Prehospital Sepsis Care

Jerrilyn Jones, MD, MPH[a,*], Benjamin J. Lawner, DO, MS, EMT-P[a,b]

KEYWORDS

• Prehospital • Emergency medical services • Sepsis • Advanced life support
• Paramedic

KEY POINTS

- Early recognition of sepsis in the prehospital environment can improve patient outcomes.
- Early recognition and aggressive fluid therapy (when appropriate) are important components of a prehospital sepsis protocol.
- Early notification of the receiving hospital and measurement of serum lactate concentrations may expedite care of the septic patient encountered in the prehospital environment.
- Additional research is needed to determine the necessary components of a prehospital sepsis protocol.

INTRODUCTION

Emergency medical services (EMS) personnel frequently provide care for individuals with time-critical illnesses and injuries. One such condition is sepsis, which represents a broad spectrum of clinical presentations requiring early recognition and rapid intervention. Interventions such as the administration of antibiotics and intravenous (IV) fluids within the first few hours have been linked to lower mortalities.[1,2] In the United States, EMS systems have a long-standing tradition of care coordination. For example, trauma victims are conveyed speedily to designated trauma centers and victims of ST-segment elevation myocardial infarction (STEMI) are delivered to waiting cardiac catheterization laboratories. Because sepsis represents a distinct medical entity that would benefit from timely medical intervention, it logically follows that a systematic approach to prehospital recognition and treatment would benefit this distinct group of patients. That said, the recognition of a sepsis syndrome during the prehospital phase of care is far more complex than teaching EMS providers to recognize varying degrees of hemodynamic instability.

Modern EMS systems incorporate a variety of professionals, and each level of EMS provider has been trained to a different level of understanding with respect to human

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[a] Department of Emergency Medicine, University of Maryland School of Medicine, 110 S. Paca Street, 6th floor, Suite 200, Baltimore, MD 21201, USA; [b] Baltimore City Fire Department, Emergency Medical Services, 3500 West Northern Parkway, Baltimore, MD 21215, USA
* Corresponding author.
E-mail address: jjones@em.umaryland.edu

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anatomy and physiology. Basic emergency medical technicians (EMTs) can interpret abnormalities in vital signs but might not be familiar with the underlying physiology. Paramedics understand the physiologic implications of a septic state but might not appreciate subtle or occult presentations of sepsis in immunosuppressed or chronically ill individuals. Because early recognition and intervention are associated with a decreased mortality, it is imperative to engage EMS systems in a comprehensive approach to the treatment of sepsis. This article explores current practices and available medical decision-making tools, job aids, and point-of-care (POC) tests in order to articulate an evidence-based approach to the prehospital recognition of sepsis.

EXISTING TRIAGE TOOLS

In 2009 and 2010, researchers from Harborview Medical Center attempted to quantify EMS providers' understanding of sepsis.[3] Providers from 3 EMS agencies, at all levels of EMS education and training, participated in an online 10-question survey focused on sepsis recognition. The study population included firefighter (FF)//EMTs, other EMTs, and paramedics. Seven hundred eighty-six EMS providers completed the survey: 408 FF/EMTs (52%), 276 other EMTs (21%), and 102 paramedics (13%). Almost all (97%) of the participants had "heard of sepsis" and appreciated its association with increased in-hospital mortality.[3] However, knowledge gaps were found when participants were asked about their understanding of sepsis. EMTs were less likely than paramedics to identify the correct definition of sepsis, and this finding persisted following logistic regression analysis. Importantly, 55% of respondents agreed that EMS providers could play a role in the early identification of patients at risk for sepsis. These results lend credence to the idea of a systemic, protocolized approach to sepsis care. Important limitations surfaced in the analysis of the study. Each EMS system has different training programs, and the results may not be readily generalizable. The survey did not incorporate clinical scenarios, and researchers were therefore unable to test a provider's ability to engage in more complex medical decision making. However, paramedics' broad and more refined familiarity with sepsis suggested that these providers could be integrated into more specific and widespread prehospital treatment strategies.

Guerra and colleagues[4] examined the utility of an aggressive, goal-directed, prehospital sepsis protocol. Before this study's results are examined, it is helpful to appreciate aspects of the regional EMS system that made such important research possible. First, physicians from a single group staffed all the emergency departments (EDs) involved in the study. The EMS system used an "all-advanced life support" (all-ALS) model of care, meaning that each ambulance crew included at least one credentialed paramedic.[4] Finally, medical direction was provided by board-certified emergency physicians affiliated with area hospitals and EMS system. Although such a collaborative arrangement might seem logical, the reality of physician oversight in EMS is far less consistent. This study featured a rather fortuitous pairing of engaged medical direction and an all-ALS system. Although basic life support (BLS) providers have a pivotal role to play in terms of recognition, EMTs are not often authorized to insert IV lines or administer medication therapy. The authors used an evidence-based triage screening tool and incorporated POC lactic acid testing into the prehospital sepsis algorithm. Patients who met predefined prehospital triage parameters were directed into a "sepsis alert" protocol. Essentially, patients had to fulfill 4 criteria: (1) age greater than 18 years and not pregnant, (2) presence of 2 systemic inflammatory response criteria, (3) suspected infection, and (4) hypoperfusion manifested by prehospital systolic hypotension or an elevated lactic acid level (>4 mmol/L). The study

population comprised 112 patients. Paramedics correctly identified 32 of 67 patients (48%) who were subsequently diagnosed as having severe sepsis. Patients dropped out of the "sepsis alert" protocol for reasons apart from provider familiarity with the sepsis definition. Of the 35 septic patients who were not identified by EMS personnel, 5 had vital signs that did not meet criteria. Thirteen additional septic patients were identified during their ED stay as a result of an elevated white blood cell count. In an unadjusted analysis that examined survival as a primary endpoint, patients classified by EMS personnel as having severe sepsis had an odds ratio of 3.19 in favor of survival (95% confidence interval [CI], 1.14–8.88). The authors also reported a lower mortality for EMS patients identified with the sepsis alert protocol as opposed to those not identified with the sepsis alert protocol. This study affirms that paramedic-level providers can identify severe sepsis and initiate appropriate treatment. Furthermore, the use of an "alert" protocol could have several positive downstream effects. Patients identified as having a time-sensitive condition are more likely to undergo timely interventions. Potentially negative effects of this specific protocol included false-positive sepsis activations and increased costs associated with paramedic education and training. It is logical to infer, however, that additional investment in training costs would be offset by the benefits gleaned from aggressive prehospital resuscitation of septic patients.

A recent retrospective study examined more than 66,000 EMS encounters for the purpose of developing a prehospital sepsis score (PRESS).[5] This score can be used by a broad range of EMS providers to facilitate the early treatment and rapid transport of septic patients to definitive care. The investigators looked at dispatch and patient characteristics associated with adverse outcomes. In an urban, 2-tiered (BLS and ALS) EMS system, a few variables emerged that were persistently linked to the inpatient diagnosis of severe sepsis or septic shock: advanced age, hot tactile temperature, low systolic blood pressure, and low oxygen saturation. Compared with other currently available triage schemes, the PRESS relies mostly on clinical assessment and 9-1-1 triage. Indeed, prehospital POC lactate analysis is not readily available in most EMS agencies, and compliance with rigorous protocols may depend at least in part on the ambulance crew's level of training. The sensitivity of the score was 91% in the derivation group and 78% in the validation group. When the predefined threshold of 2 or more points is met, the sensitivity of the PRESS increases to 86%.

This scoring technique has several important limitations. Patients in the derivation group had already met criteria for the systemic inflammatory response syndrome (SIRS). Patients deemed "at risk" for sepsis had to meet all the criteria in the prehospital setting: elevated heart rate, elevated respiratory rate, and systolic blood pressure less than 100 mm Hg. Therefore, the PRESS's respectable sensitivity would suffer following validation in an external cohort.

EARLY WARNING SCORES

The concept of an early warning score (EWS) was developed in an effort to identify deteriorating hospitalized patients rapidly.[6] These scores, most often a composite of physiologic and/or laboratory values, have become the standard of care in many parts of the world.[6] However, the utility of an EWS in the prehospital environment is less well established. There is precedent for timely prehospital intervention directed at time-sensitive conditions such as stroke, STEMI, and penetrating trauma. It follows that sepsis, which is also a time-critical illness, would benefit from the same treatment strategy. Although early treatment of sepsis shows a greater morbidity and mortality benefit than early thrombolysis and balloon angioplasty for patients with acute

coronary syndrome, until recently it received less attention and research funding.[7,8] There is current interest in developing a prehospital EWS to identify patients with critical illness and facilitate their early access to appropriate, definitive care.[6]

Developing an EWS for sepsis presents unique challenges. The first challenge is the lack of a consensus definition for sepsis. Sepsis is a clinical syndrome for which the inclusion and exclusion criteria have been changed over the years. The most recent definition by the International Committee on Sepsis was published in *Journal of the American Medical Association* in 2016.[9] The authors of that article anticipate that, as one becomes more knowledgeable about the biology behind the clinical manifestations of sepsis, the definition of the disease will be refined. For example, the term "severe sepsis" is now considered redundant, so it has been removed from the clinical spectrum.[9] Changing the nomenclature poses a problem when it comes to research and establishing evidence-based practices. Much of the data produced so far used "severe sepsis" criteria in determining whether an intervention was successful. The lack of a clear definition, as well as a lack of consensus on measurable outcomes, makes the existing body of literature heterogeneous and difficult to compare.[6] Establishing a universal EWS under these circumstances becomes complex.

The first prehospital EWS was the Rapid Acute Physiology Score (RAPS), which is an abbreviation of the APACHE-II (Acute Physiology and Chronic Health Evaluation) score.[6] RAPS was developed and tested for the aeromedical transport of critically ill patients. There are several in-hospital EWS currently in use. Attempts have been made to translate in-hospital EWSs into the prehospital environment via scoring systems such as the Modified EWS (MEWS), with varying success.[6,10]

Guerra and colleagues[4] developed a "sepsis alert" protocol that incorporates modified SIRS criteria along with prehospital lactate measurements to identify severe sepsis patients. The Robson screening tool takes into account temperature, heart rate, respiratory rate, mental status, plasma glucose concentrations, and a history suggestive of new infection.[8] The BAS tool is based on the following vital signs: oxygen saturation less than 90%, respiratory rate greater than 30, and systolic blood pressure less than 90 mm Hg (BAS 90–30–90).[1,6,11]

In 2015, German researchers developed the Prehospital Early Sepsis Detection score (PRESEP), which gives weighted values to abnormal vital signs (**Table 1**). The cutoff indicating potential septic disease is greater than or equal to 4.[7] The authors compared their scoring system with MEWS, BAS 90-30-90, and the Robson screening tool. The PRESEP score performed better than MEWS and BAS 90-30-90 in terms of sensitivity, specificity, as well as positive and negative predictive value. The Robson

Table 1
Prehospital early sepsis detection score

Vital Sign	Points
Temperature >38 C	4
Temperature <36 C	1
Heart rate >90 bpm	2
Respiratory rate >22 breaths/min	1
Oxygen saturation <92%	2
Systolic blood pressure <90 mm Hg	2

A score greater than or equal to 4 suggests sepsis.

From Bayer O, Schwarzkopf D, Stumme C, et al. An early warning scoring system to identify septic patients in the prehospital setting: the PRESEP score. Acad Emerg Med 2015;22:868–71.

score, however, had a higher sensitivity and negative predictive value but a lower specificity and positive predictive value.[7] It is important to note that the German model of prehospital care differs significantly from the American model. In Germany, ambulance crews typically include physicians. In addition, in the United States, body temperatures are not always measured by prehospital care providers, which could limit the generalizability of a scoring system that requires it.[12]

As previously mentioned, the PRESS score is 86% sensitive when the threshold of 2 points is met or exceeded.[13] The score incorporates several pieces of data that are collected routinely by both dispatch and EMS providers in the United States in order to identify patients at risk for severe sepsis.[13] Each criterion is weighted (see **Table 1**). The maximum is 24 points, and the threshold of 2 or more points can be met with a single criterion. This scoring system has several limitations, and additional validation studies are required before it can be put into widespread practice.

In a recent article in *Journal of the American Medical Association*, the Sepsis-3 Committee recommended use of the Sequential Organ Failure Assessment (SOFA) score as a marker of organ dysfunction. The SOFA score, which incorporates laboratory values such as bilirubin and creatinine levels, has been used primarily in the intensive care setting. A score greater than or equal to 2 is associated with an in-hospital mortality greater than 10%. The authors propose using a truncated SOFA score in out-of-hospital, ED, and general ward settings to identify patients at increased risk of worse outcomes related to sepsis. The criteria for this quick SOFA score (qSOFA) are respiratory rate greater than or equal to 22 breaths/min, systolic blood pressure less than or equal to 100 mm Hg, and altered mentation. The presence of 2 of these 3 criteria had similar predictive validity to the full SOFA score outside the ICU.[9]

EWSs and the prehospital care provider's ability to act on them could have the greatest impact in areas where transport times are prolonged. The mainstays of sepsis treatment are antimicrobial therapy, source control, and supportive therapy (eg, IV fluids, vasopressors) to maintain tissue perfusion.[14] Seymour and colleagues[15] found that, after multivariable adjustment, placement of a prehospital catheter with or without prehospital fluid administration was associated with a reduced odds of hospital mortality. It must be noted that decisions to administer fluids or insert a catheter were not driven by any sepsis-specific protocol. Instead, patients in whom an IV line was placed were viewed by the medics as having life-threatening or urgent conditions according to the EMS severity index.[15] These patients also had lower blood pressures, lower Glasgow Coma Scale scores, higher heart rates, and higher respiratory rates compared with those who did not have the intervention. Essentially, the patients who had an IV catheter placed with or without fluid administration were perceived by the prehospital providers to be sicker.[15] The average amount of fluid administered was a mere 500 mL, leading some to think that the hospital mortality benefit was due to early hospital notification and reduced time to intervention in the ED.[10] Indeed, some have questioned whether prehospital warnings have any measurable effect on the overall mortality.[12] Even if the actual impact of early prehospital notification remains unproven, an EMS treatment strategy that prioritizes recognition of sepsis syndromes and aggressive fluid administration when appropriate is consistent with sound medical practice.

AN IDEAL PREHOSPITAL SEPSIS PROTOCOL

Prehospital care in the United States is protocol driven. EMS providers are expected to know the protocols in their jurisdiction and to operate within and venture outside of them only in consultation with real-time medical direction. Within a given jurisdiction,

the protocols will differ according to provider level. EMTs have the baseline skill set allowed for prehospital transport. Their scope of practice is limited to obtaining vital signs, applying oxygen, and delivering a limited number of medications.[16] These individuals can recognize abnormalities but are limited in the ways they may intervene. Conversely, paramedics provide the highest level of routine prehospital care. They possess all the skills of an EMT plus are able to establish IV lines and administer IV drugs, provide cardiac care such as cardioversion and transcutaneous pacing, as well as provide definitive airway management (ie, intubation).[16] Various models of prehospital care are used—some operate solely with EMTs, some with solely paramedics, and others with a combination of the 2 levels of training and practice.

The ideal prehospital protocol for sepsis would not only provide accurate recognition but also dictate what action should follow the recognition. It should be simple to apply and take into account skills possessed by both EMTs and paramedics so that it could be applied in a wide range of systems. In light of the recommendations by the Sepsis-3 Committee, a prehospital sepsis protocol could incorporate the elements of qSOFA with the addition of a POC lactate measurement. The qSOFA components are readily calculable and easy to recall, because each component is given one point. The addition of POC lactate measurement would add specificity when used in the correct clinical context, as 2 of 3 points with qSOFA alone could be amassed in many clinical scenarios (eg, drug overdose).

POC lactate measurements correlate well with measurements from whole blood. Gaieski and colleagues[17] compared the accuracy of fingertip POC and whole blood POC lactate measurements with the reference method for lactate analysis. They also examined the time differential from fingertip POC lactate results to that obtained from the laboratory. Both fingertip and whole blood POC lactate measurements showed excellent agreement with the reference method, with intraclass correlation coefficients of 0.90 and 0.92, respectively. In addition, the average time between obtaining POC and reference laboratory results was 65 minutes (95% CI, 30–103). Although the sample size was small, the findings suggest that POC fingertip lactate results are accurate, quickly available, and suitable for use in the prehospital setting.

At present, POC lactate monitors are not widely used in the prehospital environment. Body fluid testing for information that may influence patient care decisions is regulated by the Centers for Medicare and Medicaid Services through the Clinical Laboratory Improvement Amendments (CLIA).[18] Several standards must be met before an agency can be authorized to perform the test. CLIA has established 3 categories of laboratory tests based on criteria that involve the equipment and the knowledge required to interpret the results. The categories are high complexity, moderate complexity, and waived testing. Measurement of POC lactate is considered moderate complexity, so an EMS service must be accredited and certified at that level before it can implement POC lactate testing. Whole blood glucose testing, in comparison, has been granted CLIA-waived status.[18] Several POC lactate measurement devices have been approved for clinical use by the US Food and Drug Administration. However, obtaining and maintaining these devices as well as ensuring that prehospital care providers are trained in their proper use can be costly to the system.

When a septic patient is identified, steps should be taken to ensure transport to definitive care as quickly as possible. A “sepsis alert” should be given to the receiving hospital so that the patient can be triaged in a timely manner and appropriate treatment initiated immediately. Hayden and colleagues[19] sought to determine if a triage sepsis alert and sepsis protocol reduced time to fluids and antibiotics in the ED. They found that by identifying certain sepsis criteria at triage and thus triggering a system that automated “sepsis bundle” treatment, the mean time to a fluid bolus was

reduced by 31 minutes and the mean time to antibiotics was reduced by 59 minutes.[19] Such a system triggered from the field could reduce times to fluids and antibiotics even further.

In a 2-tiered system, a sepsis protocol should include parameters that dictate when prehospital care should be escalated to ALS. Placing IV catheters and starting IV fluids is outside the scope of practice for an EMT. Any such intervention must be done by a paramedic. En route to the hospital, it might be reasonable for a paramedic to administer a fluid bolus to a hypotensive patient with sepsis. Additional therapy, such as antibiotics, should be administered only after considering transport times and in consultation with medical control. For example, in a rural EMS system for which transport times are routinely 2 hours or longer, there is likely little downside in starting broad-spectrum antibiotics for a patient who presents in septic shock. The ability to do so depends on the availability of the medication and the skill of the prehospital care providers who are present. The transport team should obtain real-time online medical direction before the administration of antibiotics. In most cases, the prehospital use of antibiotics should not be a standing order within a sepsis protocol.

Finally, an ideal sepsis protocol would give guidance regarding where patients should be transported. In systems in which ambulance diversion is used, prehospital identification of a patient in septic shock could allow an ambulance to bypass the nearest hospital for a more appropriate one if the first does not have critical care capability. Authorization for such measures would be coordinated at a regional or state level in the same way that trauma and cardiac systems of care are organized.

PARTNERS IN CARE

Prehospital personnel are often the first health care providers to reach patients with life-threatening illnesses and injuries, including sepsis. EMS units transport more patients with sepsis than with stroke or acute myocardial infarction.[20] Based on a review of 16 published studies, Lane and colleagues[20] calculated that roughly half of all patients admitted to a hospital with severe sepsis arrive by ambulance service. This volume suggests that EMS providers are uniquely positioned to play a role not only in early notification systems to hospitals when transporting a septic patient but also in illness surveillance within the community. Community paramedicine is a new model of community-based health care delivery that uses EMS personnel and systems to address issues of wellness, prevention, postdischarge care, care for the chronically ill, and medical compliance within a local population.[21] Initially designed to expand access to care in underserved rural areas, these providers perform assessments and interventions on an outpatient basis and usually do not transport patients to hospitals. Community paramedicine can be used to monitor for illness trends among high-risk populations such as nursing home residents. Using EMS skills in this way could allow identification of septic patients even earlier in their disease process and prevent adverse outcomes. Early identification and management of sepsis may allow patients to avoid the hospital all together, which could save up to $50,000 per patient, translating to annual nationwide savings of $17 billion.[22]

CHALLENGES AND THE PATH FORWARD

The clinical syndrome of sepsis is not yet completely understood. This incomplete understanding, coupled with the previously undervalued importance of the disease, has led to gaps in prehospital training modules. After all, formal, state-funded EMS systems were established in the 1970s in response to the large numbers of out-of-hospital deaths caused by trauma.[23] Studies have shown that prehospital personnel

have low rates of sepsis identification when judgment alone is used.[3] These findings indicate a need for increased education regarding the presentations of occult sepsis and for the development of protocols that incorporate objective data into the process by which septic patients can be identified. Accurate recognition of sepsis in the prehospital environment can prevent delays in definitive care and presumably improve patient outcomes.

In addition to improving the prehospital recognition of sepsis, additional research is needed in terms of delineating which parameters and biomarkers are most important in sepsis classification. Outcomes research is needed to determine whether there is a mortality benefit to prehospital intervention in sepsis and, if so, which EMS treatment conveys that benefit. Elucidating these parameters will help determine education guidelines and can help to justify the cost of additional equipment and training surrounding the out-of-hospital management of sepsis.

SUMMARY

Similar to acute myocardial infarction and stroke, sepsis is a time-sensitive condition that would benefit from early recognition and management. Many patients with sepsis and septic shock are transported to EDs via EMS. Data indicate that prehospital care providers' recognition of sepsis is low when based solely on clinical judgment. At present, there is no universally accepted scoring system that can be used to identify septic patients in the prehospital setting. In addition, there are no guidelines indicating what treatment should be initiated for a septic patient in the prehospital environment. There is suggestion that a "sepsis alert" triggered by EMS personnel might reduce the time to administration of antibiotics and fluids. Giving EMS care providers the education and tools they need to detect sepsis in the field could lead to even earlier detection of this potentially life-threatening condition and thereby improve patient outcomes. Additional research is needed to determine what role EMS should play in the chain of survival when it comes to this serious clinical syndrome.

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