American Journal of Emergency Medicine 37 (2019) 1505–1509

Contents lists available at ScienceDirect

American Journal of Emergency Medicine

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

Original Contribution

Sepsis alerts in EMS and the results of pre-hospital ETCO2☆

Steven J. Weiss *, Angel Guerrero, Christian Root-Bowman, Amy Ernst, Kurt Krumperman, Jon Femling, Phil Froman

University of New Mexico Department of Emergency Medicine, United States of America

ARTICLE INFO

Article history:
Received 14 September 2018
Received in revised form 22 October 2018
Accepted 6 November 2018

ABSTRACT

Background: Field sepsis alerts have the ability to expedite initial ED sepsis treatment. Our hypothesis is that in patients that meet EMS sepsis alert criteria there is a strong relationship between prehospital end-tidal carbon dioxide (ETCO2) readings and the outcome of diagnosed infection.
Methods: In 2014, our EMS service initiated a protocol requiring hospitals to receive notification of a "sepsis alert" on all suspected sepsis patients. The EMS service transports 70,000 patients/year to a number of urban centers. All patients transported to our major urban teaching hospital by our EMS service in one year in which a sepsis alert was announced were included in this study. The primary outcome variable was diagnosed infection and secondary outcomes were hospital admission, ICU admission and mortality. Positive lactate was defined as >4.0 mmol/L. ROC curve analysis was used to define the best cutoff for ETCO2.
Results: 351 patients were announced as EMS sepsis alert patients and transported to our center over a one year period. Positive outcomes were as follows: diagnosed infection in 28% of patients, hospital admission in 63% and ICU admission in 11%. The correlation between lactate and ETCO2 was −0.45. A ROC curve analysis of ETCO2 vs. lactate >4 found that the best cutoff to predict a high lactate was an ETCO2 of 25 or less, which was considered a positive ETCO2 (AUC = 0.73). 27% of patients had a positive ETCO2 and 24% had a positive lactate. A positive ETCO2 predicted a positive lactate with 76% accuracy, 63% sensitivity and 80% specificity. 27% of those with a positive ETCO2 and 44% of those with a positive lactate had a diagnosed infection. 59% of those with a positive ETCO2 and 89% of those with a positive lactate had admission to the hospital. 15% of those with a positive ETCO2 and 18% of those with a positive lactate had admission to the ICU. Neither lactate nor ETCO2 were predictive of an increased risk for diagnosed infection, hospital admission or ICU admission in this patient population.
Conclusion: While ETCO2 predicted the initial ED lactate levels it did not predict diagnosed infection, admission to the hospital or ICU admission in our patient population but did predict mortality.

1. Introduction

The initial evaluation of patients in the pre-hospital setting, requires EMS to properly assess vital signs to determine initial patient management and to communicate to emergency departments to prepare for receipt and treatment of transported patients. Development and implementation of disease specific field alerts, such as Field Sepsis Alerts in which certain criteria are established to deem a patient "sepsis likely" expedite initial ED sepsis treatment [1-4].

Of particular interest to our study of pre-hospital patient parameters predicting in-hospital patient outcomes was end tidal CO2 (ETCO2) and how it compares to first hospital lactate [5-8]. ETCO2 is a noninvasive method of providing another insight to patient status and patient management by EMS [9-16]. Devices that measure exhaled carbon dioxide are a mature and easy to use technology already available to field EMS. Currently, instantaneous capnography is utilized in the settings of acute asthma exacerbations, return of efficacious cardiac output following cardiac arrest, as well as a sign of a successful endotracheal intubation. In relation to sepsis, pathologically speaking, is the common development of a metabolic acidosis that is often accompanied by an apparent increase in cardiovascular carbon dioxide content as well as the production of water via carbonic anhydrase in an effort to buffer the decrease of blood pH towards physiologic normal values. As a result of this change in vascular carbon dioxide content, increased amounts should be exhaled and thus lead to a measurable decrease in blood CO2 via commonly available capnography assessment tools. Given the immediacy and ease of use of ETCO2 monitor results, an association with pre-hospital suspicion of sepsis and initiation of empiric treatment prior to gold standard lactate levels in the hospital setting has the ability to improve patient outcomes like prehospital interventions have for MI, stroke and TBI [17-19]. The sepsis literature has begun to suggest that earlier interventions are important in sepsis care [20-27].

☆ Presented at SAEM May 2017, Orlando, FL.
* Corresponding author.
E-mail address: sweiss52@aol.com (S.J. Weiss).

https://doi.org/10.1016/j.ajem.2018.11.009
0735-6757/

The purpose of our study was to further assess the possible role and scope of ETCO2 measurement to drive the commencement of evidence-proven effective early therapy, thereby maximizing treatment's ability to decrease sepsis mortality. It is essential to establish the efficacy of effective, readily available, non-invasive, and inexpensive tests that equip EMS providers and receiving emergency department health care professionals to aid suspected sepsis patients to the best of their ability. Given that EMS providers are already capable of delivering research supported early therapy, which include large volume fluid resuscitation, allowing them to carry out this care with confidence is paramount to escalating provider response to the serious threat of sepsis.

Our hypothesis was that in patients that meet EMS sepsis alert criteria there is a strong relationship between prehospital ETCO2 readings and the outcome of diagnosed infection. The secondary hypothesis was that ETCO2 also predicted hospital admission, ICU admission and death.

2. Methods

2.1. Design and setting

As of 2014, our local EMS services that deliver patients to the our hospital emergency department, the only level one trauma center in the state, as well as other local emergency departments, began to employ a Field Sepsis Alert Protocol. This EMS service transports about 70,000 patients per year to area health care centers. The Field Sepsis Alerts were to be triggered if there was a suspicion of infection plus 2 or more of the following: temperature > 38.3 C or <36 C, heart rate greater than the age adjusted expectation, and respiratory rate greater than age adjusted expectation in addition to the presence of any one of the following: hypotension, respiratory distress, or lactate >4 mmol/L (if available).

The structure of this study was a retrospective cohort study encompassing EMS run reports from Albuquerque Ambulance Service from 2014 to 2015 and subsequent Patient care reports (PCRs) from UNMH. The UNM Human Research Protections Office approved the study protocol.

All run reports that indicated that ETCO2 devices were used and data recorded, over a two year period during 2014 and 2015, were included in this study. Inclusion criteria further included delivery to our ED, a minimum of one set of lab values attained at the hospital that included a lactate value and white blood cell count as well as a minimum of one set of vital signs. Exclusion criteria was incomplete EMS run reports and hospital PCRs that did not include the minimum criteria previously mentioned. The eventual outcome variable was whether the patient was eventually diagnosed with sepsis upon admission to the hospital.

2.2. Data collection

Data collection consisted of the development of a standardized Data Collection Form for both EMS run report and ED PCR data extraction. Patients were de-identified and given matched identification numbers for the purposes of data matching of records and eventual analysis. Researchers were trained on the study protocol and method of data extraction. One researcher used run reports and mined them for patient age, pulse, respiration rate (RR), systolic blood pressure (SBP), diastolic blood pressure (DBP), temperature, primary impression, and call priority. Additionally, we investigated whether IV access was established, supplemental oxygen was employed, intraosseous access was initiated, and the ETCO2 recorded. Another pair of researchers used Cerner PowerChart patient care records and investigated them for the parameters of date, patient age, gender, ethnicity, ED Diagnosis, first set of vital signs, WBC, first lactate, disposition (AMA/LWBS, Admit, Discharge, Observation), and outcome if available.

The outcome variables measured included diagnosed infection, admission to the hospital and admission to the ICU. We defined "diagnosed infections" as finding the patient's final diagnosis of an infectious source, not necessarily based on a positive culture. This could be any one of the final charted diagnoses for the patient or a positive culture if done. We defined positive lactate to be >4.0 mmol/L.

2.3. Analysis

Data was analyzed through the utilization of stratification into live and deceased groups and means of the parameters mentioned previously with an established confidence interval of 95% throughout. Receiver Operator Characteristic Curve analysis was used to define the best cut-off value for ETCO2. This study was powered to show a difference of 15% between groups with 350 total patients. The study was approved by our IRB as expedited.

3. Results

Of all run reports for the 2014–2015 year, 351 patients were announced as Field Sepsis Alerts and transported to UNMH. On retrospective review, all patients that were included met the protocol criteria to be announced as a sepsis alert. Outcomes for these patients were as follows: 28% had an identified source of infection, 63% were admitted to the hospital, 12% were admitted to the ICU, and 8% of patients died. The mean age was 52 and 56% of the included patients were male. Per EMS all patients met at least 2 SIRS criteria; in the ED with the first set of vital signs 62% of patients met at least 2 SIRS criteria. Enroute to the hospital, 68 patients received supplemental oxygen and 55 had IV access established (see Table 1).

Upon Admission, patients stayed a mean of 5.9 days and, if admitted to ICU, stayed a mean of 11 days. Nine percent of floor admitted patients and 29% of ICU admitted patients died during their hospital stay.

Table 1
Demographics.

	N (%)
N	351
Age	52 ± 23
Gender (%males)	185/330(56%) (21 unknown)
Race	
White	122 (35%)
Hispanic	140 (40%)
American Indian	35 (10%)
African American	13 (4%)
Other/unknown	42 (11%)
Source of infection found	101 (29%)
Dispositions	
Admitted to hospital	180 (51%)
Admitted to ICU	40 (11%)
Discharged	104 (30%)
Unknown	27 (8%)
EMS urgency codes	
Level 1	70 (20%)
Level 2	18 (5%)
Level 3	108 (31%)
Level 4	151 (43%)
Level 5	4 (1%)
EMS Priority codes	
Code 1	209 (60%)
Code 2	80 (23%)
Code 3	63 (1%)
LOS –overall (Median, IQR)	4(2,8)
LOC-discharged (Median, IQR)	1 (1,1)
LOS-Admitted to floor (Median, IQR)	4 (2,7)
LOS-Admitted to ICU (Median, IQR)	8 (2,18)
Source found (%age)	100 (28%)
Floor admit (%age)	180 (51%)
ICU admit (%age)	41 (12%)
All admits (%age)	221 (63%)
Deaths (%age)	28 (8%)

The comparison of the groups based on the outcome of whether a source of infection was found is shown it Table 2. As can be seen, many of the individual variables were significantly different between the two groups. However, only prehospital SIRS criteria were significantly related to any of the outcome variables (Table 3). When we looked the patients who died using ETCO2, first lactate and Sirs criteria, only the first lactate was significantly related to death (Table 4).

The correlation between lactate levels in hospital and ETCO2 levels per EMS was −0.43. When analyzed utilizing receiver operating characteristic curve of ETCO2 vs a lactate >4 mmol/L we found that the best cutoff to predict a lactate >4 was an ETCO2 level of <25 (what we term a "positive" ETCO2). Area under curve for this ROC analysis was 0.73. Given this cut-off value, 27% of included patients had an ETCO2 <25 and 24% of patients had a lactate >4 mmol/L. Overall, our established cutoff value for ETCO2 (<25) predicted a positive lactate (>4.0 mmol/L) with 76% accuracy, 63% specificity, and 80% sensitivity (OR = 26). (see ROC curve in Fig. 1).

Primary outcome of source of infection found, was not related to either positive lactate or positive ETCO2. Twenty-seven percent of patients with a positive ETCO2 and 29% of patients with negative ETCO2 had a positive primary outcome of source of infection found. For lactate, 44% of patients with a positive lactate and 42% of patients with a negative lactate had a positive primary outcome of source of infection found.

Admission to the hospital for those with positive ETCO2 and Lactate was 15% and 18% respectively. For, those with negative ETCO and lactate, admission to the ICU was 10% and 12% respectively.

Twenty seven patients (8%) died during this hospital stay. This was the only outcome in which we found significant predictive value for lactate, SIRS criteria and ETCO2. Using continuous values, ETCO2, lactate and SIRS criteria were all significant single predictors of mortality. When the values of these three variables were dichotomized the same pattern remained. Percent differences and 95% confidence intervals for continuous variables are shown in Table 2.

4. Discussion

Our study demonstrated and reinforced findings suggesting implementation of ETCO2 as a part of initial patient parameters to be attained by EMS in lieu of the ability to quickly attain a lactate level. While this study was conducted at the largest academic hospital center in the state, it should not go without mentioning that the overall sample for Field Sepsis Alerts was relatively small compared to that of similar studies. If EMS is better equipped to use the information that is available to them through the utilization of equipment that is already standard, they can work more efficiently without any increased cost. It follows that using ETCO2 with a suggested cut off value of <25 in the context of a field sepsis alert, the optimal course of action may be early therapy including the initiation of empiric antibiotic treatment.

We were able to show the same mortality benefit of ETCO2 that was seen in other studies. However, when we looked closer at whether that mortality was associated with sepsis, we did not find a benefit in sepsis patients having a diagnosed infection, being admitted to the hospital or being admitted to an ICU. These were not evaluated in other studies.

Only two other studies looked at EtCO2 in the pre-hospital environment. Hunter et al. [26] looked at EtCO2 levels in all patients who had one recorded so their patients were undifferentiated and thus very different from the patient population in our study. A second paper by Hunter et al. [27] focused on patients who were screened for sepsis in the prehospital setting but found that almost half of them really did not meet the critical criteria to be in the study. We only included those who had protocol positive results and thus our population was also very different from those in that study. This study adds information about protocol positive patients in a prehospital environment different from the two previous studies and also looks at the outcomes of infection found, hospital and ICU admission that the other studies did not assess in this type of setting.

We were unable to show any predictive value to ETCO2 for the variables of infection found, admission to the floors and admission to the

Table 3
Univariate odds using discrete cutoffs for ETCO2, lactate and SIRS criteria in predicting a positive source of infection, admission to the hospital, admission to an ICU and death.

	Cutoff positive	Source of infection found		Admitted to the hospital		Admitted to the ICU		Death	
		OR	95% CI	OR	95% CI	OR	95% CI	OR	95% CI
ETCO2	(≤25)	0.9	0.5,1.5	0.8	0.5,1.3	1.5	0.8,3.0	**2.8**	**1.3,6.2**
Lactate	(≥4)	1	0.6,2.1	1.9	0.7,5.3	1.6	0.6,4.0	**7.7**	**3.0,19.9**
SIRS	(≥2)	**3.5**	**2.1,6.0**	**3.9**	**2.5,6.2**	1.8	0.9,3.6	**3.8**	**1.4,10.2**

Bolded values are significant at $p < 0.05$.

Table 2
Comparison of cases with outcome of infection found vs those without any infection found on admission to the hospital. Upper part of the table is continuous variables with differences and 95% CIs, lower part is dichotomous variables with odds ratios and 95% CIs.

	Cases with no source of infection found	Cases with source of infection found	p-Value	Difference	95%CI
N	251	100			
Age	51 ± 23	58 ± 22	0.02	7	1,12
Gender					
EMS vitals					
Pulse	114 ± 23	120 ± 22	0.03	6	0.8,11.0
Resp rate	30 ± 10	31 ± 10	NS	–	–
Temperature (deg C)	36.9 ± 1.0	37.3 ± 1.6	0.01	0.04	0.1,0.7
EtCO2	32 ± 10	31 ± 11	NS		
ED vitals					
Pulse	102 ± 23	112 ± 22	<0.01	10	5,16
Resp rate	23 ± 8	26 ± 10	0.01	3.0	1.0,5.0
Temp (deg C)	36.7 ± 0.7	37.0 ± 1/3	0.002	0.3	0.1,0.6
Sys BP	134 ± 35	128 ± 27	NS		
Dias BP	76 ± 16	73 ± 16	NS		
EMS Sirs	1.9 ± 0.7	2.2 ± 0.6	0.002	0.3	0.1,0.4
WBC count	11 ± 5	13 ± 9	0.001	3.0	1.1,4.2
First ED lactate	3.3 ± 3.9	3.5 ± 4.0	NS		
ED sirs	1.4 ± 1.0	2.0 ± 0.9	<0.001	0.7	0.5,0.9
Length of stay median (IQR)	3(1,7)	5(2,10)	0.007	3	–

	Cases with no source of infection found	Cases with source of infection found	p-Value	OR	95%CI
Floor admit	99(39%)	81(80%)	<0.01	6.2	3.6,10.8
ICU admit	31(12%)	10(10%)	NS	NS	NS
All admit	130(52%)	91(90%)	<0.01	8.4	4.2,17.0

Table 4
Absolute values of the predictors of mortality. Table shows actual continuous results for each variable for those patients who were alive at discharge vs those that died during hospital admission.

	Alive (mean ± SD)	Deceased (mean ± SD)	Diff (95% CI)
ETCO2	31.6 ± 9.3	26.9 ± 14.4	4.7(0.9,8.6)
First Lactate	2.9 ± 2.4	7.6 ± 8.4	**4.7**(**3.1**,**6.3**)*
SIRS Criteria	1.5 ± 1.0	2.1 ± 0.9	0.6(0.2,1.0)

* $p < 0.5$.

ICU. Patients with and without both positive ETCO2 values and lactate values were equally likely to be infected and equally likely to be admitted to either the floor or the ICU. Only SIRS criteria predicted infection, hospitalization and death.

The impact of EMS on sepsis care is still uncertain. We found that neither lactate nor end tidal CO2 are helpful in directing sepsis care. Grover et al. summarized the state of the EMS literature in 2016 on the issue of the impact of EMS on sepsis management [28]. They noted that of the severe sepsis patients, >40% arrived by EMS, that the ESM patients were sicker than walk-ins, that every hour from the onset of sepsis dropped survival 7.6% and that the odds of mortality dropped to 0.3 just by having EMS start an IV catheter. They concluded that EMS sepsis care significantly reduced overall mortality and that the addition of End tidal CO2 and/or lactate measures would be an even greater improvement. Not all of the literature has been this positive as was pointed out by Smyth et al. in an exhaustive review of published articles in the same year [29], who found that robust evidence of EMS role in sepsis care is still lacking. Because end tidal CO2 is so easily accessible to EMS providers, its addition to EMS management is significantly easier than point of care lactate. However, we were not able to determine that either lactate or end tidal CO2 improved EMS sepsis care significantly beyond the value of SIRS criteria alone.

5. Conclusions

Among our patient population, ETCO2 was effective at predicting first hospital lactate levels but it did not reliably predict finding an infection source or admission to either the floor or ICU. Lactate, given our established cutoffs, had the ability to predict in hospital mortality. SIRS criteria alone predicted source of infection found and hospital admission. Earlier establishment of metrics to assess patient status at earlier time points will only serve to improve patient outcomes in hopes of decreasing patient mortality in the setting of suspected sepsis.

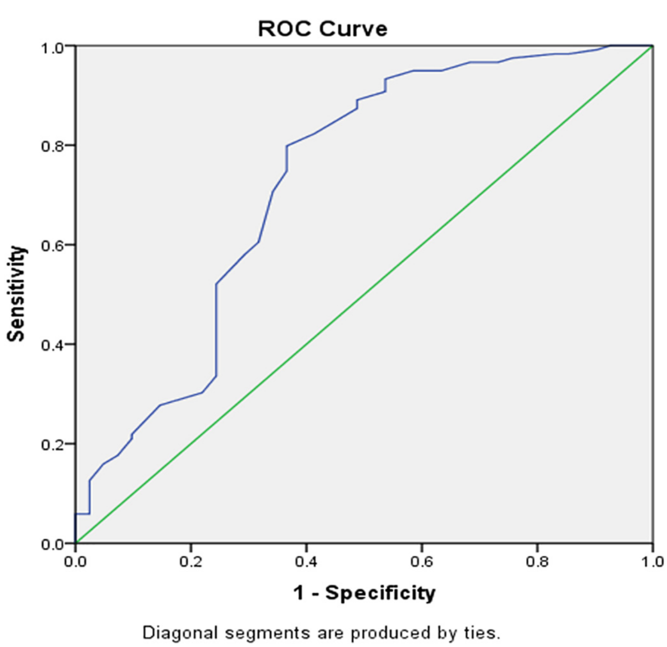
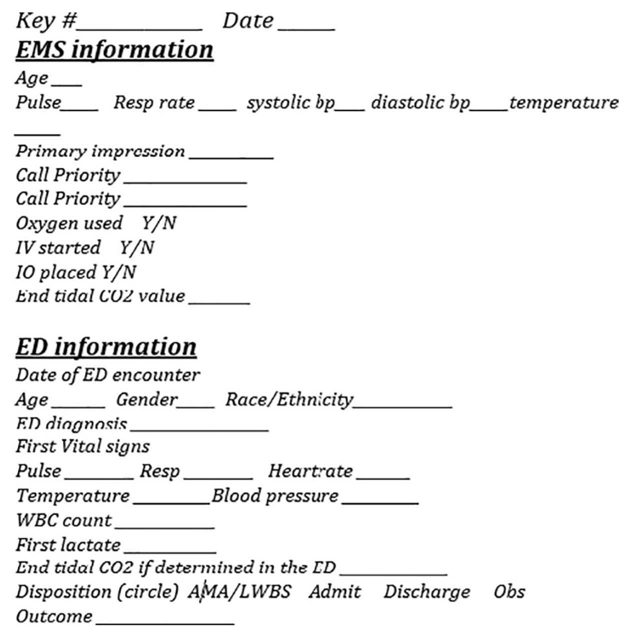


Fig. 1. ROC curve based on positive lactate looking at values of ETCO2. Based on Youden criteria, an ETCO2 < 25 represented the best cutoff when compared to a positive lactate.

Appendix A. Data collection form



Key #___________ Date _____

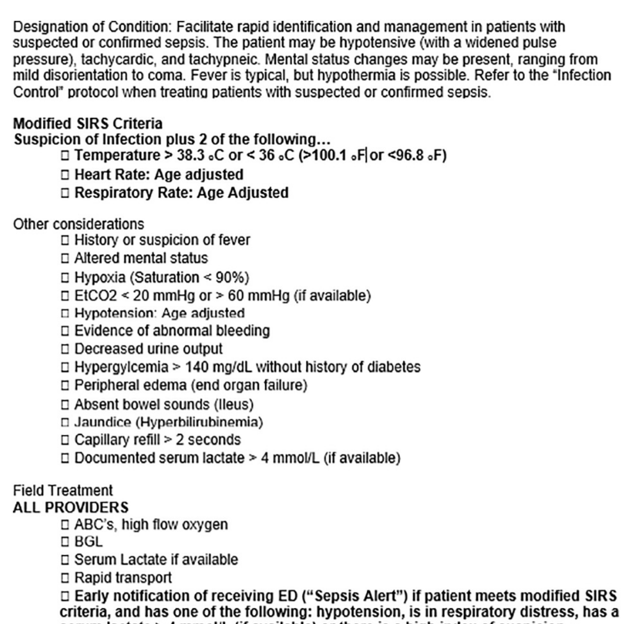
EMS information

Age ___
Pulse____ Resp rate ____ systolic bp___ diastolic bp____temperature ____
Primary impression _________
Call Priority ___________
Call Priority ___________
Oxygen used Y/N
IV started Y/N
IO placed Y/N
End tidal CO2 value ______

ED information

Date of ED encounter
Age _____ Gender____ Race/Ethnicity__________
ED diagnosis ____________
First Vital signs
Pulse ______ Resp ______ Heartrate _____
Temperature _______Blood pressure _______
WBC count _________
First lactate _________
End tidal CO2 if determined in the ED __________
Disposition (circle) AMA/LWBS Admit Discharge Obs
Outcome ____________

Appendix B. M-13 sepsis/septic shock



Designation of Condition: Facilitate rapid identification and management in patients with suspected or confirmed sepsis. The patient may be hypotensive (with a widened pulse pressure), tachycardic, and tachypneic. Mental status changes may be present, ranging from mild disorientation to coma. Fever is typical, but hypothermia is possible. Refer to the "Infection Control" protocol when treating patients with suspected or confirmed sepsis.

Modified SIRS Criteria
Suspicion of Infection plus 2 of the following…
- **Temperature > 38.3 °C or < 36 °C (>100.1 °F or <96.8 °F)**
- **Heart Rate: Age adjusted**
- **Respiratory Rate: Age Adjusted**

Other considerations
- History or suspicion of fever
- Altered mental status
- Hypoxia (Saturation < 90%)
- EtCO2 < 20 mmHg or > 60 mmHg (if available)
- Hypotension: Age adjusted
- Evidence of abnormal bleeding
- Decreased urine output
- Hypergylcemia > 140 mg/dL without history of diabetes
- Peripheral edema (end organ failure)
- Absent bowel sounds (Ileus)
- Jaundice (Hyperbilirubinemia)
- Capillary refill > 2 seconds
- Documented serum lactate > 4 mmol/L (if available)

Field Treatment
ALL PROVIDERS
- ABC's, high flow oxygen
- BGL
- Serum Lactate if available
- Rapid transport
- **Early notification of receiving ED ("Sepsis Alert") if patient meets modified SIRS criteria, and has one of the following: hypotension, is in respiratory distress, has a serum lactate > 4 mmol/L (if available) or there is a high index of suspicion**

References

[1] Rivers EP, Katranji M, Jaehne KA, Brown S, Abou Dagher G, Cannon C, et al. Early interventions in severe sepsis and septic shock: a review of the evidence one decade later. Minerva Anestesiol 2012 Jun;78(6):712–24.

[2] Perman SM, Goyal M, Gaieski DF. Initial emergency department diagnosis and management of adult patients with severe sepsis and septic shock. Scand J Trauma Resusc Emerg Med 2012;20:41.
[3] Kethireddy S, Kumar A. Mortality due to septic shock following early, appropriate antibiotic therapy: can we do better?*. Crit Care Med 2012 Jul;40(7):2228–9.
[4] Nguyen HB, Lynch EL, Mou JA, Lyon K, Wittlake WA, Corbett SW. The utility of a quality improvement bundle in bridging the gap between research and standard care in the management of severe sepsis and septic shock in the emergency department. Acad Emerg Med 2007 Nov;14(11):1079–86.
[5] Puskarich MA, Trzeciak S, Shapiro NI, Arnold RC, Heffner AC, Kline JA, et al. Prognostic value and agreement of achieving lactate clearance or central venous oxygen saturation goals during early sepsis resuscitation. Acad Emerg Med 2012 Mar;19(3):252–8.
[6] Jones AE, Shapiro NI, Trzeciak S, Arnold RC, Claremont HA, Kline JA. Lactate clearance vs central venous oxygen saturation as goals of early sepsis therapy: a randomized clinical trial. JAMA 2010 Feb;303(8):739–46.
[7] Goyal M, Pines JM, Drumheller BC, Gaieski DF. Point-of-care testing at triage decreases time to lactate level in septic patients. J Emerg Med 2010 Jun;38(5):578–81.
[8] Puskarich MA, Kline JA, Summers RL, Jones AE. Prognostic value of incremental lactate elevations in emergency department patients with suspected infection. Acad Emerg Med 2012 Aug;19(8):983–5.
[9] Band RA, Gaieski DF, Hylton JH, Shofer FS, Goyal M, Meisel ZF. Arriving by emergency medical services improves time to treatment endpoints for patients with severe sepsis or septic shock. Acad Emerg Med 2011 Sep;18(9):934–40.
[10] Studnek JR, Artho MR, Garner Jr CL, Jones AE. The impact of emergency medical services on the ED care of severe sepsis. Am J Emerg Med 2012 Jan;30(1):51–6.
[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 Dec;25(4):553–62.
[12] 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 [Apr-2010 Jun].
[13] Wang HE, Weaver MD, Shapiro NI, Yealy DM. Opportunities for emergency medical services care of sepsis. Resuscitation 2010 Feb;81(2):193–7.
[14] Guerra WF, Mayfield TR, Meyers MS, Clouatre AE, Riccio JC. Early detection and treatment of patients with severe sepsis by prehospital personnel. J Emerg Med 2013 Jun;44(6):1116–25.
[15] 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 Respir Crit Care Med 2012 Dec;186(12):1264–71.
[16] Herlitz J, Bang A, Wireklint-Sundstrom B, Axelsson C, Bremer A, Hagiwara M, et al. Suspicion and treatment of severe sepsis. An overview of the prehospital chain of care. Scand J Trauma Resusc Emerg Med 2012;20:42.
[17] Brown JP, Mahmud E, Dunford JV, Ben-Yehuda O. Effect of prehospital 12-lead electrocardiogram on activation of the cardiac catheterization laboratory and door-to-balloon time in ST-segment elevation acute myocardial infarction. Am J Cardiol 2008 Jan;101(2):158–61.
[18] Mosley I, Nicol M, Donnan G, Patrick I, Kerr F, Dewey H. The impact of ambulance practice on acute stroke care. Stroke 2007 Oct;38(10):2765–70.
[19] Hartl R, Gerber LM, Iacono L, Ni Q, Lyons K, Ghajar J. Direct transport within an organized state trauma system reduces mortality in patients with severe traumatic brain injury. J Trauma 2006 Jun;60(6):1250–6 [discussion 1256].
[20] Institute for Healthcare improvement. [Available at] http://www.ihi.org/IHI/Topics/CriticalCare/Sepsis/; 2013. [Accessed 2013 Feb 16].
[21] Nguyen HB, Van Ginkel C, Batech M, Banta J, Corbett SW. Comparison of predisposition, insult/infection, response, and organ dysfunction, acute physiology and chronic health evaluation II, and mortality in emergency department sepsis in patients meeting criteria for early goal-directed therapy and the severe sepsis resuscitation bundle. J Crit Care 2012 Aug;27(4):362–9.
[22] Jones AE, Trzeciak S, Kline JA. The Sequential Organ Failure Assessment score for predicting outcome in patients with severe sepsis and evidence of hypoperfusion at the time of emergency department presentation. Crit Care Med 2009 May;37(5):1649–54.
[23] Rivers E, Nguyen B, Havstad S, Ressler J, Muzzin A, Knoblich B, et al. Early goal-directed therapy in the treatment of severe sepsis and septic shock. N Engl J Med 2001 Nov;345(19):1368–77.
[24] Nguyen HB, Banta JE, Cho TW, Van Ginkel C, Burroughs K, Wittlake WA, et al. Mortality predictions using current physiologic scoring systems in patients meeting criteria for early goal-directed therapy and the severe sepsis resuscitation bundle. Shock 2008 Jul;30(1):23–8.
[25] Vincent JL, de Mendonca A, Cantraine F, Moreno R, Takala J, Suter PM, et al. Use of the SOFA score to assess the incidence of organ dysfunction/failure in intensive care units: results of a multicenter, prospective study. Working group on "sepsis-related problems" of the European Society of Intensive Care Medicine. Crit Care Med 1998 Nov;26(11):1793–800.
[26] Hunter CL, Silvestri S, Ralls G, Bright S, Papa L. The sixth vital sign: prehospital end-tidal carbon dioxide predicts in-hospital mortality and metabolic disturbances. Am J Emerg Med 2014;V32:160–5.
[27] Hunter CL, Salvatore 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;V34:813–9.
[28] Williams J, Cabanas J. Sepsis early recognition and treatment in prehsopital setting vital for patient outcome. JEMS [September]. 2016;41(9) [Accessed on Internet 10/22/2018 at] https://www.jems.com/articles/print/volume-41/issue-9/special-focus-septic-alert/sepsis-early-recognition-and-treatment-in-prehopsital-setting-vital-for-patient-outcomes.html.
[29] Smyth MA, Brace-McDonnell SJ, Perkins GD. Impact of prehospital care on outcomes in Sepsis: a systematic review. West J Emerg Med 2017;19(4):427–37.