



Diagnosing Sepsis: qSOFA is Not the Tool We're Looking For

The degree of organ dysfunction suffered by a critically ill patient is proportionate to that patient's risk of dying in the hospital, as confirmed by the quick Sequential Organ Function Assessment Score (qSOFA) developed in recent years for Sepsis-3.¹ Despite its ability to remind us of the grave consequences of vital organ dysfunction, however, qSOFA is not specific to sepsis under new or prior definitions, and is repeatedly shown to be under-sensitive for identifying patients with sepsis. It does not fill a void left by abandoning the systemic inflammatory response syndrome (SIRS), as our understanding of sepsis has evolved.

The 1991 American College of Chest Physicians/Society of Critical Care Medicine Consensus Conference, which defined sepsis in terms of SIRS, provided a common understanding of sepsis terminology, as well as providing the first formal diagnostic criteria. At the same time, the committee acknowledged limitations of defining sepsis in terms of SIRS, including over-sensitivity, overlap with noninfectious causes of systemic inflammation, and failure to highlight other important signs of organ dysfunction.² As pointed out in the original consensus statement, it is the organ dysfunction, then termed Multiple Organ Dysfunction Syndrome, which is the major threat to survival in sepsis.

Sepsis-3, published in 2016, provided a new definition of sepsis: life-threatening organ dysfunction, as demonstrated by an increase in the Sequential Organ Failure Assessment (SOFA) of 2 or more points, caused by a dysregulated host response to infection.¹ While this definition better reflects our current understanding of the consequences of sepsis, SOFA, like SIRS, relies on a combination of nonspecific markers and is less a measurement of sepsis than of critical illness. In an attempt to create "novel clinical criteria for sepsis" with less dependence on laboratory criteria, the

Sepsis-3 group developed a "quick" SOFA. Using this tool, any 2 of 3 criteria including altered mental status, systolic blood pressure ≤ 100 mm Hg, and respiratory rate ≥ 22 breaths per minute, was shown by the group's retrospective analysis to be associated with in-hospital mortality, "supporting its use as a prompt to consider possible sepsis."³

There are several significant problems with the use of qSOFA as a screen for sepsis. First, it is insufficiently sensitive. Lacking a gold standard for diagnosis of sepsis, the Sepsis-3 committee has made in-hospital mortality the de facto gold standard, which they have labeled "an outcome typical of sepsis." Death, it must be argued, is not typical of sepsis in present practice, because the majority of septic patients do not die during their hospital admission. The validating study for qSOFA could not have identified cases of sepsis that were appropriately treated or otherwise avoided death due to sepsis. Indeed, numerous studies undertaken since the publication of Sepsis-3 have found qSOFA to be insufficiently sensitive as the primary screening test in detection of sepsis compared with existing tools, to include SIRS.^{4–14} Next, an elevated qSOFA is not specific to sepsis.^{15–17} This is not surprising because mortality is the late outcome of all types of critical illness. Of note, the validating study for qSOFA did not account for preexisting positive qSOFA criteria due to comorbid conditions, which would skew toward risk of death in the setting of decreased physiologic reserve. Like SIRS, a positive qSOFA is not unique to sepsis, but is a nonspecific marker of mortality just as the SIRS criteria are nonspecific markers of inflammation.

Objective indicators of multiple organ dysfunction such as qSOFA are best used to characterize the trajectory of critical illness, and perhaps in prognostication. However, a screening tool is still sorely needed that identifies the dysregulated immune response of sepsis. Our goal should be to recognize and diagnose sepsis promptly to prevent organ dysfunction and its associated mortality. qSOFA misses the mark. Mortality is not the appropriate gold standard with which to develop a screening test for sepsis, and should cease to be used as the primary benchmark as our understanding of sepsis evolves.

Funding: None.

Conflict of Interest: None.

Authorship: All authors had access to the data and a role in writing the manuscript.

Requests for reprints should be addressed to Nathan S. Cutler, MD, Wake Forest Baptist Medical Center, 1 Medical Center Blvd, Winston-Salem NC, 27157.

E-mail address: nate.cutler@outlook.com

ACKNOWLEDGMENT

The views expressed in this article reflect the results of research conducted by the author and do not necessarily reflect the official policy or position of the Department of the Navy, Department of Defense, nor the United States Government.

I am a military service member or federal/contracted employee of the United States government. This work was prepared as part of my official duties. Title 17 U.S.C. 105 provides that “copyright protection under this title is not available for any work of the United States Government.” Title 17 U.S.C. 101 defines a U.S. Government work as work prepared by a military service member or employee of the U.S. Government as part of that person’s official duties.

Nathan S. Cutler, MD*

Lieutenant Commander, Medical Corps, United States Navy, Fellow, Critical Care Medicine, Wake Forest Baptist Medical Center, Winston-Salem, NC

References

1. Singer M, Deutschman CS, Seymour CW, et al. The Third International Consensus Definitions for Sepsis and Septic Shock (Sepsis-3). *JAMA* 2016;315(8):801–10.
2. American College of Chest Physicians/Society of Critical Care Medicine Consensus Conference: definitions for sepsis and organ failure and guidelines for the use of innovative therapies in sepsis. *Crit Care Med*. 1992;20(6):864-874.
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(8):762–74.
4. Henning DJ, Puskarich MA, Self WH, et al. An emergency department validation of the SEP-3 sepsis and septic shock definitions and comparison with 1992 consensus definitions. *Ann Emerg Med* 2017;70(4):544–552.e5.
5. Haydar S, Spanier M, Weems P, Wood S, Strout T. Comparison of QSOFA score and SIRS criteria as screening mechanisms for emergency department sepsis. *Am J Emerg Med* 2017;35(11):1730–3.
6. Song JU, Sin CK, Park HK, Shim SR, Lee J. Performance of the quick Sequential (sepsis-related) Organ Failure Assessment score as a prognostic tool in infected patients outside the intensive care unit: a systematic review and meta-analysis. *Crit Care* 2018;22(1):28.
7. van der Woude SW, van Doormaal FF, Hutten BA, J Nellen F, Holleman F. Classifying sepsis patients in the emergency department using SIRS, qSOFA or MEWS. *Neth J Med* 2018;76(4):158–66.
8. Goulden R, Hoyle MC, Monis J, et al. qSOFA, SIRS and NEWS for predicting in-hospital mortality and ICU admission in emergency admissions treated as sepsis. *Emerg Med J* 2018;35(6):345–9.
9. Jiang J, Yang J, Mei J, Jin Y, Lu Y. Head-to-head comparison of qSOFA and SIRS criteria in predicting the mortality of infected patients in the emergency department: a meta-analysis. *Scand J Trauma Resusc Emerg Med* 2018;26(1):56.
10. Fang X, Wang Z, Yang J, et al. Clinical evaluation of Sepsis-1 and Sepsis-3 in the ICU. *Chest* 2018;153(5):1169–76.
11. Giamarellos-Bourboulis EJ, Tsaganos T, Tsangaris I, et al. Validation of the new Sepsis-3 definitions: proposal for improvement in early risk identification. *Clin Microbiol Infect* 2017;23(2):104–9.
12. Umemura Y, Ogura H, Gando S, et al. Assessment of mortality by qSOFA in patients with sepsis outside ICU: a post hoc subgroup analysis by the Japanese Association for Acute Medicine Sepsis Registry Study Group. *J Infect Chemother* 2017;23(11):757–62.
13. Fernando SM, Tran A, Taljaard M, Cheng W, Perry JJ. Prognostic accuracy of the quick Sequential Organ Failure Assessment for mortality in patients with suspected infection. *Ann Intern Med* 2018;169(4):264–5.
14. Maitra S, Som A, Bhattacharjee S. Accuracy of quick Sequential Organ Failure Assessment (qSOFA) score and systemic inflammatory response syndrome (SIRS) criteria for predicting mortality in hospitalized patients with suspected infection: a meta-analysis of observational studies. *Clin Microbiol Infect* 2018;24(11):1123–9.
15. Jawa RS, Vosswinkel JA, McCormack JE, et al. Risk assessment of the blunt trauma victim: the role of the quick Sequential Organ Failure Assessment Score (qSOFA). *Am J Surg* 2017;214(3):397–401.
16. Kitahara O, Nishiyama K, Yamamoto B, Inoue S, Inokuchi S. The pre-hospital quick SOFA score is associated with in-hospital mortality in noninfected patients: a retrospective, cross-sectional study. *PLoS One* 2018;13(8):e0202111.
17. Cho YS, Moon JM, Chun BJ, Lee BK. Use of qSOFA score in predicting the outcomes of patients with glyphosate surfactant herbicide poisoning immediately upon arrival at the emergency department. *Shock* 2019;51(4):447–52.