Guest: Dr. Gabriel Wardi, MD MPH
Assistant Clinical Professor
Department of Emergency Medicine
Department of Medicine, Division of Pulmonary, Critical Care, and Sleep Medicine

Key Article

Yealy DM, Mohr NM, Shapiro NI, Venkatesh A, Jones AE, Self WH. Early Care of Adults With Suspected Sepsis in the Emergency Department and Out-of-Hospital Environment: A Consensus-Based Task Force Report. Annals of Emergency Medicine. 2021 Apr 9.

BACKGROUND:

- Greater than 850,000 sepsis visits occur in US emergency departments each year
- Majority (around 85%) of sepsis is present on admission and nearly all these patients receive sepsis-related care in the ED and about 75% of ED sepsis patients are treated in the out-of-hospital environment by emergency medical services (EMS) providers
- Despite evidence showing many aspects of emergency sepsis care improve outcomes, inherent difficulties exist in early diagnosis of sepsis, what therapies should be provided when competing diagnoses exist, and the impact of sepsis-related therapies on patients who ultimately do not have sepsis must be considered
- SEP-1, a national quality measure, became publicly reportable in 2018, yet only about 50% of septic patients received full CMS-recommended bundle for emergency and hospital care
- The Surviving Sepsis Campaign (SSC) offers recommendations on comprehensive sepsis care designed to improve outcomes, but they do not address undifferentiated patients before the diagnosis of sepsis can be confirmed
- In 2019, ACEP convened a task for to address controversies and opportunities for improvement in emergency care of patients with sepsis in acute early care settings

RECOGNIZING SEPSIS and SEPTIC SHOCK IN THE FIRST MINUTE TO HOURS OF CARE

Principles of Sepsis Recognition

- Sepsis is a confirmed or suspected infection with new or worsening organ dysfunction and dysregulated host dysfunction (organ dysfunction defined by $\geq$ 2 increase in SOFA score from baseline)
- Septic shock exists in a subset of sepsis patients with circulatory dysfunction and confers higher mortality
- <u>Sepsis is challenging to diagnose, particularly when there is diagnostic uncertainty in the ED, therefore guidance is most appropriate when the diagnosis is established, rather than considered among other causes of illness</u>
    - 20-40% of patients with suspected sepsis in ED are ultimately diagnosed with another noninfectious sepsis mimic
- Recognition that patients with infection-induced hypotension require time-sensitive care, even if they do not meet criteria for septic shock

Early Screening and Detection of Those with Sepsis

- Standardized early sepsis screening tools may improve sepsis recognition however there is no validated evidence-based tool or strategy to accomplish this in the ED
- Although screening systems have improved timeliness of care, there are concerns about reliability and lack of data to suggest patient-centered outcomes are improved and it is incumbent on clinicians to understand which elements of screening lead to improved outcomes

INITIAL CARE STEPS IN THE EMERGENCY DEPARTMENT and OUT-OF-HOSPITAL ENVIRONMENT

Principles of Early Sepsis Management

- History and physical examination may help to detect infection and organ dysfunction
- Emphasis on usual care and prompt action to treat infection and reverse (or prevent) hypotension are important but time thresholds must be based on distinguishing sepsis from other clinical diagnoses

Out-of-Hospital Care

- EMS providers can expedite care by completing a focus history and obtaining corroborating data prior to transport and rapidly bringing patients to an ED capable of early sepsis care
- Current evidence does not support out-of-hospital antibiotic therapy and this cannot be recommended for routine use

Evaluation for Source of Infection

- Recommend obtaining blood cultures in ED without delaying care in those with suspected sepsis before antibiotic administration, unless culture collection will delay antibiotic therapy
- Targeted evaluation and imaging studies based on clinical suspicion

Severity Assessment

- Initial measurement of arterial of venous lactate and repeating lactate after initial resuscitation only if elevated above 4 mmol/L or there is suspicion of clinical deterioration
- No scoring systems accurately stratifies individual sepsis risk in the early stages, but the group recommends using the SOFA score as a reasonable systematic approach
- qSOFA score: less sensitive, more specific than SIRS for short-term mortality, and is a potentially useful tool to identify patients at highest risk for clinical deterioration, but is not sensitive enough to screen for sepsis (nor was it intended to identify patients with infection)
    - 1/3 patients who are qSOFA (+) on admission have an infection, and 1/6 have sepsis

Intravenous Fluid and Timing of Vasopressors

- An intravenous fluid bolus is important during initial management of patients who have hypotension or signs of hypoperfusion, absent signs of fluid overload
- The group does NOT recommend a prespecified volume or body-mass adjusted volume for all patients, although recognizes many patients benefit from 30 mL/kg of crystalloid
- No recommendations of a specific minimum fluid amount prior to starting vasoactive support
- The group supports using balanced crystalloid solutions as the primary resuscitation fluid in patients with sepsis, especially if volumes > 1 L are provided

Vasopressors:

- Norepinephrine is an excellent first line vasopressor and targeting a MAP of at least 65 mm Hg is a reasonable approach, although some patients may require higher amounts, particularly those with chronic hypertension
- Vasopressin is reasonable to administer in patients with high norepinephrine requirements are present
- For patients with ongoing hypotension or evidence of myocardial depression, epinephrine is a reasonable choice

Antimicrobials and Infection Source Control:

- Strongest evidence for antibiotics comes from patients with septic shock and the group supports early antibiotics once sepsis is diagnosed or deemed likely
- Shorter time to antibiotics is preferred, but precise timeframe to optimally support outcomes remains to be defined
    - Group agrees that once the diagnosis of sepsis is made, rapid and comprehensive therapy (including antibiotics) is optimal
- Emerging data will help address the impact of subsequent dosing of antibiotics, particularly those who remain in the ED due to lack of an appropriate inpatient bed
- Patients with an unidentified pathogen should receive broad-spectrum antibiotics directed against gram positive and gram-negative bacteria, according to local susceptibility patterns
- The group supports early identification of infections requiring source control although acknowledges no specific timing threshold exists

TITRATION OF CARE, *delivering ongoing fluids, vasopressors, respiratory support, other interventions based on the individual response to the first care steps*

Ongoing Fluid Administration

- Fluids after administration of initial bolus should be individualized based on patient and response to therapy
- No single approach (clinical evaluation or quantitative evaluation) is superior and the group recommends multiple assessments
- Dynamic over static quantitative resuscitation approaches are recommended, if used

Vascular Access and Invasive Monitoring

- Early vasopressors can be administered through a well-secured non-distal peripheral IV or intraosseous catheters is acceptable for short-term use
- Invasive hemodynamic devices, including central lines and arterial catheters may aid but are not routinely needed in early sepsis care

Subsequent Doses of Antibiotics and Adjunctive Early Sepsis Therapies

- Patients who remain in the ED for prolonged periods of time should have subsequent doses of antibiotics administered according to optimal dosing for each medication
- Corticosteroids are recommended if there is concomitant adrenal insufficiency or patient is on high-dose corticosteroids prior to onset of sepsis
- AGII, vitamin C, vitamin D, thiamine, alone or in combination – are not recommended due to lack of strong evidence supporting benefit

Role of Interhospital Transfer, Inpatient Boarding and Care Transitions in Sepsis Management

- ED boarding (prolonged care awaiting inpatient transfer) presents additional risks for patients with sepsis and if local facilities do not have the capabilities to care for critically ill patients, the group recommends transfer to a facility that can provide appropriate care
- Every institution should create a plan to explicitly define accountability for sepsis patients receiving prolonged ED care

RELATED CONTROVERSIES

- The group supports recommendations and quality assessment tools required by government or regulatory bodies as important ways to improve outcomes of patients with sepsis, but also believe these should be based on best available evidence and undergo regular re-evaluation
- Such guidelines and recommendations should include all relevant stakeholders at each phase of care and incorporate assessment of impact of care on both targeted patients and other receiving care

Sepsis Care in Constrained Settings

- Recognition that resource-constrained settings place limitations on care options available and care must be modified in those settings

TAKE-AWAY POINTS

- **Sepsis is a heterogenous condition that requires a thoughtful approach to the management of patients while in the pre-hospital and emergency department setting**
- **The ACEP taskforce provides an evidence-based approach to the care of patients with sepsis and septic shock that has some notable differences from prior guidelines and quality measures including:**
    - **An emphasis that treatment guidance and bundles are most appropriate when it is clear sepsis is present and such bundles may result in patient harm when there is significant uncertainty in the diagnosis of sepsis.**
    - **Usual care and prompt action to treat infection and reverse (or prevent) hypotension are important but time thresholds must be based on distinguishing sepsis from other clinical diagnoses.**
    - **No scoring systems accurately stratifies individual sepsis risk in the early stages, but the group recommends using the SOFA score as a reasonable systematic approach**
    - **There is no pre-defined fluid bolus amount that should be administered to patients. Although many patients benefit from a 30 mL/kg fluid bolus, others may require less (or more) fluid. Balanced crystalloids are the preferred fluid type in the resuscitation of septic patients, particularly if > 1 L is used. Subsequent fluid administration should be guided by either clinical or quantitative assessment of patient status.**
    - **The strongest evidence for antibiotics comes from patients in septic shock and antibiotics should be promptly administered once sepsis is diagnosed or deemed likely**
    - **Numerous controversies exist in the care of septic patients that are limited by lack of high-quality evidence. Including relevant stakeholders from all phases of care and ensuring the impact of care on targeted patients (and others) receiving care is evaluated is important in the development of guidelines and policy statements**