Sepsis-3 and simple rules

Bernard A Foëx

Sepsis is a complex syndrome, where complexity is defined as having multiple interdependent parts. It has been a challenge to define it, and, as our understanding has evolved, so its definition has changed from the first iteration in 1991,[1] to the second in 2001[2] and now a third in 2016.[3]

At its most basic sepsis is defined as life-threatening organ dysfunction caused by a dysregulated host response to infection.[3] Singer *et al* have suggested that this organ dysfunction can be identified using an acute change in the Sequential Organ Failure Assessment (SOFA) score ≥2 points as a result of the infection.[3]

The problem with the SOFA score is that it does rely on some laboratory data, which makes it difficult to use outside hospital or at the 'front door'. Singer *et al* then developed what they described as a 'parsimonious clinical model', which they termed the qSOFA (quick SOFA)[3] based only on RR, systolic BP and altered mental state. One point is scored for (1) a RR ≥22 breaths per minute, (2) a systolic BP of ≤100 mm Hg and (3) altered mental state (GCS<15). A score of ≥2 in a patient with infection was associated with an increased risk of death.[3]

The new definition of sepsis and the role of qSOFA has aroused controversy (eg, refs.[4–7]). Two papers in this issue of the journal join in the controversy.

Rodriguez *et al*, in their cohort study from the USA, compared qSOFA with what they described as 'the most commonly used current ED sepsis identification tools', namely Systemic Inflammatory Response Syndrome (SIRS), severe sepsis criteria and lactate levels for their ability to identify patients who would either die in hospital, require vasopressor support or be admitted to intensive care within 72 hours of presentation to the ED.[8] From the five EDs, 3743 patients were admitted with an infectious disease-related illness and 512 (13.7%) fulfilled one or more of the composite outcome criteria. A qSOFA score ≥1 was equally sensitive as SIRS (86.1% vs 86.7%, respectively), but more specific 56.7% versus 45.6%, respectively (hardly surprising since the RR criterion in qSOFA is ≥22 vs >20 for SIRS). Specificity is much better with a qSOFA ≥2 (89.1%), better than the specificity of 'severe sepsis' (77.5%) and that of lactate ≥2 (71.6%), and better still when qSOFA is 3 (98.3%), outperforming lactate ≥4 (96.0%).

From their data it is clear that a patient in the ED with an infection who scores a 3 on qSOFA or has a blood lactate ≥4 should be considered very high risk.

Goulden *et al* were also interested in the prognostic accuracy of qSOFA in relation to hospital mortality and intensive care unit (ICU) admission.[9] In a retrospective cohort of 1818 patients admitted and treated as sepsis in one UK centre, they compared qSOFA with SIRS criteria used as a score and the National Early Warning Score (NEWS).[10] Although the outcomes in the two studies were not the same, the percentages of patients fulfilling the primary outcome criteria were similar (15% in Goulden *et al* and 13.7% in Rodriguez *et al*).

There were other differences in the two study cohorts. In the study by Goulden *et al*, the mean age was 68 years (SD 19) and the mortality rate 15% with 3% admitted to the ICU, while in Rodriguez *et al* the median age was 58 years (IQR 44–72) and the mortality rate was 1.9% and the composite outcome was observed in 13.7%. The majority of deaths in Goulden *et al* occurred outside the ICU (only 7% of deaths occurred on the ICU).

Goulden *et al* found SIRS to have a sensitivity similar to that in Rodriguez (80%), but the sensitivity of qSOFA ≥2 was only 37%.[9] Specificity of qSOFA (79%) was similar to Rodriguez *et al* but the specificity of SIRS was less (only 21%). They considered that NEWS with a score ≥5 performed better than either qSOFA ≥2 or SIRS≥2: area under the Receiver Operating Characteristic (ROC) curve was 0.65 for NEWS ≥5 compared with 0.62 for qSOFA ≥2 and 0.49 for SIRS≥2. However, although the sensitivity was higher (74%), the specificity was only 43%.[9]

Based on their results, Goulden *et al* argue that qSOFA should not replace NEWS, where the latter is already being used. It depends very much on perspective. Early warning scores used in hospital are there to act as triggers for action. I would argue that specificity is important. In their cohort, qSOFA had a better positive predictive value than the other scores.

Screening for sepsis in the ED populations described is fundamentally different from some other forms of screening. Screening in general terms, such as for phenylketonuria in the newborn, assumes there is no pathology. The condition is rare and the consequences of missing it are devastating. The screening test must be exquisitely sensitive to avoid missing a case. Specificity is almost irrelevant. False positives are a small price to pay.

Screening for sepsis in the ED is a very different situation. In both the studies presented,[8 9] these are patients for whom the decision to admit had already been made. Hospitals, as WHO defines them, are 'health care institutions that have an organized medical and other professional staff and inpatient facilities, and deliver services 24 hours a day, 7 days per week'. So the screening process in ED is not a 'one chance to get it right'. Sensitivity is much less important. A qSOFA ≥2 does not need to be a highly sensitive test in the context of patients who are already being admitted to hospital. In this cohort, the highly sensitive screening has already been done. Now what is needed is appropriate allocation of a scarce resource, namely assessment by an intensive care practitioner and, possibly, an intensive care bed. Singer has already alluded to the problem of 'alert fatigue' when there are too many 'false positives'.[6]

In their book, *Simple Rules. How to thrive in a complex world*, Sull and Eisenhardt explain that simple rules are shortcut strategies that save time and effort by focusing our attention and simplifying the way we process information.[11]

Simple rules have common traits. Their simplicity makes them easy to remember and focuses on what really matters. They apply to a well-defined activity or decision and they can provide clear guidance, but also allow flexibility to alter the decision. They can help decision-making when there is little information and promote consistency in decision-making. As such, simple rules provide a powerful weapon against the complexity that threatens to overwhelm individuals, organisations and society as a whole.[11] qSOFA is an example of a 'simple rule'. As Vincent *et al* eloquently point out, qSOFA is not part of the new definitions.[7] It may help in deciding which patients need assessment in the ED and on arrival which patients need to be seen sooner rather than later. The

Correspondence to Dr Bernard A Foëx, Emergency Department, Manchester Royal Infirmary, Manchester M13 9WL, UK; bernard.foex@mft.nhs.uk

Emerg Med J: first published as 10.1136/emermed-2018-207668 on 2 May 2018. Downloaded from http://emj.bmj.com/ on 7 June 2018 by Dr R A PEARSON 4 Hun Avenue. Protected by copyright.

focus on sepsis and qSOFA also risks prioritising sepsis as a cause of critical illness or deterioration at the expense of other diagnoses. But sepsis is just one of the possible causes of the critical illness syndrome for which more complex scoring systems may perform better, as suggested by Churpek *et al*.[12] As Inada-Kim and Nsutebu point out, 'We must guard against blinkered, condition specific approaches in both assessment and measurement'.[13] They argue, cogently, in favour of a single 'early warning' scoring system, such as NEWS 2.[14 15] qSOFA should not replace more complex 'track and trigger' systems but should complement them, particularly in (relatively) resource-poor settings, such as primary care, and for research.

Funding The authors have not declared a specific grant for this research from any funding agency in the public, commercial or not-for-profit sectors.

Competing interests None declared.

Patient consent Not required.

Provenance and peer review Commissioned; internally peer reviewed.

© Article author(s) (or their employer(s) unless otherwise stated in the text of the article) 2018. All rights reserved. No commercial use is permitted unless otherwise expressly granted.

Check for updates

To cite Foëx BA. *Emerg Med J* 2018;**35**:343–344.

Received 27 March 2018
Revised 28 March 2018
Accepted 29 March 2018
Published Online First 2 May 2018

Linked

► http://dx.doi.org/10.1136/emermed-2017-207120
► http://dx.doi.org/10.1136/emermed-2017-207383

Emerg Med J 2018;**35**:343–344.
doi:10.1136/emermed-2018-207668

REFERENCES

1 Bone RC, Balk RA, Cerra FB, *et al*. Definitions for sepsis and organ failure and guidelines for the use of innovative therapies in sepsis. The ACCP/SCCM Consensus Conference Committee. American College of Chest Physicians/Society of Critical Care Medicine. *Chest* 1992;101:864–74.
2 Levy MM, Fink MP, Marshall JC, *et al*. 2001 SCCM/ESICM/ACCP/ATS/SIS International Sepsis Definitions Conference. *Intensive Care Med* 2003;29:530–8.
3 Singer M, Deutschman CS, Seymour CW, *et al*. The third international consensus definitions for sepsis and septic shock (sepsis-3). *JAMA* 2016;315:801–10.
4 Simpson SQ, Criteria NS*CHEST* 2016;149:1117–8.
5 Sprung CL, Schein RMH, Balk RA. The new sepsis consensus definitions: the good, the bad and the ugly. *Intensive Care Med* 2016;42:2024–6.
6 Singer M. The new sepsis consensus definitions (Sepsis-3): the good, the not-so-bad, and the actually-quite-pretty. *Intensive Care Med* 2016;42:2027–9.
7 Vincent JL, Martin GS, Levy MM. qSOFA does not replace SIRS in the definition of sepsis. *Crit Care* 2016;20:210.
8 Rodriguez R, *et alEmergency Medicine Journal* 2018.
9 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;35:345–9.
10 McGinley A, Pearse RM. A national early warning score for acutely ill patients. *BMJ* 2012;345:e5310.
11 Sull D, Eisenhardt K. *Simple Rules. How to thrive in a complex world*. London: John Murray, 2015:280.
12 Churpek MM, Snyder A, Han X, *et al*. Quick sepsis-related organ failure assessment, systemic inflammatory response syndrome, and early warning scores for detecting clinical deterioration in infected patients outside the intensive care unit. *Am J Respir Crit Care Med* 2017;195:906–11.
13 Inada-Kim M, Nsutebu E. NEWS 2: an opportunity to standardise the management of deterioration and sepsis. *BMJ* 2018;360:k1260.
14 Royal College of Physicians. National Early Warning Score (NEWS). 2017. https://www.rcplondon.ac.uk/projects/outputs/national-early-warning-score-news-2
15 Royal College of Physicians. *National Early Warning Score (NEWS) 2: standardising the assessment of acute-illness severity in the NHS*. London: RCP, 2017.

Emerg Med J: first published as 10.1136/emermed-2018-207668 on 2 May 2018. Downloaded from http://emj.bmj.com/ on 7 June 2018 by Dr R A PEARSON 4 Hun Avenue. Protected by copyright.