ED via EMS. Early recognition of sepsis will allow medical personnel to initiate sepsis protocol and decrease an important variable in sepsis mortality, time. We demonstrated that the use of a pre-hospital sepsis screening tool was associated with significant improvement in 3-hour bundle compliance, likely due to improved recognition of sepsis. Further studies should be conducted to increase sample size and power. More data is needed to determine the impact that pre-hospital sepsis screening has on outcomes such as mortality and progression to septic shock.

Declarations of interest

None.

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