

Perspectives and implications of the new sepsis clinical practice guidelines

Denise McCormack¹, Miriam Kulkarni², Steven E. Keller³

¹Department of Emergency Medicine, Rutgers University - New Jersey Medical School, Newark, NJ, USA; ²Department of Emergency Medicine, Albert Einstein College of Medicine, Jacobi Medical Center, Bronx, New York, USA; ³Family Medicine and Emergency Medicine, Rutgers University - New Jersey Medical School, Newark, NJ, USA

Correspondence to: Denise McCormack, MD, MPH. Resident, Emergency Medicine, Department of Emergency Medicine, Rutgers University - New Jersey Medical School, 185 South Orange Avenue, Medical Science Building - E609, Newark, NJ 07103, USA. Email: Mccormde@njms.rutgers.edu.

Submitted Sep 16, 2016. Accepted for publication Sep 20, 2016.

doi: 10.21037/jtd.2016.09.58

View this article at: <http://dx.doi.org/10.21037/jtd.2016.09.58>

The Surviving Sepsis Campaign (SSC) advocates for early recognition and prompt treatment to decrease mortality from sepsis (1). Currently, the mortality rate associated with septic shock is greater than 40%, which makes early detection imperative (2-4). In the article by Zhang and colleagues entitled, “AME evidence series 001—The Society for Translational Medicine: clinical practice guidelines for diagnosis and early identification of sepsis in the hospital”, the authors discuss recent evidence that supports early recognition of sepsis (5). The comprehensive analysis examines the new definition of sepsis based on the guidelines published by the Third International Consensus Definitions for Sepsis and Septic Shock (Sepsis-3) and provides a detailed assessment of sepsis screening using the Grades of Recommendation Assessment, Development and Evaluation (GRADE) framework.

Zhang and colleagues provide an insightful introduction of Sepsis-3 which encompasses a new definition of sepsis and updated criteria for determining sepsis versus septic shock, based on the Sequential Organ Failure Assessment (SOFA) score and its counterpart quick SOFA (qSOFA). Prior to Sepsis-3, multiple sepsis scoring systems were evaluated as a way to predict mortality, however qSOFA was found to be the most reliable (6-10). The qSOFA score, has three components, new altered mental status or Glasgow Coma Scale (GCS) ≤ 13 , respiratory rate ≥ 22 and systolic blood pressure ≤ 100 mmHg and can be performed rapidly by physicians based on clinical presentation. Zhang and

colleagues point out, “*the diagnosis of sepsis is challenging because there is no gold standard*”. Although Sepsis-3 does not provide a gold standard for diagnosing sepsis, the use of qSOFA does offer physicians a few advantages.

As the authors state, qSOFA can “*provide rapid and repeated assessments of patients without laboratory tests*”. In addition, Sepsis-3 divides sepsis into two components—sepsis or septic shock. The consensus determined that the terminology of severe sepsis was redundant and concluded that sepsis should be defined as, “life-threatening organ dysfunction caused by a dysregulated host response to infection” and septic shock defined as, “a vasopressor requirement to maintain a mean arterial pressure of 65 mm Hg or greater and serum lactate level greater than 2 mmol/L in the absence of hypovolemia” (1-4). The definition is significant because it accentuates the critical nature of sepsis and emphasizes that immediate intervention is warranted as soon as sepsis is suspected.

The new definition lowers the lactate threshold for septic shock from 4 to 2 mmol/L, which may capture a larger number of patients earlier in the disease course and prevent progression to organ failure and death. This change remains controversial because there is marginal evidence to support an ideal lactate value that predicts sepsis mortality (11,12). Moreover, the SSC recommended treatment bundles are based on studies performed using “severe sepsis” and lactate ≥ 4 mmol/L (1,13-15). In order to decrease sepsis-related mortality, the updated guidelines should also address early interventions, such as intravenous fluids and antibiotics,

which remain crucial to sepsis survival.

In addition, Zhang and colleagues note that there are relevant disadvantages associated with using qSOFA. One disadvantage is that the qSOFA score is validated in intensive care unit (ICU) patients in the United States and does not include patients presenting to the emergency department (ED) or patients in low and middle-income countries. Emergency Medicine physicians are usually first line providers for patients presenting with a “black box” of signs and symptoms and may not have the same clinical reference point as physicians who diagnose sepsis in the ICU, hence there is a strong need for studies validating the use of qSOFA in the ED.

For physicians practicing in low and middle-income countries, with limited access to resources, the use of lactate may not be applicable to the diagnosis of septic shock based on the Sepsis-3 definition. Instead, the diagnosis of septic shock may rely upon physical exam findings and the type of infectious pathogen involved. Despite these disadvantages, the ultimate goal of Sepsis-3 is to expedite sepsis recognition and decrease mortality.

In an effort to improve early sepsis identification, Zhang and colleagues analyzed the usefulness of novel biomarkers and automated electronic sepsis alert systems (AeSAS) utilizing the GRADE system. The purpose of their analysis was to clarify which screening tools are superior based on randomized controlled trials (RCT) and observational studies. They found that the biomarker procalcitonin (PCT) demonstrated promising results for differentiating true sepsis from non-infectious systemic inflammatory respiratory syndrome (SIRS), which is a considerable finding since SIRS criteria is thought to miss up to 1 in 8 patients with sepsis (16). The application of PCT as a sepsis screening tool could potentially decrease false positive rates and unnecessary costly interventions. As summarized by Zhang and colleagues, “*it may shorten the duration of antibiotic exposure and therefore could reduce financial cost and development of antibiotic resistance*”. These results reported are favorable and further research is necessary to deduce how PCT testing can be incorporated into the Sepsis-3 paradigm.

One of the most noteworthy screening tools discussed by the authors is the use of an AeSAS that would establish a standardized approach to sepsis screening. The AeSAS

creates an alert when a patient exhibits clinical criteria consistent with sepsis, such as abnormal vital signs or an elevated lactate. The incorporation of dependable technology into sepsis screening is paramount and may help to reduce human error. The greatest challenge associated with the AeSAS is that it emphasizes early diagnosis but has not been shown to decrease mortality. Zhang and colleagues argue that “*AeSAS have only poor to moderate diagnostic performance*”, which may impede its universal application in the clinical setting. In the future, advanced modifications of AeSAS may establish it as a reliable screening tool.

In conclusion, the article presented by Zhang and colleagues provides an important analysis of the evolving definition of sepsis and future implications of Sepsis-3. The authors highlight the advantages and disadvantages of the new guidelines and also expound upon the usefulness of multiple novel screening tools, such as qSOFA, PCT and AeSAS for early sepsis detection. The literature summarized by the authors will continue to have a strong impact on sepsis screening. However, there is still an urgent need for RCTs that identify validated and reliable screening methods that can be used universally to accurately detect sepsis early, specifically those that improve patient outcomes and decrease mortality.

Acknowledgements

None.

Footnote

Provenance: This is an invited Commentary article commissioned by Editor-in-chief Nanshan Zhong (Academician, Chinese Academy of Engineering, Guangzhou Institute of Respiratory Disease, Guangzhou, China).

Conflicts of Interest: The authors have no conflicts of interest to declare.

Comment on: Zhang Z, Smischney NJ, Zhang H, *et al.* AME evidence series 001—The Society for Translational Medicine: clinical practice guidelines for diagnosis and early identification of sepsis in the hospital. *J Thorac Dis* 2016;8:2654-65.

References

1. Dellinger RP, Levy MM, Rhodes A, et al. Surviving Sepsis Campaign: international guidelines for management of severe sepsis and septic shock, 2012. *Intensive Care Med* 2013;39:165-228.
2. Singer M, Deutschman CS, Seymour CW, et al. The Third International Consensus Definitions for Sepsis and Septic Shock (Sepsis-3). *JAMA* 2016;315:801-10.
3. Seymour CW, Liu VX, Iwashyna TJ, et al. Assessment of Clinical Criteria for Sepsis: For the Third International Consensus Definitions for Sepsis and Septic Shock (Sepsis-3). *JAMA* 2016;315:762-74.
4. Shankar-Hari M, Phillips GS, Levy ML, et al. Developing a New Definition and Assessing New Clinical Criteria for Septic Shock: For the Third International Consensus Definitions for Sepsis and Septic Shock (Sepsis-3). *JAMA* 2016;315:775-87.
5. Zhang Z, Smischney NJ, Zhang H, et al. AME evidence series 001—The Society for Translational Medicine: clinical practice guidelines for diagnosis and early identification of sepsis in the hospital. *J Thorac Dis* 2016;8:2654-65.
6. Nguyen HB, Van Ginkel C, Batech M, et al. 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;27:362-9.
7. Macdonald SP, Arendts G, Fatovich DM, et al. Comparison of PIRO, SOFA, and MEDS scores for predicting mortality in emergency department patients with severe sepsis and septic shock. *Acad Emerg Med* 2014;21:1257-63.
8. Calle P, Cerro L, Valencia J, et al. Usefulness of severity scores in patients with suspected infection in the emergency department: a systematic review. *J Emerg Med* 2012;42:379-91.
9. Sivayoham N, Rhodes A, Cecconi M. The MISSED score, a new scoring system to predict Mortality In Severe Sepsis in the Emergency Department: a derivation and validation study. *Eur J Emerg Med* 2014;21:30-6.
10. McCormack D, Ruderman A, Menges W, et al. Usefulness of the Mortality in Severe Sepsis in the Emergency Department score in an urban tertiary care hospital. *Am J Emerg Med* 2016;34:1117-20.
11. Nguyen HB, Rivers EP, Knoblich BP, et al. Early lactate clearance is associated with improved outcome in severe sepsis and septic shock. *Crit Care Med* 2004;32:1637-42.
12. Arnold RC, Shapiro NI, Jones AE, et al. Multicenter study of early lactate clearance as a determinant of survival in patients with presumed sepsis. *Shock* 2009;32:35-9.
13. Nguyen HB, Jaehne AK, Jayaprakash N, et al. Early goal-directed therapy in severe sepsis and septic shock: insights and comparisons to ProCESS, ProMISe, and ARISE. *Crit Care* 2016;20:160.
14. ARISE Investigators, ANZICS Clinical Trials Group, Peake SL, et al. Goal-directed resuscitation for patients with early septic shock. *N Engl J Med* 2014;371:1496-506.
15. Mouncey PR, Osborn TM, Power GS, et al. Protocolised Management In Sepsis (ProMISe): a multicentre randomised controlled trial of the clinical effectiveness and cost-effectiveness of early, goal-directed, protocolised resuscitation for emerging septic shock. *Health Technol Assess* 2015;19:i-xxv, 1-150.
16. Kaukonen KM, Bailey M, Pilcher D, et al. Systemic inflammatory response syndrome criteria in defining severe sepsis. *N Engl J Med* 2015;372:1629-38.

Cite this article as: McCormack D, Kulkarni M, Keller SE. Perspectives and implications of the new sepsis clinical practice guidelines. *J Thorac Dis* 2016;8(10):E1355-E1357. doi: 10.21037/jtd.2016.09.58