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Protocol Based Screening Tools to Identify Sepsis Patients Transported by Emergency Medical Services

Isaiah Moser
University of Central Florida

PROTOCOL BASED SCREENING TOOLS TO IDENTIFY SEPSIS PATIENTS TRANSPORTED BY EMERGENCY MEDICAL SERVICES

by

ISAIAH S. MOSER

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Abstract

Sepsis is a complicated disorder in which an infection has reached the bloodstream and caused a cascade of events that in time will lead to death. Interventions aimed at identifying sepsis early in its progression are imperative to stopping the process. The purpose of this study is to examine the current state of the literature regarding sepsis screening tools utilized by emergency medical services. A literature review exploring the various tools in place was conducted to see their value in predicting sepsis and secondary what the initiation of a sepsis alert has on the patients' outcome. Results found included that sepsis screening tools when in place decrease time to identification, decrease time to antibiotics, increase amount of fluid administration, and overall reduce hospital stay and mortality rate. With these findings educational training for EMS providers and the introduction of generalized protocols are of the upmost importance. Further research is needed to be done to create a consistent tool to be used by all EMS agencies that has a validated predictive value of sepsis.

Dedication

I would like to dedicate this work to first responders: EMS, fire, and police, who everyday put their lives at risk to save others. I am forever grateful for the sacrifices you make to keep my family, my community, and me safe. God bless you all.

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List of Abbreviations

ED: Emergency Department

EMS: Emergency Medical Services

$ETCO_2$: End-Tidal Carbon Dioxide

ICU: Intensive Care Unit

SIRS: Systemic Inflammatory Response Syndrome

SOFA: Sequential Organ Failure Assessment

Background

Sepsis is a systemic response to infection that can progress to organ failure and eventually death (Uppu, Ghosh, & Haldar, 2015). Severe sepsis and septic shock affects millions of people worldwide each year killing as many as one in four people (Dellinger et al., 2012). With Emergency Medical Service (EMS) only identifying 19% of patients exhibiting severe sepsis based on clinical judgement, new interventions are being introduced (Politio et al., 2015). Initiatives to decrease mortality associated with sepsis start with protocol-based screening tools and treatment guidelines (van Zanten et al., 2014). In an effort to identify patients with possible sepsis as early as possible, these tools are now being used in the prehospital environment, which means EMS providers play an essential role in identifying at risk patients (Studnek, Artho, Garner, & Jones, 2012). EMS provides the first point of contact for many sepsis patients. Thus their recognition of sepsis is paramount in the initial treatment once reaching the Emergency Department (ED).

In the last 5-10 years, research has been initiated to evaluate the effectiveness of EMS activated "sepsis alerts" to the receiving hospital. The goal of an alert system is to notify the receiving hospital of the patient's status prior to arrival. An important level in the diagnosis of sepsis drawn in the hospital is a lactate level as it identifies those in danger for rapid deterioration due to organ failure (Aluisio et al., 2016). Initial lactate level ≥ 4 has a significantly higher 28 day mortality rate than those < 4, warranting its usefulness (Berger et al., 2013). Although this value is sometimes drawn by EMS systems with predictive value of sepsis, due to the limitations of many and to decrease cost, noninvasive screening tools are utilized

(Shiuh et al., 2012). A common tool used by prehospital providers in addition to vital signs is End Tidal CO_2 Capnography ($ETCO_2$). This device measures the maximal fraction of carbon dioxide present at the end of exhalation or a singular breath. This tool is noninvasive, provided in real time, and does not require any additional monitor equipment to be carried by the EMS provider. Various studies have shown the inverse relationship between a low $ETCO_2$ and an elevated lactate level (Caputo et al., 2012; Guirgis et al., 2014; Hunter, Silvestri, Dean, Falk, & Papa, 2013). Lactate levels are important in the prediction risk of sepsis related mortality specifically when combined with hypotension (Singer, Deutschman, Seymour, & et al., 2016).

A practical reliable tool utilized within the EMS system would in theory allow for earlier recognition and expedite treatment leading to improved outcomes (Polito et al., 2015). Once reaching the hospital guideline bundles for treatment could be introduced within ICU admitted patients which could decrease the risk of mortality (van Zanten et al., 2014). With guidelines in place adherence increases reducing the in hospital mortality rate once admitted. The goal is early recognition, prompt treatment, and to maintain consistency in care once admitted.

Problem

Identifying sepsis early has been a difficult task assigned to EMS and hospital personnel. Sepsis alerts initiated by EMS providers in the field require time-sensitive allocation of limited and specialized resources at the receiving hospital. Many times alert systems are utilized due to the high mortality rate associated with delayed diagnosis and the inability to rule out if sepsis is occurring (Shetty et al., 2016). Emergency Department and other personnel are required to prioritize assessments and interventions for the sepsis alert patient.

If, however, the patient does not meet sepsis alert criteria or if these time-sensitive interventions do not impact patient outcomes, these limited and specialized resources may be misallocated. When resources are misused the cost impact on the hospital increases and drives patient care expenses up. Another issue is that human and diagnostic resources are inappropriately allocated to patients for whom no benefit has been reported. While these resources are being used by the "inappropriate" patient, they are not available for appropriate ones. It may also contribute to the ED divert problem in which EMS is forced to go to another receiving hospital due to overcrowding. The problem that currently exist is if initiating a sepsis alert is improving the outcome of the patient. If the outcome is improving and the noninvasive screening tools being used show signs of positive predictive value the sepsis alert being called would be validated. If early interventions do not improve patient outcomes, there is no added value to EMS calling a sepsis alert. Knowing this would allow EMS providers and hospital staff to shift their focus from time-sensitive interventions to secondary measures and seeing more critical patients.

Purpose

The aim of this thesis is to assess the current state of the science regarding the early identification and treatment of sepsis by providing an integrated review of the literature. This review will identify the factors that contribute to positive patient outcomes with sepsis. It will incorporate the roll that EMS providers contribute to the identification and alert system of the receiving hospital. Recommendations for future practice and research will be made.

Methods

The researcher examined the current published literature on sepsis screening tools utilized by the prehospital and in hospital systems. The specific focus of this research was to evaluate the use and relevancy of protocols that include non-invasive measures to screen for sepsis. Databases used to find studies included CINHAL, MEDLINE, Academic Search Premier. These databases were accessed electronically through UCF's online library system. The goal of this search was to find original research studies that have been peer reviewed, up to date literature reviews, and published dissertations, if applicable. In order to screen articles abstracts were read to evaluate their applicability to this literature review.

The following terms were used to search the databases: Sepsis AND Screening AND Adult. Using those search terms a total of 213 articles were found; Medline 141, CINHAL 52, and Academic Search Premier 20. Articles were included if they were of adult patients, published from 2010-2017, and had an abstract available. Articles were excluded if they included studies of pediatric aged patients, if the article was not available in full text, and if the article was not published in English. Studies were also excluded if their focus was not on sepsis screening and the use of protocols. This process reduced the total of articles to 29; Medline 13, CINHAL 12, and Academic Search Premier 4. Further reduction was done by eliminating repeat articles which brought the overall article count to 22. Some articles were located after the initial search while reviewing found articles and finding further sources through references. These additions were evaluated using the same inclusion and exclusion criteria.

Findings

The literature review search revealed three major themes present in the current research:

1. Sepsis definition and identification is a rapidly changing topic.

2. There are various screening tools in place to recognize sepsis.

3. EMS play an important role in recognition and treatment of sepsis.

Sepsis Identification Rapidly Changing

Recently, the definition of sepsis has changed and has shown that SIRS criteria is not as helpful in diagnosing sepsis as once thought. SIRS criteria includes the following (Singer et al., 2016):

- Temperature >38°C or <36°C
- Pulse >90 BPM
- RR >20 BPM or $PaCO_2$ < 32 mm Hg
- WBC > 12,000 or < 4000 or >10% immature bands

Many protocols that have been implemented throughout the last ten years have included SIRS criteria as their diagnostic tool and now will need to adjust to updated research. New guidelines by Singer et al., suggest that a Sequential Organ Failure Assessment (SOFA) score be used in the diagnosis and ongoing treatment of sepsis presented in Figure 1 below (2016). This includes a broader scoring system in the recognition of sepsis and organ failure beyond the current guidelines of SIRS criteria. This score incorporates various blood values such as creatinine, bilirubin, and platelets with also some non-invasive measurements such as mean

arterial pressure and Glasgow Coma Scale. Once a patient reaches a SOFA score of 2 or greater they have approximately an overall mortality risk of 10%, higher than current rates for acute myocardial infarction (Singer et al., 2016).

Unfortunately, some of this scoring system is not feasible for EMS providers because blood laboratory values necessary to obtain a complete score are not available in the prehospital environment. These values also are expensive and with routine use would drive up the cost of an ambulance transport. However, the authors also proposed a quick SOFA (qSOFA) that does not require blood laboratory values and is easily applied by EMS providers. The qSOFA includes the following criteria (Singer et al., 2016):

- Respiratory rate $\geq$ 22/min
- Altered mentation (Reduced from baseline GCS)
- Systolic blood pressure $\leq$ 100 mm Hg

A useful addition to the qSOFA is the ETCO2 as it associated is with metabolic disturbances specifically elevated lactate levels (Hunter, Silvestri, Dean, Falk, & Papa, 2013). Protocols incorporating qSOFA and ETCO2 can help EMS providers recognize patients at greater risk for sepsis in the prehospital environment. No matter the protocol in place relying on lab values to guide treatment outcomes causes a significant delay in care.

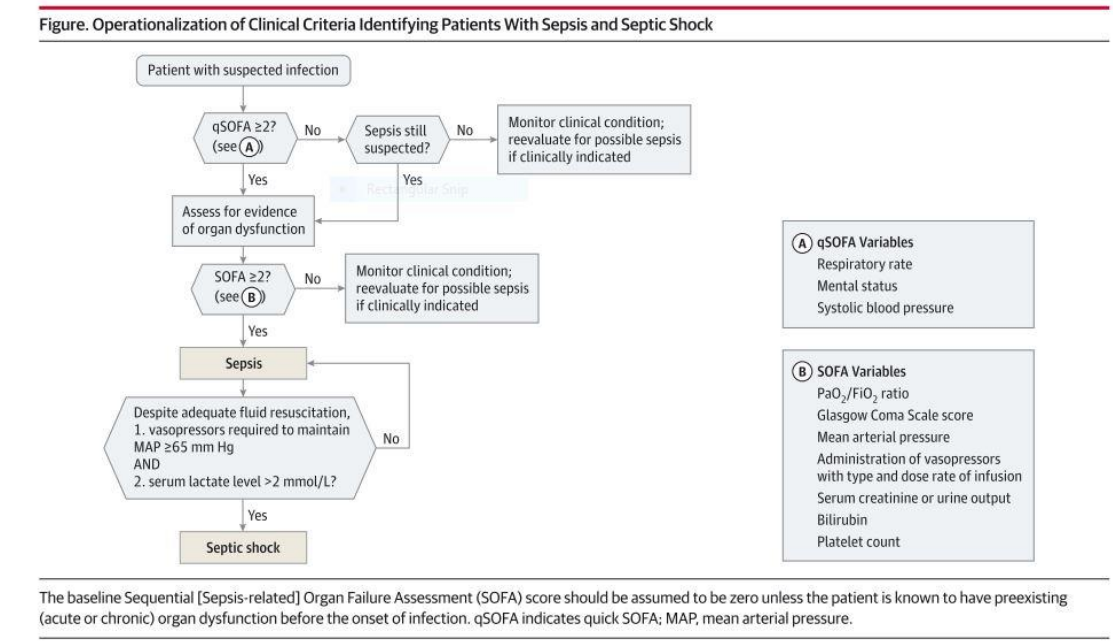

Figure 1 taken from: Singer, M., Deutschman, C. S., Seymour, C., & et al. (2016). The third international consensus definitions for sepsis and septic shock (sepsis-3). *JAMA*, *315*(8), 801-810.

Recognizing Sepsis and EMS Role

Early identification of sepsis has recently become part of the 911 dispatch information, requiring emergency medical dispatchers to ask valuable questions that can signal in to sepsis such as breathing and level of conscious changes (Bohm, Kurland, Bartholdson, & Castrèn, 2015). EMS transports nearly half of all patients that are diagnosed with sepsis, many of which had progressed to severe sepsis and septic shock (Studnek et al., 2012). Protocols and diagnostic screening tools such as the PRESEP score, TREWScore, or utilizing ETCO2 measurements along with SIRS criteria that have shown predictive values for recognizing sepsis (Alsolamy et al., 2014; Bayer et al., 2015; Henry, Hager, Pronovost, & Saria, 2015; Hunter et al., 2016; Suffoletto et al., 2011). The current science suggests the need for consistent evidenced based

screening tools to identify those with sepsis and at risk (Wallgren, Antonsson, Castrén, & Kurland, 2016).

There is limitations to the identification of sepsis as to this day it is not fully understood with clinical symptoms the primary model for diagnosis (Uppu, Ghosh, & Haldar, 2015). Currently patients exhibiting signs and symptoms consistent with sepsis initiates the EMS provider to call a "Sepsis Alert" to notify the receiving hospital of the patient's status (Guerra, Mayfield, Meyers, Clouatre, & Riccio, 2013; Polito et al., 2015). This can be challenging for providers in the field as they do not have access to the laboratory and imaging test that are available to ED personnel. With this though EMS personnel are still able to recognize sepsis to a high degree, one study found up to 78.2% of the time when a protocol is in place (Green et al., 2016). This study was conducted in Canada with different levels of training given to providers compared to the curriculum in the U.S. The goal of calling a sepsis alert is to decrease time to critical interventions and improve patient outcomes.

Improved recognition of sepsis allows EMS providers to initiate early prehospital treatment and decrease invasive interventions needed at the hospital. In one study patients were intubated about 27% less frequently and had a 10% less mortality rate if a sepsis alert protocol was initiated (Guerra, Mayfield, Meyers, Clouatre, & Riccio, 2013) . The rate of intubation is significant as it is associated with longer length of stays thus driving up cost (Hunter et al., 2013). Prolonged hypotension in the septic patient is detrimental to their overall prognosis. With this, early fluid administration is associated with greater rates of survival in patients with severe sepsis and septic shock (Lee et al., 2014). Patients receiving intravascular fluids at a higher rate

within the first three hours have a decreased mortality rate (Lee et al., 2014). Access to intravenous lines and fluid administration is nearly universal across the U.S in the prehospital arena. Although it is readily available to providers one study showed that a mere 40% of patients transported by EMS in septic shock received prehospital fluids (Seymour et al., 2010). Lee et al., goes on to suggest that the current guidelines of initial fluid bolus of 20ml/kg be increased to 30ml/kg due to improved outcomes with greater amounts of fluids within the first 6 hours (2014). With EMS carrying equipment to initiate this procedures this process could be implemented before patients ever reach the hospital.

When patients are transported by EMS services time to antibiotics and goal therapy are reduced significantly (Studnek, Artho, Garner, & Jones, 2012). One study found that when their sepsis protocol was implemented time to antibiotics can be decreased as much as 59 minutes and fluid administration 31 mins than when the protocol was not in place (Hayden et al., 2016). Historically each hour of delay in the administration of antimicrobials past 6 hours for the sepsis patient decreases their chance of survival by 7.6% with only 50% of septic shock patients receiving these medications within six hours of prolonged hypotension (Kumar et al., 2006).

Table 1 in Appendix A examines the differences and results of various screening tools. A consistent theme is seen throughout where evaluation consist of non-specific signs of global infection such as heart rate elevation, respiratory rate increases, and elevated or decreased temperature. These themes although can be present with other conditions such as diabetic ketoacidosis, trauma related injuries, and metabolic disturbances not consistent with sepsis. It is important for the provider to rule out other causes before initiating a sepsis alert. A

comprehensive in depth analysis of screening tools done by Smyth, Brace-McDonnell, & Perkins in 2016 reflects similar themes and is referenced.

A major challenge found associated with protocols is provider compliance. In one study, about 40% of sepsis alert notifications did not meet protocol criteria (Hunter et al., 2016). Most of these false alerts were called despite an ETCO2 level inconsistent with metabolic acidosis. Clinician judgement, although not part of the protocol criteria, may be a factor in the incidence of false sepsis alerts. Providers have been educated that longer time to antibiotics with nonspecific presentations can have a negative impact on patient outcomes, so EMS providers may error on the side of caution (Wallgren, Antonsson, Castrén, & Kurland, 2016). EMS providers are charged with combining protocols, clinical judgement, and limited diagnostic tools to identify patients at increased risk for systemic infection. However, studies report that clinical judgment is inferior to protocol based identification of sepsis (Harrison et al., 2015; Wallgren, Castrén, Svensson, & Kurland, 2014).

During the literature review, some have challenged that timing metrics such as time to antibiotics and automated sepsis alerts did not significant reduce mortality rates in patients with severe sepsis and septic shock (Makam, Nguyen, & Auerbach, 2015; Sterling, Miller, Pryor, Puskarich, & Jones, 2015). The analysis done by Sterling et al., in 2015 was later challenged to its validity and the impact that antibiotics do contribute to changes in mortality (Youkee et al., 2016). One study found that focused on EMS transported sepsis patients showed that although time was reduced from initial antibiotic therapy and further treatment algorithms, there was not a statistically significant reduction in mortality rate seen (Band et al., 2011).

Implications for Practice

As mentioned previously the need for a non-invasive consistent, reliable, and valid tool to assess for sepsis is needed as the amount of patients being diagnosed with sepsis continues to grow (Stoller et al., 2016). The advancement of the prehospital provider both in skill set and tools allows for a development in the recognition of metabolic disorders. With the combination of protocol based training and the utilization of non-invasive monitoring the EMS provider will be able to identify sepsis to a higher degree.

The findings of this literature review did not reveal significant training being given to EMS in regards to the identification of sepsis. Many of which were done through electronic media sources or placed in protocol resources to be followed. The implementation of in person training with hands on simulation may be required to reinforce the recognition of sepsis. As some practicing providers began before the utilization of $ETCO_2$ this tool may not be as familiar to them. Also sepsis screening is new to EMS over the past 5-10 years and may have not been included in their educational program. Although there is cost associated with doing simulation training; if done this may reduce the amount of false sepsis alerts called, increase the amount of recognized sepsis patients, and have better control over resource allocation. Length of stay is known to be decreased when sepsis protocols and early treatment algorithms are in place (Castellanos-Ortega et al., 2010).

In one small study a cost reduction of over $2000 was seen when sepsis identification tools were utilized (Judd, Stephens, & Kennedy, 2014). Although this number may be even greater especially in areas where higher level of care is needed for a longer period of time due to

the capacity of the hospital. In turn the amount of money saved by reducing a hospital stay by one to two days through early treatment and resuscitation may warrant the training for providers.

When examining the current state of the literature the following protocol was developed to be used to screen for sepsis based on the current body of knowledge:

A "Sepsis Alert" is to be initiated by the prehospital provider if the following are present:

1. Suspected Infection

2. Two or more of the following Present:

- *Systolic B/P ≤ 100 mm Hg or Mean Arterial Pressure < 70 mm Hg*
- *Altered Mentation (from baseline) GCS < 15*
- *Respiratory Rate ≥ 22 Breaths Per Minute*
- *$ETCO_2 \leq 25$*

In addition to aspects of SIRS criteria this protocol adds two parameters included in the SOFA scoring system which had been shown to have better predictability of mortality (Raith et al., 2017). The two parameters included are the MAP < 70 mm Hg and altered mentation, if the patient exhibited these two findings they would have a SOFA score of at least two depending on level of dysfunction (Singer et al., 2016). It should be noted that these noninvasive measurements of altered mentation, tachypnea, and hypotension are commonly associated with an elevated SOFA score (Seymour et al., 2010). Although neither SIRS nor SOFA protocols include $ETCO_2$ within their screening algorithms, its correlation with bedside lactate levels warrants its use (Hunter et al., 2013). However if an EMS provider in their best clinical

judgement believe that a patient would benefit from a sepsis alert being called this intervention should not be withheld as a high portion of non-protocol compliant patients are diagnosed with sepsis (Hunter et al., 2016). There may be further indication to notify receiving emergency room staff of suspicion of sepsis without initiating an alert, it could decrease allocation of resources without having negative patient outcomes. With this protocol the prehospital provider would be able to assess the sepsis patient non-invasively with a blood pressure cuff and End-Tidal capnography present. Due to the nature of the protocol being significant signs of sepsis such as decreased MAP it may be limited to "severe sepsis" and "septic shock" categories although these patients may benefit the most from an alert system. The time associated with these measurements is minimal and should be used routinely on suspected infection patients.

Further research is needed to be conducted to evaluate the outcome based measurements of sepsis when a "sepsis alert" is initiated by the EMS provider. The current state of the research shows various forms of screening tools that are in use most of which are using SIRS criteria guidelines. With the current consensus of a SOFA score being more accurate than SIRS criteria and qSOFA, new protocols need to be implemented (Raith et al., 2017). A cost effective intervention to be included in routine patient care as a vital sign is the $ETCO_2$ as it use extends beyond that of sepsis recognition (Nagurka et al., 2014). Further research is needed in developing an adequate screening tool that is generalized throughout the EMS system that is reliable in the prediction of clinically significant outcomes (Williams, Tohira, Finn, Perkins, & Ho, 2016). There may also be some validity to adding keywords related to symptom presentation in the alert system of sepsis, although more research needs to be done before this becomes common practice (Wallgren, Bohm, & Kurland, 2017).

This research project focused on the use of the non-invasive protocols to be utilized by EMS systems although the practicality of this tool could be implemented throughout the hospital setting. The cost-effectiveness of the measurement and limited training needed could propose a triage tool to be utilized by the ED nurse when evaluating the level of acuity to assign to a patient or on a medical floor when screening for sepsis. This may lead to the development of accurate automatic warning systems that can be used in electronic health records to identify sepsis.

Limitations

One of the limitations to this search review is the selection of the articles only from the period of January 2010-2017. This parameter excludes studies conducted before this date which may have valuable research in regards to sepsis algorithms. Many of the studies conducted are of singular hospital systems with protocols initiated for that area which may not represent a larger population.

A concern that is noted is that currently most of the research conducted is by Medical Doctors not with collaborative management of other specialties. It is interesting that studies found involve interventions to be carried out by emergency medical personnel or ED staff (nurses, respiratory therapy, etc.) yet they are not listed as investigators.

Another limitation is that many of the positive results coming from protocol based screening tools are from research studies outside of the United States. It is crucial that more research is done here to see if there are differences in outcomes based on region and level of training.

APPENDIX A: REVIEW OF SCREENING TOOLS

Sepsis Electronic Health Record Screening Tool (Alsolamy et al., 2014) *Not in use in EMS evaluated for future research	1. >14 Years old 2. Two or more SIRS Criteria • Temperature >38℃or <36℃ • Pulse >90 BPM • RR >20 BPM • WBC >12,000 or <4,000 ml 3. One Organ Dysfunction • Systolic B/P <90to 86 mm Hg with IV fluids or <86 regardless • Blood Oxygen Saturation <90% to 85 with oxygen or <85% without oxygen • Lactate >2mmol/L OR • Two of the organ dysfunction criteria	• At 95% Confidence Interval : Predictive Value for Sepsis ○ Sensitivity – 0.93 ○ Specificity – 0.98 ○ Positive Predictive Value – 0.21 ○ Negative Predictive value – 0.99 • Test does not include laboratory testing or presenting symptomology • Implications for further practice could include earlier time of recognition of sepsis preceding ICU admissions • Alert system utilized through Nursing worklist system which in turn they alert the attending physician • Only conducted on patients who were admitted to the ICU
Early Warning Scoring System PRESEP Score (Bayer et al., 2015)	1. Temperature > 38℃ = 4 or Temperature < 36℃ = 1 2. Heart Rate >90 BPM = 2 3. Respiratory Rate >22 BPM = 1 4. SaO_2 < 92% = 2 5. Systolic Blood pressure < 90 mm Hg = 2 Score ≥ 4 = Possible septic disease process	• Simple tool and fast to calculate as all measurements included in the study are readily available • Tool performed more accurately than the Modified Early Warning Score (MEWS) • Non-invasive and does not require any additional equipment to be implemented • Sensitivity of 0.85 • Specificity of 0.86 • Positive predictive value of 0.63 • Negative predictive value of 0.95 • AUC 0.93 ($p \leq 0.001$, CI 95%)

Prehospital Screening Tool (Guerra et al., 2013)	1. >18 years old and not pregnant 2. Two SIRS Criteria • Temperature >38°C or <36°C • Pulse >90 BPM • RR >20 BPM 3. Suspected infection 4. Presence of Hypoperfusion by one of the following • SBP <90 mm Hg • MAP <65 mmHg • Lactate Level ≥ 4 mmol/L	• Trained EMS providers identified 47.8% of severe sepsis patients • Overall mortality for 112 patients was 26.7% • Mortality for sample whom Sepsis Alert Protocol was initiated was 13.6% (p=0.040) • Sepsis Alert Protocol Patients were intubated less frequently than non-Alert patients 8% vs 35% (p=0.003) • Hospital length of stay about 1 day shorter than Non-Alert patients (p=0.65) although not statistically significant
"Sepsis Alert" Prehospital Screening tool (Hunter et al., 2016)	1. Suspected Infection 2. Two or more of the following: • Temperature >38°C or <36°C • RR >20 BPM • Pulse > 90 BPM 3. $ETCO_2 \leq 25$ mmHg	• 41% of protocol compliant patients admitted to ICU • 78% of protocol compliant patients diagnosed with sepsis compared to 43% non-compliant • Protocol complaint group 6% higher mortality rate • Protocol non-compliant group had significantly higher mean temperatures • Area under ROC curve predicting sepsis was 0.99 for $ETCO_2$ (95% CI $P < 0.001$)
Prehospital recognition of severe sepsis (Polito et al., 2015)	Risk Factor 1. EMD Chief Complaint : sick person (3 points) 2. Nursing home transport (4 points) 3. Age (0-4 points) 4. Hot tactical temperature (3 points) 5. Systolic blood pressure (0-5 points) 6. Oxygen Saturation (0-5 points) Total Points (0-24) 2 points = increased risk for severe sepsis	• Prehospital severe sepsis (PRESS) screening tool is simple, practical and demonstrates a sensitivity of 86% and specificity of 47% • Does not require any additional equipment or data beyond that of current standards • Incorporates the use of Emergency Medical Dispatch chief complaint category into scoring system • Positive predictive value of 19% • Negative predictive value of 96% • EMS personnel recognized 19% of patients with severe sepsis based on clinical judgement

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