American Journal of Emergency Medicine 37 (2019) 114–117

Contents lists available at ScienceDirect

American Journal of Emergency Medicine

journal homepage: www.elsevier.com/locate/ajem

Brief Report

Prehospital sepsis alert notification decreases time to initiation of CMS sepsis core measures

Christopher L. Hunter [a,b,*], Salvatore Silvestri [a], Amanda Stone [a], Anne Shaughnessy [a], Stacie Miller [a], Alexa Rodriguez [a], Linda Papa [a,b]

[a] Department of Emergency Medicine, Orlando Regional Medical Center, Orlando, FL, United States of America
[b] University of Central Florida College of Medicine, Orlando, FL, United States of America

ARTICLE INFO

Article history:
Received 6 August 2018
Received in revised form 20 September 2018
Accepted 22 September 2018

Keywords:
Prehospital
Sepsis
End-tidal carbon dioxide
Antibiotics

ABSTRACT

Objective: To determine if prehospital identification of sepsis will affect time to Centers for Medicare and Medicaid services (CMS) sepsis core measures and improve clinical outcomes.
Methods: We conducted a retrospective cohort study among septic patients who were identified as "sepsis alerts" in the emergency department (ED). Metrics including time from ED registration to fluid resuscitation, blood cultures, serum lactate draws, and antibiotics administration were compared between those who had pre-arrival notification by EMS versus those that did not. Additionally, outcomes such as mortality and intensive care unit (ICU) admission were recorded.
Results: Of the 272 total patients, 162 had pre-arrival notification (prehospital sepsis alerts) and 110 did not. The prehospital sepsis alert group had significantly lower times to intravenous fluid administration (6 min 95%CI 4–9 min vs 41 min 95%CI 24–58 min, $p < 0.001$), blood cultures drawn (12 min 95%CI 10–14 min vs 34 min 95%CI 20–48 min, $p = 0.003$), lactate levels drawn (12 min 95%CI 10–15 min vs 34 min 95%CI 20–49 min, $p = 0.003$), and administration of antibiotics (33 min 95%CI 26–40 min vs 61 min 95%CI 44–78 min, $p = 0.004$). Patients with prehospital sepsis alerts also had a higher admission rate (100% vs 95%, $p = 0.006$), and a lower ICU admission rate (33% vs 52%, $p = 0.003$). There was no difference in mortality (11% vs 14%, $p = 0.565$) between groups.
Conclusions: Prehospital sepsis alert notification may decrease time to specific metrics shown to improve outcomes in sepsis.

1. Introduction

Sepsis, defined by organ failure in response to severe infection, may develop into septic shock and is responsible for significant morbidity and mortality [1-3]. Early identification and aggressive treatment, including fluid resuscitation, broad spectrum antibiotics, and close monitoring of perfusion, has been shown to improve survival [4-6]. Recently, the Centers for Medicare and Medicaid Services (CMS) adopted a quality process aimed at standardizing the treatment of sepsis and septic shock and encouraging protocols that stress early identification and treatment strategies [7]. Although they remain controversial, these core measures are tied to reimbursement and quality metrics. They include obtaining serum lactate and blood cultures, as well as administering antibiotics and intravenous fluids [7]. In response, many hospitals have established standing orders and alert processes to help identify these patients and improve compliance.

Delays in first medical contact to antibiotic administration increase mortality in septic patients [8]. Although sepsis is common among patients transported by emergency medical services (EMS) [9-11] and outcomes improve with appropriate prehospital care [9,12-15], studies suggest personnel are undertrained in recognition of the disorder [16]. Multiple screening tools have been studied to improve upon recognition, including the quick sequential organ failure assessment (qSOFA) score [17]. Recently, we described a screening tool utilizing end-tidal carbon dioxide (ETCO2) that was shown to be sensitive and specific in the prehospital environment [18] and may outperform qSOFA in this setting [19].

The current study compares the compliance with CMS sepsis core measures between septic patients in the emergency room that were identified by prehospital providers as "sepsis alerts" versus those that were not. We hypothesized that patients identified by EMS providers would have decreased times to initiation of fluid resuscitation and antibiotic administration, as well as lactate and blood culture draws.

* Corresponding author at: Orlando Health Emergency Medicine Residency, Orange County EMS System, Orlando Health Air Care Team, 86 W. Underwood Street, Suite 200, MP 31, Orlando, FL 32806, United States of America.
E-mail address: christopher.hunter@orlandohealth.com (C.L. Hunter).

https://doi.org/10.1016/j.ajem.2018.09.034
0735-6757/

2. Methods

2.1. Design and setting

We conducted a retrospective cohort study among adult patients (≥18 years old) diagnosed with sepsis who were identified as "sepsis alerts" in the emergency department (ED) at Orlando Regional Medical Center (ORMC) during a 3-year period from 4/13–4/16. Orange County, Florida is an urban/suburban region with a population of approximately 1.2 million individuals. The OCEMS system consists of eight Advanced Life Support EMS agencies utilizing the same medical protocols, providing over 100,000 transports annually. ORMC is a large, urban, tertiary receiving hospital with approximately 90,000 ED visits annually. Principle diagnosis of sepsis was defined by International Classification of Disease version 9 (ICD-9). The institutional review board at the participating hospitals approved the study protocol.

Inclusion criteria consisted of any case where a "sepsis alert" was activated by the ED. Sepsis alerts can be activated by ED staff at the time of triage or clinician evaluation, as well as by arriving Orange County EMS System (OCEMS) transport vehicles. Emergency Department "sepsis alerts" are defined by physician discretion based on clinical presentation or an internal nursing screening tool consisting of three or more of the following criteria: RR > 30 breaths/min, oxygen saturation < 93%, new altered mental status, systolic blood pressure < 100 mm Hg, ETCO < 26 mm Hg, age > 65 years old, or immunocompromised patient. These patients may arrive through ED triage or from a non-OCEMS EMS agency that does not have sepsis alert protocols. Per OCEMS 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 mm Hg. Regardless of whether it is activated by ED or prehospital staff, the sepsis alert at ORMC brings additional physician, nursing, and phlebotomy staff to the patient's bedside, allows for standing orders including intravenous access, laboratory and radiographic tests, and notifies nursing administration for potential ICU disposition.

Patients were excluded if they were not activated as a sepsis alert in the ED. Exclusion criteria also included pediatric patients (<18 years old), and patients without available prehospital or hospital records.

2.2. Data collection

Patient age, gender, mortality, admission to hospital or intensive care unit (ICU), initial ED vital signs including ETCO2, and serum lactate levels were obtained from the hospital chart. Time to blood culture draw, serum lactate draw, initiation of intravenous fluids, and initiation of antibiotics were calculated from the hospital chart utilizing patient registration into the emergency department as time zero. Charting of these tasks is performed by nursing staff and time-stamped by the electronic medical record (All Scripts/Sunrise®). Prehospital sepsis alerts were verified by linking EMS and hospital data.

The primary outcomes were time to blood culture draw, time to serum lactate draw, time to initiation of IVF, and time to initiation of antibiotics. We also measured mortality and patient disposition described as discharge, hospital admission, or ICU admission.

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's Exact test and independent sample *t*-tests with pooled or separate variance as appropriate. Significance was set at 0.05. Data were analyzed using STATA (StataCorp, College Station, TX).

3. Results

Of the 272 total patients, 162 had pre-arrival notification (prehospital sepsis alerts) and 110 did not. The average age was 67 years old (SD17), with the prehospital sepsis alert group being statistically older (69 versus 64 years old, $p = 0.024$, see Table 1), and 49% of patients were female. Ninety eight percent of all patients were admitted to the hospital and 41% were admitted to the ICU. The average lactate level was 3.3 mM/L (95%CI 2.9–3.6 mM/L), and there was an overall mortality rate of 12% (see Table 1).

The prehospital sepsis alert group had significantly lower times to intravenous fluid administration (6 min 95%CI 4–9 min vs 41 min 95% CI 24–58 min, $p < 0.001$), blood cultures drawn (12 min 95%CI 10–14 min vs 34 min 95%CI 20–48 min, $p = 0.003$), lactate levels drawn (12 min 95%CI 10–15 min vs 34 min 95%CI 20–49 min, $p = 0.003$), and administration of antibiotics (33 min 95%CI 26–40 min vs 61 min 95%CI 44–78 min, $p = 0.004$, see Fig. 1). Patients with prehospital sepsis alerts also had a higher admission rate (100% vs 95%, $p = 0.006$), and a lower ICU admission rate (33% vs 52%, $p = 0.003$, see Table 1). The prehospital sepsis alert group had a slightly higher RR (27 bpm 95%CI 25–28 bpm vs 24 bpm 23–26 bpm, $p = 0.044$) and pulse (112 bpm 95%CI 108–116 bpm vs 102 bpm 95%CI 97–106 bpm, $p = 0.001$, see Table 1). The prehospital sepsis alert group also had a lower mean DBP (67 mm Hg 95%CI 64–71 mm Hg vs 82 mm Hg 95%CI 79–85 mm Hg, $p < 0.001$, see Table 1). ETCO2 levels were lower in the prehospital sepsis alert group (22 mm Hg 95%CI 20–23 mm Hg vs 32 mm Hg 95%CI 28–35 mm Hg, $p < 0.001$). However, there was no difference in mortality (11% vs 14%, $p = 0.565$) or lactate levels (3.4 mM/L 95%CI 2.9–3.8 mM/L vs 3.1 mM/L 95%CI 2.7–3.6 mM/L, $p = 0.528$), see Table 1) between groups.

4. Discussion

This study suggests that a prehospital sepsis alert screening tool decreases time to workup and subsequent CMS sepsis bundle compliance. However, in this cohort there was no change in mortality. Prehospital sepsis alerts were associated with a higher overall hospital admission rate but a lower ICU admission rate, which may reflect upon successful early resuscitative efforts. Both groups had similar mortality and lactate levels, suggesting that a differing disease severity was not the cause for these findings.

Sepsis care has evolved over the last decade, with a current focus on early identification and aggressive therapy. Large trials have shown aggressive fluid resuscitation, frequent monitoring of perfusion status, and early antibiotic administration improves outcomes [5]. As incentive to standardize best practices, CMS initiated timed sepsis bundles to encourage compliance with core measures [7]. Within the first 3 h of presentation, hospitals must obtain lactate levels and blood cultures, and administer antibiotics. For patients with septic shock, they must also complete a 30 mL/kg resuscitation with crystalloid fluids prior to perfusion reassessment. Sepsis bundles require reassessment of perfusion status within 6 h of presentation. Compliance with such measures requires early identification and significant resources for patient registration, phlebotomy, and drug administration. Prehospital sepsis alerts may improve upon these metrics by providing pre-arrival notification, allowing the facility to prepare for immediate offload, gathering of staff and equipment, and physician assessment. By encouraging recognition of septic patients in the field, the current protocol also directed EMS providers to obtain IV access and begin crystalloid resuscitation. These processes – pre-arrival notification, IV access, and immediate fluid administration – were likely responsible for improvement of the CMS bundle compliance. While the CMS core measures were designed with best practices in mind, it is currently unknown if compliance improves survival in septic patients.

Several prior studies have noted an association between prehospital identification of sepsis and improved outcomes [12-15]. In the current

Table 1
Comparison of characteristics of patients with no prehospital sepsis alert versus prehospital sepsis alert.

	No prehospital sepsis alert N = 110 [95%CI]	Prehospital sepsis alert N = 162 [95%CI]	Total N = 272 [95%CI]	p-Value
Age	64 (SD18)	69 (SD16)	67 (SD17)	0.024
Gender (% female)	56 (51%)	78 (48%)	134 (49%)	0.347
Admission (n = 255)	104 (95%)	145 (100%)	249 (98%)	0.006
ICU admission (n = 254)	57 (52%)	48 (33%)	105 (41%)	0.003
Mortality (n = 255)	15 (14%)	16 (11%)	31 (12%)	0.565
Time to IV fluids (min) (n = 248)	41 [24–58]	6 [4–9]	19 [13–26]	<0.001
Time to blood cultures (min) (n = 241)	34 [20–48]	12 [10–14]	21 [15–28]	0.003
Time to antibiotics (min) (n = 240)	61 [44–78]	33 [26–40]	45 [37–54]	0.004
Time to lactate (min) (n = 241)	34 [20–49]	12 [10–15]	22 [15–28]	0.003
Lactate levels (n = 246)	3.1 [2.7–3.6]	3.4 [2.9–3.8]	3.3 [2.9–3.6]	0.528
ETCO2 (n = 206)	32 [28–35]	22 [20−23]	24 [22–25]	<0.001
ED temp (n = 228)	100.4 [99.9–100.9]	100.5 [100.1–100.8]	100.5 [100.2–100.8]	0.889
ED respiratory rate (n = 235)	24 [23–26]	27 [25–28]	25 [24–27]	0.044
ED BP systolic (n = 236)	128 [123−133]	122 [117–127]	125 [121–128]	0.114
ED BP diastolic (n = 235)	82 [79–85]	67 [64–71]	74 [72–77]	<0.001
ED pulse (n = 237)	102 [97–106]	112 [108–116]	107 [104–110]	0.001
ED O2 saturation (n = 234)	94 [91–96]	95 [94–96]	94 [93–95]	0.254

study, mortality was unchanged by those with prehospital sepsis alerts, despite decreased time to important benchmarks. Mortality is a difficult primary outcome to interpret in early sepsis intervention considering many septic patients are older, have multiple co-morbidities, and may have advanced directives for end of life care. There was a decrease in ICU admission in the patients identified by prehospital providers, which may reflect that successful early resuscitative efforts stabilized these patients. However, the decision for ICU admission is multifactorial and may not necessarily reflect upon initial patient care.

The most important intervention for septic patients is early antibiotic administration [20,21]. Highly sensitive and specific sepsis screening tools may allow for out of hospital antibiotic administration. However, austere prehospital conditions limit laboratory access and the multitudes of sepsis screening tools described in the literature have varying sensitivity and specificity [19,22,23]. Overall, none of these tools are as accurate as necessary, and further study is required to improve upon them. Regardless, there are reports demonstrating prehospital antibiotics may be given safely for suspected sepsis, but none have shown survival benefit [24,25]. Larger studies will be required to determine if EMS sepsis alert protocols or antibiotic administration decrease overall inpatient mortality or improve upon other functional outcomes.

Limitations included the observational nature of the study which may introduce selection bias. To avoid potential bias, patients were only included if they were had both a principal (ICD-9) diagnosis of sepsis and a documented sepsis alert from the ED. This was done to exclude those initially considered sepsis alerts that were found not to have an appropriate diagnosis to continue with the CMS sepsis bundle treatments (for example, intoxication or metabolic encephalopathy), as well as those who were not initially identified as potentially being septic in the ED. Data was collected from chart review, and we cannot confirm the veracity of these time logs. It is possible that the reduced times were due solely to EMS transport versus walk ins, however, patient characteristics were largely the same suggesting a relatively equivalent level of disease severity at presentation. A prospective comparison consisting of only EMS transported patients may further elucidate the effect of the sepsis alert protocol among that group. The study was performed at a single site using a single set of protocols and may not be generalizable to a broader population. This study was performed as a quality improvement initiative to promote compliance with CMS sepsis bundles, and therefore the primary outcome measures were time to intervention metrics rather than patient centered. While secondary outcomes for clinical disposition showed potential for improvement with prehospital sepsis alerts (decreased ICU admission), mortality was unchanged.

5. Conclusion

Creating systems that link prehospital and ED standards of care have drastically improved upon trauma, ST segment elevation myocardial infarction, and stroke. Extending the reach of sepsis alerts to EMS may improve the flow of patient care and decrease time to life saving interventions. In this study, we show decreased time to clinical

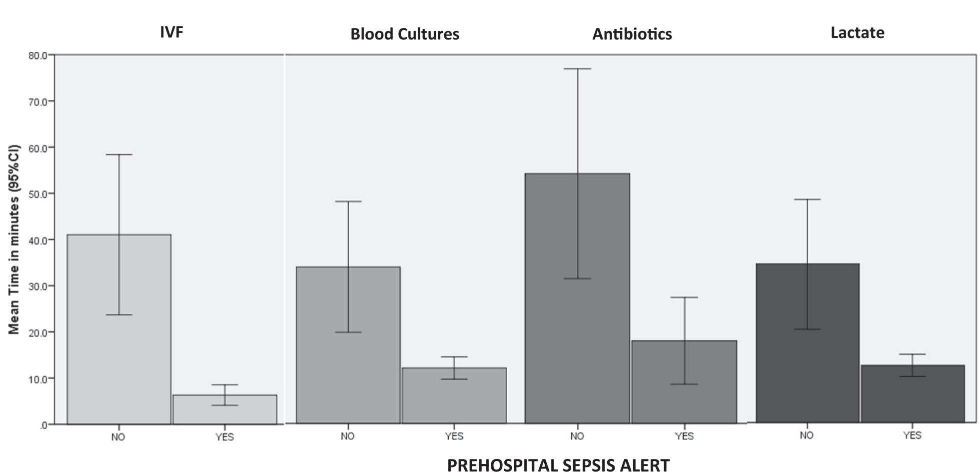

Fig. 1. Changes in core measures following institution of prehospital sepsis alert.

interventions that improve outcomes when EMS providers activate a sepsis alert from the field. Improved training for prehospital providers, validated sepsis screening tools, and further integration of prehospital and in-hospital care may improve outcomes for septic patients in the future.

Acknowledgements

This study is published in memory of Dr. Sal Silvestri.

References

[1] Dellinger RP, Cartlet JM, Masur H, Gerlach H, Calandra T, Cohen J, et al. Surviving sepsis campaign for management of severe sepsis and septic shock. Crit Care Med 2004; 32:858–73.
[2] Dellinger RP, Levy MM, Carlet JM, Bion J, Parker MM, Jaeschke R, et al. Surviving Sepsis Campaign: international guidelines for management of severe sepsis and septic shock: 2008. Crit Care Med 2008;36(1):296–327.
[3] Dellinger RP, Carlet JM, Masur H, Gerlach H, Calandra T, Coheen J, et al. Surviving Sepsis Campaign guidelines for management of severe sepsis and septic shock. Crit Care Med 2004;32(3):858–73.
[4] Dellinger RP, Levy MM, Rhodes A, Annane D, Gerlach H, Opal SM, et al. Surviving sepsis campaign: international guidelines for management of severe sepsis and septic shock: 2012. Crit Care Med 2013;41(2):580–637.
[5] Osborn TM. Severe Sepsis and Septic shock trials (ProCESS, ARISE, ProMISe): What is optimal resuscitation? Crit Care Clin 2017;33(2):323–44.
[6] Rhodes A, Evans LE, Alhazzani W, Levy MM, Antonelli M, Ferrer R, et al. Surviving Sepsis Campaign: international guidelines for management of sepsis and septic shock: 2016. Crit Care Med 2017;45(3):486–552.
[7] Centers for Medicare and Medicaid Services. Sepsis bundle project (SEP) specifications manual for national hospital inpatient quality measures discharges 10-01-15 (4Q15) through 06-30-16 (2Q16). Available at https://www.nhfca.org/psf/resources/Updates1/SEP-1%20Measure%20Information%20Form%20(MIF).pdf; 2012, Accessed date: 11 November 2016.
[8] Seymour CW, Khan JM, Martin-Gill C, Callaway CW, Yealy DM, Scales D, et al. Delays from first medical contact to antibiotic administration for sepsis. Crit Care Med 2017;45(5):759–65.
[9] Studnek JR, Artho MR, Garner CL, Jones AE. The impact of emergency medical services on the ED care of severe sepsis. Am J Emerg Med 2012;30(1):51–6.
[10] Wang HE, W. MD, Shapiro NI, Yealy DM. Opportunities for emergency medical services care of sepsis. Resuscitation 2010;81(2):193–7.
[11] Seymour CW, Band RA, Cooke CR, Mikkelsen ME, Hylton J, Rea TD, et al. Out-of-hospital characteristics and care of patients with severe sepsis: a cohort study. J Crit Care 2010;25(4):553–62.
[12] Seymour CW, Rea TD, Kahn JM, Walkey AJ, Yealy DM, Angus DC. Severe sepsis in pre-hospital emergency care: analysis of incidence, care, and outcome. Am J Resp Crit Care Med 2012;186(12):1264–71.
[13] Halimi KF, Agcaoili C, Choy K, Claridge F, Jacobs M, Taigman M. Prehospital identification of sepsis patients and alerting of receiving hospitals: impact on early goal-directed therapy. Crit Care 2011;15:S14.
[14] Seymour CW, Cooke CR, Mikkelsen ME, Hylton J, Rea TD, Goss CH, et al. Out-of-hospital fluid in severe sepsis: effect on early resuscitation in the emergency department. Prehosp Emerg Care 2010;14(2):145–52.
[15] Seymour CW, Cooke CR, Heckbert SR, Spertus JA, Callaway CW, Martin-Gill C, et al. Prehospital intravenous access and fluid resuscitation in severe sepsis: an observational cohort study. Crit Care 2014;18:533.
[16] Park J, Hwang SY, Shin TG, Jo IJ, Yoon H, Lee TR, et al. Emergency medical services personnel need to improve knowledge and attitude regarding prehospital sepsis care. Clin Exp Emerg Med 2017;4(1):48–55.
[17] Seymour CW, Liu VX, Iwashyna TJ, Brunkhorst FM, Rea TD, Scherag A, et al. Assessment of clinical criteria for sepsis: for the third International Consensus Definitions for Sepsis and Septic Shock (Sepsis-3). JAMA 2016;315:762–74.
[18] Hunter CL, Silvestri S, Ralls G, Stone A, Walker A, Papa L. A prehospital screening tool utilizing end-tidal carbon dioxide predicts sepsis and severe sepsis. Am J Emerg Med 2016;34:813–9.
[19] Hunter CL, Silvestri S, Ralls GR, Stone A, Walker A, Mangalat N, et al. Comparing quick sequential organ failure assessment scores to end tidal carbon dioxide as mortality predictors in prehospital patients with suspected sepsis. West J Emerg Med 2018;19(3):446–51.
[20] Ferrer R, Martin-Loeches I, Phillips G, Osborn TM, Townsend S, Dellinger RP, et al. Empiric antibiotic treatment reduces mortality in severe sepsis and septic shock from the first hour: results from a guideline-based performance improvement program. Crit Care Med 2014;42(8):1749–55.
[21] Kumar A, Roberts D, Wood KE, Light B, Parrillo JE, Sharma S, et al. Duration of hypotension before initiation of effective antimicrobial therapy is the critical determinant of survival in human septic shock. Crit Care Med 2006;34(6):1589–96.
[22] Wallgren UM, Castren M, Svensson AE, Kurland L. Identification of the adult septic patient in the pre-hospital setting: a comparison of two screening tools and clinical judgment. Eur J Emerg Med 2014;21(4):260–5.
[23] Hwang SY, Jo IJ, Lee TR, Yoon H, Cha WC, Sim MS, et al. Low accuracy of positive qSOFA criteria for predicting 28 day mortality in critically ill septic patients during the early period after emergency department presentation. Ann Emerg Med 2018; 71(1):1–9.
[24] Alam N, Oskam E, Stassen PM, Exter PV, van de Ven PM, Haak HR, et al. Prehospital antibiotics in the ambulance for sepsis: a multicenter, open label, randomized trial. Lancet Respir Med 2018;6(1):40–50.
[25] Walchok JG, Pirrallo RG, Furmanek D, Lutz M, Shope C, Giles B, et al. Paramedic-initiated CMS sepsis core measure bundle prior to hospital arrival: a stepwise approach. Prehosp Emerg Care 2017;21(3):291–300.