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Can Serial qSOFA Measurement Aid in Sepsis Identification and Triage Decisions?

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Early identification and intervention are important goals of sepsis management and the focus of ongoing research (1). Although recent data suggest that early goal-directed resuscitation efforts increase the cost of care without improving outcomes (2), early fluid resuscitation and antibiotic delivery remain the mainstay of sepsis management (1, 3, 4). Thus, clinical tools, which can reliably identify sepsis, are critically important to early intervention efforts and may also aid triage decision-making through the identification of patients at risk for poor outcomes.

In 2016, the Sepsis-3 expert panel developed a new consensus definition for sepsis, which they mandated the presence of “life threatening organ dysfunction” as defined by a 2 point increase in the Sequential [Sepsis-related] Organ Failure Assessment (SOFA) score (5). Because of the SOFA score’s reliance upon multiple laboratory values, the panel anticipated the unfeasibility of its routine use outside of an ICU setting and created an alternative scoring tool known as the quick SOFA (qSOFA).

The qSOFA was conceived as a simple and pragmatic tool based solely on bedside clinical assessments that can quickly be performed outside of an intensive care unit (ICU) including in resource poor settings (6). It uses a three-point scoring system with one point being assigned for each of three physiologic derangements: 1) a systolic blood pressure ≤ 100 mmHg, 2) a respiratory rate ≥ 22 breaths per min, and 3) a Glasgow Coma Scale score < 15 . While designed as a tool to identify the presence of sepsis in patients admitted with suspected infection, its predictive validity has been measured by its association with negative patient outcomes anticipated to occur with sepsis: in-hospital mortality and ICU length of stay ≥ 3 days. In its initial evaluation, the initial qSOFA score demonstrated a superior ability to discriminate between survivors and non-survivors among patients cared for outside of an ICU (area under the receiver operating characteristic curve [AUC], 0.81) when compared to the presence of the systemic inflammatory response syndrome (SIRS) (AUC,

0.76) (7). Further, initial qSOFA scores ≥ 2 were associated with substantial increased risk of in-hospital mortality suggesting this score's importance as a clinically relevant cut-off. However, a subsequent meta-analysis suggested that the qSOFA tool was less accurate at predicting death among non-ICU patients (sensitivity 51.2%, specificity 79.6%) but was limited by inter-study heterogeneity (8). Although these studies are thought provoking, they have been limited by the fact that they have each analyzed the predictive validity of the qSOFA score at one moment in time, early in the course of the suspected infection. Thus, our understanding of how changes in the qSOFA score may predict outcomes in a dynamic illness such as sepsis is incomplete.

In this issue of *Critical Care Medicine*, Kievlan et al. attempt to address this gap in knowledge with an innovative retrospective analysis of serial qSOFA scores obtained from a subset of the cohort of patients used to initially derive the qSOFA score (9). The investigators calculated the peak SOFA score for each 6 hour epoch over the 48 hour window subsequent to when infection was first suspected and then analyzed the predictive abilities of the mean and maximum qSOFA scores over 48 hours as well as the qSOFA score trajectory. Using Group Based Trajectory Modeling (GBTM), they identified 5 distinct qSOFA trajectories: 1) started low (qSOFA = 0) and remained low, 2) increasing, 3) started moderate (qSOFA = 1) and remained moderate, 4) started high (qSOFA ≥ 2) and remained high, and 5) decreasing. They observed that while the addition of the initial qSOFA score did improve the predictive capability of a baseline multivariate model including demographics and comorbidity burden (AUC, 0.79 vs. 0.63, $p < 0.001$), the addition of serial measures of qSOFA to the baseline model provided superior predictive validity. Specifically, adding the mean qSOFA score over 48 hours or the qSOFA trajectories to the baseline model resulted in the highest AUC's (0.86 and 0.85, respectively). This pattern of superior performance by the mean qSOFA score and the qSOFA score trajectories was further witnessed in sensitivity analyses across all deciles of baseline risk and among patients receiving care both in and outside of ICUs.

Intuitively, the authors' observations that serial measurements of the qSOFA score perform superior to one initial measurement appear valid. Patients present to medical attention at different points along the sepsis timeline so it would be logical to assume that initial qSOFA scores may vary even among patients with sepsis who are at high risk for a complicated course. Alternatively, serial measurements would likely mitigate these variations in qSOFA scores by incorporating more than just a single snapshot in time. However, the data presented by Kievlan et al. raise the obvious question of how their statistically significant observations can be meaningfully applied to clinical practice. qSOFA has been validated as a tool to predict poor outcomes in patients admitted with infection, specifically, in-hospital mortality. Thus, as the investigators allude to in the manuscript, a potential application for its use in clinical practice is as a decision aid when triaging care location. If a patient's serial qSOFA scores suggests a high risk of mortality, then they should be triaged to an ICU whereas low risk serial scores should lead to a non-ICU triage decision. When conceptualizing how serial qSOFA scores could be applied to triage decision-making, it is helpful to carefully scrutinize the presented data.

Two-thirds of the patients in the cohort had initial qSOFA scores of 0 and, among these patients, 95% of them had scores which remained at 0 or 1 over the subsequent 48 hours and their mortality rate was < 2%. These data suggest that the vast majority of patients with an initial score of 0 will likely not need to be triaged to an ICU based solely on their initial score. Conversely, in the 7% of patients whose initial qSOFA score was high (2), the majority (78%) had serial qSOFA scores which remained high during the next 48 hours and 25% of these patients died in the hospital. However, the mortality rate in the minority of patients whose qSOFA started high and then decreased over time was still as high as 11%. Thus, a valid argument could be made that any patient with an initially high qSOFA score warrants triage to an ICU irrespective of their serial values. The group of patients where serial qSOFA measurements may offer the greatest potential benefit for triage decision making are those whose initial score is moderate (qSOFA = 1). Among this group, 25% increased to a high qSOFA score over the next 48 hours and experienced a 16% in-hospital mortality rate whereas the remaining 75% who did not increase their qSOFA scores experienced only a 4% mortality rate. Thus, serial qSOFA monitoring in this population could provide additive predictive abilities and should be explored as an adjunct to existing early warning scoring tools (10).

This study has several strengths. The large data set provided robust sample sizes even after accounting for missing qSOFA scores, which was a common occurrence. Further, the use of multiple different analytical approaches (i.e. mean, maximum, trajectories) allowed for a thorough investigation into the predictive validity of serial measurements. The authors' use of robust sensitivity analyses including stratification of their findings across baseline risk deciles enhances the validity of their observations. Finally, the performance of serial qSOFA scores, which consist of simple and fast bedside assessments, represents a potentially feasible monitoring system even in resource poor environments. A significant limitation of the study was the large amount of missing data including 22% of initial qSOFA scores from the cohort. While the authors demonstrated through multiple imputations that the missing data do not significantly affect their findings, the frequency of missing qSOFA scores raises questions regarding potential barriers to implementation of serial qSOFA monitoring.

The qSOFA score is a simple sepsis screening tool that may represent an attractive and pragmatic method for appropriately triaging patients admitted with suspected infection. Kievelan et al. has advanced our understanding of its potential applicability by examining the predictive validity of serially measured scores. However, as with all good research, we are left with more questions than answers including can we apply these findings clinically or will the utility of serial qSOFA measurement largely be confined to a research tool? Further investigation is required to develop, embed, and test serial qSOFA-based decision aids into electronic health records before we can begin to answer that unknown.

References

1. Rhodes A, Evans LE, Alhazzani W, Levy MM, Antonelli M, Ferrer R, et al. Surviving Sepsis Campaign: International Guidelines for Management of Sepsis and Septic Shock: 2016. *Crit Care Med.* 2017;45(3):486–552. [PubMed: 28098591]

2. Investigators P, Rowan KM, Angus DC, Bailey M, Barnato AE, Bellomo R, et al. Early, Goal-Directed Therapy for Septic Shock - A Patient-Level Meta-Analysis. *N Engl J Med*. 2017;376(23):2223–34. [PubMed: 28320242]
3. Kumar A, Roberts D, Wood KE, Light B, Parrillo JE, Sharma S, et al. Duration of hypotension before initiation of effective antimicrobial therapy is the critical determinant of survival in human septic shock. *Crit Care Med*. 2006;34(6):1589–96. [PubMed: 16625125]
4. Liu VX, Fielding-Singh V, Greene JD, Baker JM, Iwashyna TJ, Bhattacharya J, et al. The Timing of Early Antibiotics and Hospital Mortality in Sepsis. *Am J Respir Crit Care Med*. 2017;196(7):856–63. [PubMed: 28345952]
5. Singer M, Deutschman CS, Seymour CW, Shankar-Hari M, Annane D, Bauer M, et al. The Third International Consensus Definitions for Sepsis and Septic Shock (Sepsis-3). *JAMA*. 2016;315(8):801–10. [PubMed: 26903338]
6. Rudd KE, Seymour CW, Aluisio AR, Augustin ME, Bagenda DS, Beane A, et al. Association of the Quick Sequential (Sepsis-Related) Organ Failure Assessment (qSOFA) Score With Excess Hospital Mortality in Adults With Suspected Infection in Low- and Middle-Income Countries. *JAMA*. 2018;319(21):2202–11. [PubMed: 29800114]
7. Seymour CW, Liu VX, Iwashyna TJ, Brunkhorst FM, Rea TD, Scherag A, 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. [PubMed: 26903335]
8. Fernando SM, Tran A, Taljaard M, Cheng W, Rochwerg B, Seely AJE, et al. Prognostic Accuracy of the Quick Sequential Organ Failure Assessment for Mortality in Patients With Suspected Infection: A Systematic Review and Meta-analysis. *Ann Intern Med*. 2018;168(4):266–75. [PubMed: 29404582]
9. Kievlan DRZ LA; Chang CH; Angus DC; Seymour CW Evaluation of repeated qSOFA measurements among patients with suspected infection. *Crit Care Med*. 2018 in press.
10. Subbe CP, Kruger M, Rutherford P, Gemmel L. Validation of a modified Early Warning Score in medical admissions. *QJM*. 2001;94(10):521–6. [PubMed: 11588210]