qSOFA for Identifying Sepsis Among Patients With Infection

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The identification of patients with possible sepsis is vitally important because timely recognition and appropriate, effective treatment substantially improves survival. Unlike some other life-threatening conditions (such as myocardial infarction), for which highly accurate diagnostic tests are available, no rapid diagnostic tests are currently available to accurately identify patients with sepsis (or those at high risk of developing sepsis) to help clinicians determine the best course of action. Development of such tests for sepsis will involve consideration of a number of key issues, such as whether sepsis is just one or, rather, multiple entities; whether degrees of having sepsis exist; which test is the gold standard (an accepted benchmark against which similar tests can be compared and diagnostic accuracy assessed); what levels of accuracy are sufficient for use in clinical practice; and which tests based on what markers are the most cost-effective. In the meantime, however, clinicians must rely on clinical judgment, potentially augmented by clinical criteria validated to identify sepsis among patients with infection.

In 2016, sepsis was redefined as a life-threatening organ dysfunction caused by a dysregulated host response to infection.1 Along with this new conceptual definition for sepsis, members of the Third International Consensus Definitions for Sepsis and Septic Shock (Sepsis-3) task force proposed qSOFA (quick Sequential [Sepsis-related] Organ Failure Assessment)—an empirically derived score using simple clinical criteria—to potentially assist bedside clinicians in identifying, among patients with infection, those with sepsis or those likely to develop it.2 To develop this score, Seymour et al2 and the Sepsis-3 Task Force analyzed several, very large, hospital databases, selecting patients with suspected infection (defined by a combination of use of antibiotics and body fluid culture within a specific time-window). Based on routinely available, clinical data, the authors identified the most parsimonious model, over and above baseline risk, that could distinguish a suspected infection likely to be, or lead to, sepsis from one that likely was not or would not.

When a gold standard exists for a disease or condition, it is possible to assign true-positives, false-positives, and false-negatives and calculate traditional metrics such as sensitivity and specificity. However, when there is no gold standard, true vs false assignment cannot be determined. Instead, the value of a test must be assessed on its performance across different aspects of validity, reliability, and usefulness. The principal domain used to assess qSOFA was predictive validity. Specifically, Seymour et al explored the extent to which qSOFA and other more complex measures predicted excess deaths or prolonged intensive care unit (ICU) stay beyond that explained by baseline risk. These outcomes were used because, if sepsis differs from a simple infection because of organ dysfunction and increased threat to life, then death or prolonged ICU stay should be more common among patients with sepsis than among those with simple infection.

After validation in 4 external data sets and multiple sensitivity analyses, the final qSOFA model included 3 parameters: Glasgow Coma Scale score of less than 15 (1 point), systolic blood pressure of 100 mm Hg or less (1 point), and respiratory rate of 22/min or more (1 point). Among patients with infection outside the ICU, qSOFA had similar or better predictive validity for the selected outcomes expected to be more common following sepsis than the more complex measures tested—SOFA3 and the Logistic Organ Dysfunction System4—that require a greater number of clinical and laboratory variables. However, among patients with infection in the ICU, qSOFA had statistically worse predictive validity.

Both the new definition of sepsis and qSOFA have been discussed and debated.5-10 qSOFA and, more specifically, its measurement properties appear to have generated and attracted the most concern. Two studies in this issue of JAMA, despite apparently focusing on prognosis (predicting outcome, regardless of the cause of the outcome) rather than diagnosis (identifying a disease or condition—the original intention of qSOFA), provide an opportunity to revisit qSOFA and its measurement properties both outside and inside the ICU.11,12 Because so many patients worldwide are at risk of sepsis and because evaluation for sepsis may occur in the ambulatory setting, emergency department (ED), or during hospitalization, understanding whether qSOFA is a good measure is an enormously important question.

Freund et al13 evaluated the predictive validity of qSOFA in a prospective study of patients presenting to EDs in France, Switzerland, Spain, and Belgium.13 Among 879 patients (median age 67 years, 379 with respiratory tract infection, in-hospital mortality of 8%) presenting with suspected infection to 30 EDs over a 4-week period, the investigators confirmed that the predictive validity of qSOFA in the ED setting was similar to that of the full SOFA score and that the addition of lactate did not improve predictive validity. The in-hospital mortality was 3% for patients with a qSOFA score of less than 2 and 24% for qSOFA score of 2 or more. qSOFA performed better than systemic inflammatory response syndrome (SIRS) criteria and severe sepsis to predict in-hospital mortality. The study does have some limitations. Patients who were initially suspected to have infection but subsequently adjudicated not to have infection...
ing was already reported by Seymour et al in their initial forms as well as the SOFA score in the ICU, given that this finding or developing sepsis.

In another report, Raith et al evaluated the predictive validity of qSOFA in a retrospective analysis of the large, internationally respected, Australian and New Zealand Intensive Care Society (ANZICS) Adult Patient Database of admissions to adult general ICUs. Among 184,875 patients (mean age, 62.9 years; most common diagnosis, bacterial pneumonia [17.7%]; in-hospital mortality, 18.7%) with an infection-related primary diagnosis admitted to 182 ICUs over a 16-year period, the authors confirmed that the predictive validity of qSOFA in the ICU setting was inferior to the full SOFA score. The SOFA score increased by 2 or more points in 90.1% of the patients; 86.7% manifested 2 or more SIRS criteria, and 54.4% had a qSOFA score of 2 or more. Based on area under the receiver operating curve (AUROC) analysis, SOFA (0.753; 99% CI, 0.750–0.757) demonstrated significantly greater prognostic accuracy for in-hospital mortality than did SIRS (0.589; 99% CI, 0.585–0.593) or qSOFA (0.607; 99% CI, 0.603–0.611). It is neither surprising that qSOFA did not perform as well as the SOFA score in the ICU, given that this finding was already reported by Seymour et al in their initial work, nor is it critically important because qSOFA is more likely to be useful outside of the ICU setting.

Thus, the findings from these 2 studies support the results reported by Seymour et al that qSOFA is potentially helpful in settings outside the ICU in rapidly identifying patients with suspected infection who have, or will likely develop, sepsis. However, qSOFA still warrants further testing, particularly in lower- and middle-income settings where context (for example, timing of presentation to the hospital among patients with a suspected infection) might vary considerably and such contextual factors might affect predictive validity. In addition, prospective studies may evaluate the utility of qSOFA when used longitudinally, with repeated measurements throughout the hospital stay. Arguably, the highest-quality evidence for validation of any tool to support clinical decision making would come from an analysis to establish whether decisions made with the support of the tool lead to better patient outcomes than those made by clinical judgment alone.

Ultimately, the utility of qSOFA will likely become surpassed if and when highly accurate, rapid diagnostic tests for sepsis emerge. For now, however, outside the ICU in the high-income settings where it has been tested, qSOFA appears a simple, rapid, inexpensive, and valid way to identify—among patients with suspected infection—those at a higher risk of having or developing sepsis.