



## Ⓞ The Quick Sepsis-related Organ Failure Assessment Score in Brazil: Insights for Future Use in Diverse Settings

Sepsis is a common and deadly disease that poses a global threat, with nearly 20 million estimated cases annually (1). The burden of sepsis is highest in low- and middle-income countries (LMICs), including Brazil, with mortality as high as 55% in some LMIC settings (2, 3). Early recognition and resuscitation are both cornerstones of sepsis management. However, in the absence of a gold-standard diagnostic test, how best to recognize patients who are likely to be septic, and those who are at high risk of poor outcome, remains unclear. In 2016, the Sepsis-3 Task Force introduced the Quick Sepsis-related Organ Failure Assessment (qSOFA) score, a tool comprised of three clinical variables: respiratory rate, systolic blood pressure, and Glasgow Coma Score (4, 5). The qSOFA score had an equivalent predictive validity for sepsis compared with the more complex SOFA score in patients outside of the ICU and was thus recommended as a tool with which to identify, from among non-ICU patients with suspected infection, those more likely to be septic (4, 5).

Since the release of the qSOFA score in 2016, there has been a high level of interest in the “who,” “where,” and “how” of its application, and there have been over 300 publications on its performance in a variety of settings and disease states. Retrospective studies in both high- and low-income settings, as well as prospective studies in high-income areas, have evaluated the predictive validity of the qSOFA score for the identification of sepsis, as measured by excessive hospital mortality beyond baseline risk factors. Although the qSOFA score generally performed well in both high-income settings and LMICs, the predictive validity varied widely among LMIC cohorts (4, 6). Other retrospective studies and meta-analyses have evaluated the qSOFA score’s prognostic accuracy for mortality both inside and outside the ICU and have found it to have variable accuracy (7, 8). However, the prognostic accuracy of the qSOFA score for mortality in LMICs has never before been studied prospectively. Given the simplicity of the score and its potential usefulness in low-resource settings, better understanding of its performance in a range of LMIC settings is vital. In addition, it is critical to evaluate a variety of potential applications of the qSOFA score, including adjustment of the cut-point used to define a positive test, or combination of the score with additional test.

In this issue of the *Journal*, Machado and colleagues (pp. 789–798) report the predictive accuracy of the qSOFA score for hospital mortality in adult, non-ICU patients in Brazil from

May 2016 to March 2017 (9). This large, multicenter, prospective study evaluated two patient cohorts. Cohort 1 consisted of patients with suspected infection, and cohort 2 consisted of patients with a clinical diagnosis of sepsis, as defined by the Surviving Sepsis Campaign guidelines (10). The worst qSOFA score from the time of initial presentation until the time of suspected sepsis was recorded for patients in the emergency department, and the worst score in the 24 hours before suspected sepsis was recorded for patients in the hospital wards. Patients with missing data for any of the three score components were excluded from the study. The authors compared the prognostic accuracy of qSOFA score  $\geq 2$  to other commonly available prognostic tools, including modified qSOFA (qSOFA  $\geq 1$ ), qSOFA  $\geq 1$  or lactate  $> 2$  mmol/L, SOFA score  $\geq 2$ , systemic inflammatory response syndrome (SIRS) criteria  $\geq 2$ , and presence of any organ dysfunction.

Cohort 1 was comprised primarily of patients with suspected infection who were admitted to private hospitals (95.7%), and overall in-hospital mortality was 14%. In cohort 2, comprised of patients with sepsis, 30.8% of patients were admitted to public hospitals and the overall mortality rate was 28.4%. In cohort 1, a qSOFA score of  $\geq 2$  had the lowest sensitivity (53.9% [95% confidence interval (CI)], 50.3–57), but the highest specificity (83.6 [95% CI, 82.5–84.6]) for predicting mortality among all seven evaluated tests. Reducing the threshold for a positive qSOFA score to 1 substantially improved sensitivity (84.9% [95% CI, 89.0–93.2]), and a test allowing either qSOFA  $\geq 1$  or lactate  $> 2$  mmol/L had the highest sensitivity of all seven tools (91.3% [95% CI 89.0–93.2]), as well as one of the highest areas under the receiver operating characteristic curve (82.4 [95% CI, 80.8–83.9]). Cohort 2 provided an opportunity for a descriptive analysis of the prognostic tools in a cohort of patients with a diagnosis of sepsis who were from a more balanced mix of private and public hospitals. The majority of patients had a qSOFA score  $\leq 1$  (62.3%), and although mortality increased with each additional qSOFA point, the mortality of patients with a qSOFA of  $\leq 1$  was high (17.3%). Overall, the authors conclude that, in these LMIC hospitals, a qSOFA score  $\geq 2$  has a low sensitivity for predicting hospital mortality, and using alternate tools, such as a qSOFA score  $\geq 1$ , or a qSOFA score  $\geq 1$  or lactate  $> 2$  mmol/L, increases the sensitivity for predicting death in patients with suspected infection or sepsis.

This study provides important, new, high-quality data to help clinicians and hospitals make more informed choices when selecting a tool to assist in identifying patients with suspected infection or sepsis who are at high risk of poor outcome. In LMICs, where the burden of sepsis remains high and resources may be limited, clinicians wishing to use a tool to help identify patients whose initial resuscitation must be prioritized should consider lowering the

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cut-off for a positive qSOFA score to 1 and consider drawing a lactate level to help capture patients that are at a high risk of death from sepsis.

The study's inclusion of a large number of patients who were prospectively enrolled from a wide variety of hospital settings is an important strength. Though clinical research studies are often skewed toward academic centers and hospitals in major metropolitan areas, 37% of hospitals included in this study were located in the countryside of Brazil, and 45% of hospitals were nonacademic. Through its inclusion of both public and private hospitals, this study highlights the disparities that exist within many countries' health care systems, with a staggering difference in mortality between the public and private hospitals. Although prior publications have emphasized differences in health care systems between some high- and low-income countries and the potential implications for sepsis care, this study brings these differences into sharp focus, even within the same country (11, 12). In this study, the mortality of patients in cohort 2 who were admitted to private hospitals (18.7%) was similar to that reported in many high-income countries (13, 14). In contrast, the mortality among cohort 2 patients admitted to public hospitals was over twice as high (50.3%).

This study provides important new data demonstrating that the qSOFA score, when used with a traditional cut-off value of 2, has marginal predictive accuracy for mortality in this middle-income country, especially among patients with sepsis admitted to public hospitals. In a disease where time truly matters and resources may be limited, clinicians may need to modify their use and interpretation of the qSOFA score. ■

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