Could the Quick Sequential Organ Failure Assessment Predictive Accuracy Be Affected by Site of Infection?

To the Editor:

We read with interest the article by Machado and colleagues (1) concerning the evaluation of the quick Sequential Organ Failure Assessment (qSOFA) score as a screening tool for mortality in two cohorts in Brazil. The authors state that a qSOFA score ⩾2 has low sensitivity for predicting death in patients with suspected infection and may miss patients who ultimately die. Taking into consideration the opportunity of these two large cohorts of patients, it would be interesting to explore whether the site of infection plays any role in this observation. As we have previously argued, qSOFA score is potentially biased by its very parameters, because they are affected by different sites of infection (2). qSOFA could perform adequately or overperform in cases in which the infection site could involve score parameters (e.g., respiratory tract infections [RTIs] and respiratory rate) but not in cases in which potential parameters are not included in the qSOFA score but in which the underlying inflammatory response could still be expressed otherwise and drive poor outcomes (e.g., thrombocytopenia and hyperbilirubinemia).

For this reason, we performed a retrospective cohort study to evaluate qSOFA performance in the assessment of mortality, depending on site of infection. Patients admitted with signs of infection (RTI, urinary tract infection [UTI], gastrointestinal [GI] tract infection, hepatobiliary [HB] system infection, and primary bacteremia [PB]) in the medical ward of a tertiary university hospital between May 1, 2016, and May 1, 2018, were included in this study (ethics committee approval 96/15.04.16). Patient disease severity according to systemic inflammatory response syndrome (SIRS) and qSOFA score was calculated upon presentation; epidemiological parameters were recorded; and outcomes were followed for 28 days. Using IBM SPSS Statistics version 25 software (IBM Corp.), we performed receiver operating characteristic curve analysis to assess the performance of qSOFA scores ⩾2 in predicting survival for different sites of infection. A total of 614 patients were finally included in this study, involving RTI ($n = 132$), UTI ($n = 232$), PB ($n = 47$), GI tract infection ($n = 104$), and HB system infection ($n = 99$). The mean age of the population was 63 years, and 48% were male. Ninety-eight percent of patients with PB fulfilled the SIRS criteria for sepsis, followed by 74%, 72%, 55%, and 50% of patients with UTI, HB system infection, RTI, and GI tract infection, respectively. A qSOFA score ⩾2 was recorded in 22, 13, 12, 11, and 6% of PB cases, UTIs, RTIs, HB system infections, and GI tract infections. Mortality rates were higher for PB (34%), followed by RTI (17%), HB system infection (14%), UTI (7%), and GI tract infection (2%). Receiver operating characteristic curve analysis to assess the performance of qSOFA scores ⩾2 in predicting mortality, depending on site of infection, showed an adequate area under the curve for UTI (0.799), RTI (0.715), and GI tract infection (0.720) but fair to poor predictive value for PB (0.619) or HB system infection (0.590).

It appears that a qSOFA score ⩾2 may not behave the same at different sites of infection. This is reflected in diverse areas under the curve for different infection sites. Previous authors have tried to assess qSOFA performance in emergency departments or non-ICU settings (3), with variable results. Even though real-life validation data have raised questions regarding the performance of qSOFA in these settings, no efforts have been made to distinguish its performance on the basis of type of infection as a potential cause of misclassification. Ranzani and colleagues have previously observed overestimation of mortality and miscalibration of qSOFA score in patients with pneumonia (4), findings that could be attributed to respiratory rate being affected by the disease itself and not an underlying inflammatory response mirroring severity. Discrepancies could be attributed to the fact that the qSOFA score does not necessarily reflect an underlying inflammatory response, which could vary on the basis of the type of infection (5). After all, on the one hand, SIRS and Sepsis-3 (Third International Consensus Definitions for Sepsis and Septic Shock) criteria tend to complement each other, rather than substitute for each other. On the other hand, additional laboratory markers such as lactate could significantly improve qSOFA performance, as previously described (1, 6). Even though the qSOFA represents a valuable "queue" assessment in endless waiting lines of emergency departments, caution and further studies are pivotal to elucidate where its exact limitations lie in everyday clinical practice. ■

Author disclosures are available with the text of this letter at www.atsjournals.org.

Karolina Akinosoglou, M.D., Ph.D.*
Anne-Lise deLastic, M.D., Ph.D.
Vasiliki Niarou, M.D.
Dimitrios Ziazias, M.D.
Christos Davoulos, M.D.
Martha Kolosaka, M.D.
Foteini Kosmopoulou, M.D.
Spyridoula Theodoraki, M.D., Ph.D.
Christina-Panagiota Koutsouri, M.D.
Charalambos Gogos, M.D., Ph.D.
University General Hospital of Patras
Patras, Greece

ORCID ID: 0000-0002-4289-9494 (K.A.).

*Corresponding author (e-mail: akin@upatras.gr).

Author Contributions: K.A. wrote the manuscript and oversaw the study. K.A. and A.-L.d. analyzed the data. K.A., V.N., D.Z., C.D., M.K., F.K., S.T., and C.-P.K. collected the data. C.G. critically corrected the manuscript.

Originally Published in Press as DOI: 10.1164/rccm.202003-0552LE on April 6, 2020

References

1. Machado FR, Cavalcanti AB, Monteiro MB, Sousa JL, Bossa A, Bafi AT, *et al*.; Instituto Latino-Americano de Sepsis network investigators. Predictive accuracy of the quick sepsis-related organ failure assessment score in Brazil: a prospective multicenter study. *Am J Respir Crit Care Med* 2020;201:789–798.
2. Akinosoglou K, Gogos C. Sepsis-3 in community-acquired pneumonia: how reliable is it? [letter]. *Am J Respir Crit Care Med* 2018;197:537.

3. Williams JM, Greenslade JH, McKenzie JV, Chu K, Brown AFT, Lipman J. Systemic inflammatory response syndrome, quick sequential organ function assessment, and organ dysfunction: insights from a prospective database of ED patients with infection. *Chest* 2017;151:586–596.
4. Ranzani OT, Prina E, Menéndez R, Ceccato A, Cilloniz C, Méndez R, *et al*. New sepsis definition (Sepsis-3) and community-acquired pneumonia mortality: a validation and clinical decision-making study. *Am J Respir Crit Care Med* 2017;196:1287–1297.
5. Akinosoglou K, Theodoraki S, Gkavogianni T, Pistiki A, Giamarellos-Bourboulis E, Gogos CA. How well does qSOFA correspond to underlying systemic inflammatory response? *Cytokine* 2018;110:288–290.
6. Akinosoglou K, Theodoraki S, Xanthopoulou I, Perperis A, Gkavogianni T, Pistiki A, *et al*. Platelet reactivity in sepsis syndrome: results from the PRESS study. *Eur J Clin Microbiol Infect Dis* 2017;36:2503–2512.

Reply to Topeli *et al.* and to Akinosoglou *et al.*

From the Authors:

We would like to thank Topeli and colleagues and Akinosoglou and colleagues for their interest in our manuscript (1).

We carefully read the discussion by Topeli and colleagues on our data and their own results regarding quick sepsis-related organ dysfunction (qSOFA) and other scores for sepsis' mortality prediction in Turkey. We congratulate the authors for their initiative, as we believe it is very important to have data from low- and middle-income countries (LMICs). These countries represent more than 80% of world population, and the data from these settings on sepsis epidemiology and mortality are scarce (2).

There are important similarities between the authors' results and ours. They found that qSOFA score has the worst sensitivity to predict mortality in septic patients, which adds to previous LMICs' studies showing that qSOFA has low sensitivity to predict sepsis mortality in this population (3, 4). However, there are also major differences comparing both results. Their study is a single-center retrospective cohort with a limited number of patients, as can be suggested by the large confidence intervals of the data. Additionally, they collected qSOFA variables from patients at 48 hours before ICU admission, whereas we collected qSOFA data considering only the worst values prior to the suspicion of infection or sepsis, which may have contributed to more accurate findings in our study. The time window is crucial in assessing the sensitivity of a screening tool, as it is expected that if the interval of data collection is increased, more patients that deteriorate and eventually die will have a qSOFA $\geq$2. It would also be important to evaluate in Topeli's data whether the use of a single qSOFA variable would increase the sensitivity of the score, as we demonstrated in our study. This modified score could be suggested as an alternative to improve its accuracy in determining mortality in LMICs.

Akinosoglou and colleagues assessed the role of qSOFA according to site of infection in a cohort of 614 septic patients from their institution. They identified that qSOFA accuracy to predict survival is dependent on the focus of infection. Because mortality rates are variable with the site of sepsis, and qSOFA variables may also be affected by the disease itself, their data are very reasonable. It would be interesting to assess data from other series to confirm if qSOFA can have adequate performance in all sepsis sites, or if we should modify the score according to the probable site of infection. ■

Author disclosures are available with the text of this letter at www.atsjournals.org.

Luciano C. P. Azevedo, Ph.D.*
Alexandre B. Cavalcanti, Ph.D.
Flavia R. Machado, Ph.D.
Instituto Latino-Americano de Sepsis
São Paulo, Brazil

*Corresponding author (e-mail: lucianoazevedo@uol.com.br).

References

1. Machado FR, Cavalcanti AB, Monteiro MB, Sousa JL, Bossa A, Bafi AT, *et al*.; Instituto Latino-Americano de Sepsis network investigators. Predictive accuracy of the quick sepsis-related organ failure assessment score in Brazil: a prospective multicenter study. *Am J Respir Crit Care Med* 2020;201:789–798.
2. Machado FR, Azevedo LCP. Sepsis: a threat that needs a global solution. *Crit Care Med* 2018;46:454–459.
3. Chen YX, Wang JY, Guo SB. Use of CRB-65 and quick sepsis-related organ failure assessment to predict site of care and mortality in pneumonia patients in the emergency department: a retrospective study. *Crit Care* 2016;20:167.
4. Boillat-Blanco N, Mbarack Z, Samaka J, Mlaganile T, Mamin A, Genton B, *et al*. Prognostic value of quickSOFA as a predictor of 28-day mortality among febrile adult patients presenting to emergency departments in Dar es Salaam, Tanzania. *PLoS One* 2018;13:e0197982.

The funding source is the Instituto Latino Americano de Sepsis, a nonprofit organization. As an institution, the sponsor of the study had no role in study design, data collection, data analysis, data interpretation, or writing of the report. The corresponding author had full access to all the data in the study and had final responsibility for the decision to submit for publication.

Originally Published in Press as DOI: 10.1164/rccm.202003-0628LE on April 6, 2020

Erratum: Pitolisant for Daytime Sleepiness in Patients with Obstructive Sleep Apnea Who Refuse Continuous Positive Airway Pressure Treatment. A Randomized Trial

There are errors in the article by Dauvilliers and colleagues (1), published in the May 1, 2020, issue of the *Journal*. In the list of HAROSA II Study Group collaborators that appears before the references, one of its members, Dr. Yüksel Peker, is incorrectly listed as Yeksel Peker. In addition, Dr. Peker's current affiliation