MURDOCH RESEARCH REPOSITORY

**Ho, K.M. and Lan, N.S.H. (2017) Combining quick Sequential
Organ Failure Assessment with plasma lactate concentration is
comparable to standard Sequential Organ Failure Assessment
score in predicting mortality of patients with and without
suspected infection. Journal of Critical Care, 38 . pp. 1-5.**

http://researchrepository.murdoch.edu.au/35697/
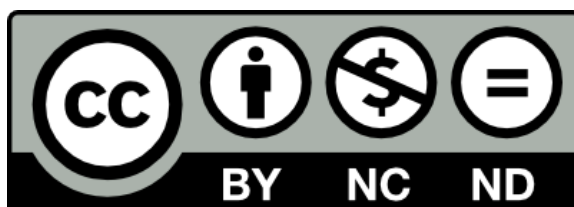
Accepted Manuscript

Combining Quick Sequential Organ Failure Assessment (qSOFA) with plasma lactate concentration is comparable to standard SOFA score in predicting mortality of patients with and without suspected infection

Kwok M. Ho FCICM, MPH, PhD, Norris S.H. Lan BCom

Combining Quick Sequential Organ Failure Assessment (qSOFA) with plasma lactate concentration is comparable to standard SOFA score in predicting mortality of patients with and without suspected infection

Short running title: Validity of qSOFA scores

Authors:

Kwok. M. Ho, FCICM , MPH, PhD [1,2,3] , Norris S.H. Lan, BCom[4]

[1] Department of Intensive Care, Royal Perth Hospital, Perth, Australia. Email: kwok.ho@health.wa.gov.au
[2] School of Population Health, University of Western Australia, Perth, Australia
[3] School of Veterinary & Life Sciences, Murdoch University, Perth, Australia
[4] School of Medicine and Pharmacology, University of Western Australia, Perth, Australia

Correspondence to: *Dr K.M. Ho, ICU, Royal Perth Hospital, Wellington Street, Perth, WA 6000,*

Australia. Fax: 61-8-92243668; Email: kwok.ho@health.wa.gov.au

Conflict of interest statements

The authors have no involvement with organisation(s) with financial interest in the subject matter of this study.

Word count: abstract 200, text 2649

Tables: 2

Figures: 3

1

Abstract

Purpose: We sought to determine whether Quick Sequential Organ Failure Assessment (qSOFA) score can be used to predict mortality of patients without suspected infection.

Materials and Methods: Using prospectively collected data within the *first hour* of intensive care unit (ICU) admission, the predictive ability of qSOFA was compared to the Simplified-Acute-Physiology-Score (SAPS III), Admission Mortality-Prediction-Model (MPM_0 III), Acute Physiology and Chronic Health Evaluation (APACHE II) model, and standard (full-version) SOFA score using area under the receiver-operating-characteristic (AUROC) curve and Brier score.

Results: Of the 2322 patients included, 279 (12.0%) died after ICU admission. The qSOFA score had a modest ability to predict mortality of all critically ill patients (AUROC 0.672, 95% confidence interval [CI] 0.638-0.707; Brier score 0.099) including the non-infected patients (AUROC 0.685, 95%CI 0.637-0.732; Brier score 0.081). The overall predictive ability and calibration of the qSOFA was comparable to other prognostic scores. Combining qSOFA score with lactate concentrations further enhanced its predictive ability (AUROC 0.730, 95%CI 0.694-0.765; Brier score 0.097), comparable to the standard SOFA score.

Conclusions: The qSOFA score had a modest ability to predict mortality of both septic and non-septic patients; combining qSOFA with plasma lactate had a predictive ability comparable to the standard SOFA score.

Abbreviations

APACHE, Acute Physiology and Chronic Health Evaluation

AUROC, area under the receiver-operating-characteristic

ICU, intensive care unit

qSOFA, Quick Sequential Organ Failure Assessment

MPM, Mortality Prediction Model

SAPS, Simplified Acute Physiology Score

Introduction

The ability to identify patients who are at risk of subsequent deterioration and mortality, starting from prehospital care, emergency department to acute hospital ward and intensive care unit (ICU) is important [1]. Many prognostic models have been developed in the past three decades and each has its own strengths and weaknesses [2]. Some prognostic models, including the Acute Physiology and Chronic Health Evaluation (APACHE II-IV models), use the worst physiological parameters of the patients within a period of time to estimate the risk of death [3], while others – including the Admission Mortality Prediction Model (MPM_0 III), Admission APACHE II and Simplified Acute Physiology Score (SAPS III) models – rely solely on patient characteristics on admission to the ICU to estimate the patient's risk of death [4-6]. None of these scores can be considered simple and user friendly enough to be used in the hospital ward and emergency department settings as an early warning score.

Using a composite score of different physiological parameters, many different medical emergency alert systems have been developed and are in use to identify patients who are at risk of deterioration in many healthcare institutions [7]. The 'quick Sequential Organ Failure Assessment' (qSOFA) score has recently been developed to facilitate early identification of patients who are at risk of mortality from suspected infection [8,9]. The qSOFA score uses only three physiological parameters (respiration rate $\geq$ 22 breaths/minute, altered mental state [Glasgow Coma Score <15] and systolic blood pressure $\leq$100mm Hg: total score ranges between 0 and three) and, despite its simplicity, it had a reasonable ability predict mortality for patients with sepsis both in the ICU (area under the receiver-operating-characteristic [AUROC] 0.66) and hospital ward (AUROC 0.81)[9].

Although the standard full-version SOFA score has been shown to predict outcomes of both septic and non-septic critically ill patients [10-12], it is uncertain whether qSOFA is only useful to predict mortality of patients with suspected infection. In this study, we assessed the ability of ICU admission qSOFA score in predicting mortality in critically ill patients with and without suspected infection, using the physiological and biochemical data of patients obtained within the *first hour* of ICU admission. Specifically, we also compared the prognostic significance of the qSOFA score, either on its own or in combination with plasma lactate concentration, with four well-established ICU admission prognostic scores (including the SAPS III, Admission MPM_0 III, Admission APACHE II models, and the standard full-version admission SOFA score)[4-6,10].

Materials and Methods

This prospective audit study was initiated in 2008 when the study center started to collect physiological and biochemical data obtained within the *first hour* of ICU admission for all ICU admissions. In this study, we utilized the data of patients, admitted between January 1st 2008 and December 31st 2013, including those who died within 24 hours of ICU admission. The clinical data analyzed were de-identified, and as such, this study was exempt from review by the Royal Perth Hospital Ethics Committee and registered as a clinical audit with the Clinical Safety and Quality Unit (150521/02). During the study period, Royal Perth Hospital was an 800-bed university teaching hospital and the 22-bed ICU was a tertiary ICU that admitted critically ill adult patients of all specialties and was staffed by fully trained intensivists.

During the study period, all the components of the SAPS III and APACHE scores including both admission (obtained within the *first hour* of an ICU admission) and worst first 24-hour physiology and biochemical data were recorded for all patients admitted to the ICU. After the patient was discharged from ICU, the data were checked for transcription errors and completeness by a designated trained clerical staff member using data from the computerized laboratory database and going through the ICU vital signs flow chart again before the data were transferred to the computer. A single data-custodian has been responsible for ensuring data quality. The data were reviewed for internal consistency before annual lock-down, and there were no patients lost to follow-up or with missing data. ICU readmissions during same hospitalization were excluded from this study [3].

The SAPS III, MPM_0III and Admission APACHE scores and predicted mortality were calculated as described by Moreno *et al*., Higgins *et al*., and Knaus *et al*., respectively [3-6], and were described in our previous publications [13,14]. Because the qSOFA score requires an assessment of a patient's mental state, all patients who were intubated and received invasive mechanical ventilation within the *first hour* of ICU admission were excluded from this study, as sedation would be needed for such patients making the assessment of the mental state of the patients inaccurate. In this study, there was no missing data to generate qSOFA and the three ICU admission prognostic scores, but arterial lactate concentrations within the *first hour* of ICU admission were available only in 1910 patients (82.3%).

Statistical analysis

The primary outcome of interest of this study was hospital mortality. The secondary outcomes were patients who required invasive mechanical ventilation

within 24 hours of ICU admission and length of ICU stay >10 days. We used the AUROC to assess the ability of the qSOFA and other prognostic scores to discriminate the primary and secondary outcomes. The difference in AUROC curves derived from the same cases was calculated by the z statistic as described by Hanley and McNeil [15]. The calibration of the model was also assessed by the Hosmer-Lemeshow chi-square statistics [16] and a calibration plot, with a p value < 0.05 suggestive of imperfect calibration.

We used the Brier score to assess the overall performance of the qSOFA and other prognostic scores [17]. This overall performance index ices will reflect both the discrimination and calibration of a prediction model [17]. Brier score is calculated as $\sum (y_i - p_i)^2 / n$, where y denotes the observed outcome while p denotes the predicted probability of death for subject i in the data set of n subjects. Brier scores range from 0 to 0.25, with a Brier score of zero indicates a perfect prediction model and a Brier score of 0.25 signifies a useless prediction model [17].

In addition to assessing the qSOFA score as a continuous predictor, we also assessed the sensitivity, specificity, positive and negative predictive values, and likelihood ratios of qSOFA ≥ 2 in predicting hospital mortality [9]. Because plasma lactate concentration was shown to have an additive prognostic effect with qSOFA score [9], we also analyzed the prognostic effect of a combination of plasma lactate concentration (grouped as <2mmol/L, 2-4mmol/L and >4mmol/L) and qSOFA. Finally, we also tested whether adding an interaction term between plasma lactate concentration and qSOFA would have any prognostic significance; if yes, it would suggest that plasma lactate concentration will have synergistic (rather than just additive) prognostic significance to the qSOFA score. In this study, a p-value <0.05 was taken as significant and all statistical analyses were performed by SPSS for

Windows (version 22.0, IBM, USA), MedCalc for Windows (version 12.5, Ostend, Belgium), and S-PLUS (version 8.0, 2007; Insightful Corp., Seattle, Washington, USA).

As a sensitivity analysis, we also assessed whether the qSOFA score, either alone or in combination with plasma lactate concentration, would be useful to predict mortality of all critically ill patients including those who required mechanical ventilation within the first hour of ICU admission (N=9458) by using the pre-intubation Glasgow Coma Score (GCS) to estimate the qSOFA score.

Results

Characteristics of the patients

Of the 9549 patients admitted to the study center during the study period, 2322 patients (24.3%) were not intubated within the first hour of ICU admission and were eligible for further analysis. Of the 2322 patients included in the study, 163 (7.0%) required non-invasive ventilation at the time of ICU admission, 345 patients (15%) required invasive mechanical ventilation within 24 hours of ICU admission, and 279 patients (12.0%) died during the same hospital stay. Patient admission characteristics including age, admission source, chronic health conditions, and admission diagnosis were significantly different between the survivors and non-survivors (**Table 1**).

Prognostic significance of qSOFA and other prognostic scores

The qSOFA score had a modest ability to discriminate between survivors and non-survivors for all critically ill, non-intubated, patients (AUROC 0.672, 95% confidence interval [CI] 0.638-0.707), and also those admitted with a non-infective diagnosis (AUROC 0.685, 95%CI 0.637-0.732; Brier score 0.081)(**Figure 1 and**

Table 2). Furthermore, the qSOFA score also had a modest ability to predict those who would subsequently require invasive mechanical ventilation within 24 hours of ICU admission (AUROC qSOFA: 0.641, 95%CI 0.596-0.686 *vs.* APACHE II: 0.640, 95%CI 607-673; SAPS III: 0.608, 95%CI 0.575-0.642; MPM$_0$III: 0.604, 95%CI 0.570-0.638; standard SOFA: 0.632, 95%CI 0.599-0.666), and those who had a prolonged ICU stay longer than 10 days (AUROC 0.622, 95%CI 0.582-0.661) comparable to other ICU admission prognostic scores.

As expected, the ability of the qSOFA score to discriminate between survivors and non-survivors was slightly inferior to those of the SAPS III, MPM$_0$ III, APACHE II models, and the standard (full-version) admission SOFA score (all p<0.001), but the qSOFA's overall predictive ability, as measured by the Brier scores (Brier score: 0.099), was not too different from those of the SAPS III (Brier score: 0.089), MPM$_0$ III (Brier score: 0.096), Admission APACHE II models (Brier score: 0.096), and admission SOFA score (Brier score: 0.105). Restricting our analyses to patients with septic shock or sepsis alone produced similar results (**Table 2**). In terms of calibration, the qSOFA also appeared to be reasonably well calibrated (**Table 2**) compared to other prognostic scores, and had a relatively linear relationship with the observed mortality (**Figure 2**).

Using qSOFA ≥2 as a warning sign and combining qSOFA with plasma lactate concentration

Using a qSOFA ≥2 on admission to ICU as a cut-point [9] , the sensitivity, specificity, positive predictive value, negative predictive value, positive and negative likelihood ratios for subsequent hospital mortality were 0.46 (95%CI 0.40-0.51), 0.81

(95%CI 0.80-0.83), 24.8% (95%CI 21.2-28.7), 91.6% (90.3-92.8), 2.4 (95%CI 2.1-2.8) and 0.7 (95%CI 0.6-0.8), respectively.

When the qSOFA was combined with arterial lactate concentrations (grouped in three categories), its ability to predict hospital mortality was further enhanced (AUROC 0.730, 95%CI 0.694-0.765; Brier score 0.097) (**Figure 3 and Table 2**) and became comparable to the standard (full-version) admission SOFA (AUROC 0.727, 95%CI 0.695-0.759; Brier score 0.105). The odds ratio (OR) for mortality per increment of qSOFA was 2.0 (95%CI 1.7-2.4), and ORs for lactate: 2-4mmol/L and lactate>4mmol/L were 1.7 (95%CI 1.2-2.4) and 4.1 (2.9-6.0), respectively, compared to patients with lactate <2mmol/L. An interaction term between lactate and qSOFA was not significant (p=0.685) in predicting mortality, suggesting that qSOFA score and plasma lactate concentration only had an additive, but not synergistic, prognostic significance.

Sensitivity analysis

Using pre-intubation GCS to estimate the ICU admission qSOFA scores, its ability to discriminate between hospital survivors and non-survivors for all ICU admissions (AUROC 0.663, 95%CI 0.648-0.679) remained similar to restricting the analysis only to those not requiring mechanical ventilation within the first hour of ICU admission (AUROC 0.672, 95%CI 0.638-0.707). Combining admission lactate concentration with qSOFA score further improved their overall ability to discriminate between hospital survivors and non-survivors regardless of whether they were mechanically ventilated on ICU admission (AUROC 0.734, 95%CI 0.718-0.751), almost comparable to predictive ability of the standard admission SOFA score (AUROC 0.763, 95%CI 0.749-0.777).

Discussion

This study showed that the qSOFA score within the *first hour* of ICU admission had a modest ability to differentiate between survivors and non-survivors for both septic and non-septic critically ill, non-intubated, patients, comparable to some well-established ICU admission prognostic scores. Combining qSOFA with lactate concentration further enhanced its ability to predict mortality of critically ill patients, comparable to the standard (full-version) admission SOFA score. In addition, the qSOFA score also had a modest ability to predict the risk of requiring invasive mechanical ventilation within 24 hours of ICU admission and prolonged ICU stay when applied to both septic and non-septic patients who were not ventilated on admission to the ICU. These results are clinically relevant and require further discussion.

First, our results confirmed that the qSOFA score had a modest ability to discriminate between survivors and non-survivors (AUROC 0.67) when applied to all critically ill non-intubated patients, very similar to the results reported in the qSOFA validation study when only septic ICU patients were included (AUROC 0.66)[9]. Because qSOFA score is easy and simple to use, it has a huge potential to be incorporated as an early warning tool for hospitalized patients, beyond identifying septic patients who are at risk of subsequent mortality [9]. Using a qSOFA score ≥2 as a sole criterion, it had a high negative predictive value and a low negative likelihood ratio, suggesting that a qSOFA <2 would be useful to 'rule out' hospitalized patients who are at high risk of subsequent deterioration and mortality. Our results also confirmed the additive (but not synergistic) prognostic significance of plasma lactate and qSOFA score reported in the qSOFA validation study [9] and, indeed, their

11

combined predictive ability became almost comparable to the standard (full-version) SOFA score (**Table 2**). For instance, when combined with plasma lactate concentrations >4mmol/L, a qSOFA score of 2 and 3 were associated with a substantial risk of subsequent mortality (at 35% and 55% respectively) compared to <5% mortality for patients with a qSOFA of zero and normal lactate concentration (<2mmol/L)(**Figure 3**). Even a moderate increase in lactate concentration (between 2 and 4mmol/L) would substantially increase the risk of mortality for patients with a qSOFA ≥2 (mortality 25% and 42% for qSOFA scores 2 and 3 respectively). As such, when combined with an elevated lactate concentration (>2mmol/L), a qSOFA≥2 would be very useful to 'rule a patient in' as a high-risk patient who is likely to deteriorate resulting in subsequent mortality. Taken together with the data from the recent large qSOFA validation study [8,9], our results strongly support the utility of qSOFA in combination with plasma lactate concentration as a simple, and yet reasonably sensitive, tool to identify both infected and non-infected hospitalized patients who are at risk of subsequent deterioration and mortality. Because qSOFA with lactate concentration is much easier to use than the standard SOFA score, qSOFA with lactate concentration may be particularly applicable in the hospital ward, emergency department, and pre-hospital settings where a quick assessment is needed to stratify patients' risk of subsequent deterioration [18].

Second, although qSOFA score had a modest ability to discriminate between survivors and non-survivors, it can, by no means, possible to replace other well-established ICU prognostic scores for quality assurance and research purposes. This is because qSOFA score would not be accurate once sedation is used. In addition, its overall discrimination ability is still not as good as the SAPS III, MPM_0 III or APACHE models [3-6](**Table 2**).

Third, we would like to acknowledge the limitations of this study. Although we had included a reasonable number of patients, this was still a single center study and our results may not be applicable to centers with very different case-mix [19]. Because the coefficients of the qSOFA mortality prediction equation were not available in the public domain, we could not compare the slope and intercept of the calibration curve of the qSOFA score with those from other ICU admission prognostic scores in this study. Finally, our study was underpowered to assess the difference in performance of the qSOFA score in patients with different admission diagnoses [3-6], and this merits further investigation by a multicenter study.

In conclusion, qSOFA score had a modest ability to predict requirement for invasive mechanical ventilation, prolonged ICU stay, and mortality of septic and non-septic critically ill patients. Its ability to predict mortality was further enhanced when combined with lactate concentration, resulting in a predictive ability comparable to the full-version SOFA score. Combining qSOFA score with plasma lactate concentration represents a simple, and yet reasonably sensitive, tool to identify both septic and non-septic patients who are risk of subsequent deterioration and mortality. Use of qSOFA with plasma lactate concentration as an early warning tool for hospitalized patients, both with and without suspected infection, should be seriously considered.

References

[1] Ghosh R, Pepe P. The critical care cascade: a systems approach. *Curr Opin Crit Care* 2009;15:279-83.

[2] Gunning K, Rowan K. ABC of intensive care: outcome data and scoring systems. *BMJ* 1999;319:241-4.

[3] Knaus WA, Draper EA, Wagner DP, Zimmerman JE. APACHE II: a severity of disease classification system. *Crit Care Med* 1985;13:818-29.

[4] Higgins TL, Kramer AA, Nathanson BH, Copes W, Stark M, Teres D. Prospective validation of the intensive care unit admission Mortality Probability Model (MPM$_0$-III). *Crit Care Med* 2009;37:1619-23.

[5] Moreno RP, Metnitz PG, Almeida E, Jordan B, Bauer P, Campos RA, et al.; SAPS 3 Investigators. SAPS 3--From evaluation of the patient to evaluation of the intensive care unit. Part 2: Development of a prognostic model for hospital mortality at ICU admission. *Intensive Care Med* 2005;31:1345-55.

[6] Ho KM, Dobb GJ, Knuiman M, Finn J, Lee KY, Webb SA. A comparison of admission and worst 24-hour Acute Physiology and Chronic Health Evaluation II scores in predicting hospital mortality: a retrospective cohort study. *Crit Care* 2006;10:R4.

[7] Royal College of Physicians. National Early Warning Score (NEWS): Standardising the assessment of acute-illness severity in the NHS. Report of a working party. London: RCP. 2012.

[8] Singer M, Deutschman CS, Seymour CW, Shankar-Hari M, Annane D, Bauer M, Bellomo R, Bernard GR, Chiche JD, Coopersmith CM, Hotchkiss RS, Levy MM, Marshall JC, Martin GS, Opal SM, Rubenfeld GD, van der Poll T, Vincent JL, Angus

DC. The Third International Consensus Definitions for Sepsis and Septic Shock (Sepsis-3). *JAMA* 2016;315:801-10.

[9] Seymour CW, Liu VX, Iwashyna TJ, Brunkhorst FM, Rea TD, Scherag A, Rubenfeld G, Kahn JM, Shankar-Hari M, Singer M, Deutschman CS, Escobar GJ, Angus DC. Assessment of Clinical Criteria for Sepsis: For the Third International Consensus Definitions for Sepsis and Septic Shock (Sepsis-3). *JAMA* 2016;315:762-74.

[10] Vincent JL, Moreno R, Takala J, Willatts S, De Mendonça A, Bruining H, Reinhart CK, Suter PM, Thijs LG. The SOFA (Sepsis-related Organ Failure Assessment) score to describe organ dysfunction/failure. On behalf of the Working Group on Sepsis-Related Problems of the European Society of Intensive Care Medicine. *Intensive Care Med* 1996;22:707-10.

[11] Ho KM, Lee KY, Williams T, Finn J, Knuiman M, Webb SA. Comparison of Acute Physiology and Chronic Health Evaluation (APACHE) II score with organ failure scores to predict hospital mortality. *Anaesthesia* 2007;62:466-73.

[12] Ho KM. Combining sequential organ failure assessment (SOFA) score with acute physiology and chronic health evaluation (APACHE) II score to predict hospital mortality of critically ill patients. *Anaesth Intensive Care* 2007;35:515-21.

[13] Ho KM, Williams TA, Harahsheh Y, Higgins TL. Using patient admission characteristics alone to predict mortality of critically ill patients: a comparison of 3 prognostic scores. *J Crit Care* 2016;31:21-5.

[14] Ho KM, Lan NS, Williams TA, Harahsheh Y, Chapman AR, Dobb GJ, Magder S. A comparison of prognostic significance of strong ion gap (SIG) with other acid-base markers in the critically ill: a cohort study. *J Intensive Care* 2016;4:43.

15

[15] Hanley JA, McNeil BJ. A method of comparing the areas under receiver operating characteristic curves derived from the same cases. *Radiology* 1983;148:839-43.

[16] Lemeshow S, Hosmer DW. A review of goodness of fit statistics for use in the development of logistic regression model. *Am J Epidemiol* 1982;115:92-106.

[17] Arkes HR, Dawson NV, Speroff T, Harrell FE Jr, Alzola C, Phillips R, et al. The covariance decomposition of the probability score and its use in evaluating prognostic estimates. *Med Decis Making* 1995;15:120-131.

[18] Williams TA, Tohira H, Finn J, Perkins GD, Ho KM. The ability of early warning scores (EWS) to detect critical illness in the prehospital setting: A systematic review. *Resuscitation* 2016;102:35-43.

[19] Kramer AA, Higgins TL, Zimmerman JE. Comparing observed and predicted mortality among ICUs using different prognostic systems: why do performance assessments differ? *Crit Care Med* 2015;43:261-9.

Figure legends

Figure 1. Areas under the receiver-operating-characteristic (AUROC) of quick Sequential Organ Failure Assessment (qSOFA) score and other intensive care prognostic scores. APACHE, Acute Physiology and Chronic Health Evaluation. SAPS, Simplified Acute Physiology Score. MPM_0, Admission Mortality Prediction Model.

Figure 2. Relationship between quick Sequential Organ Failure Assessment (qSOFA) score of non-intubated critically ill patients within the *first hour* of intensive care unit admission and the risk of subsequent hospital mortality.

Figure 3. Association between the quick Sequential Organ Failure Assessment (qSOFA) score of non-intubated critically ill patients within the *first hour* of intensive care unit admission and risk of subsequent hospital mortality, stratified by concomitant plasma lactate concentrations.

Figure 1
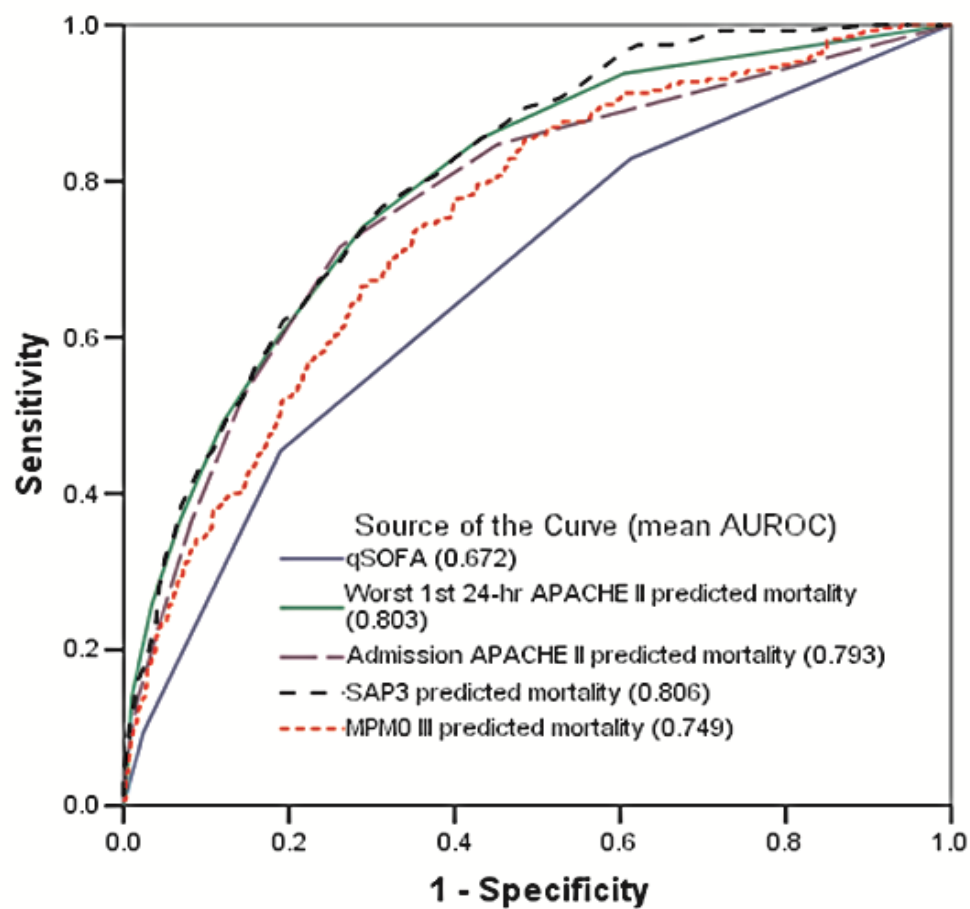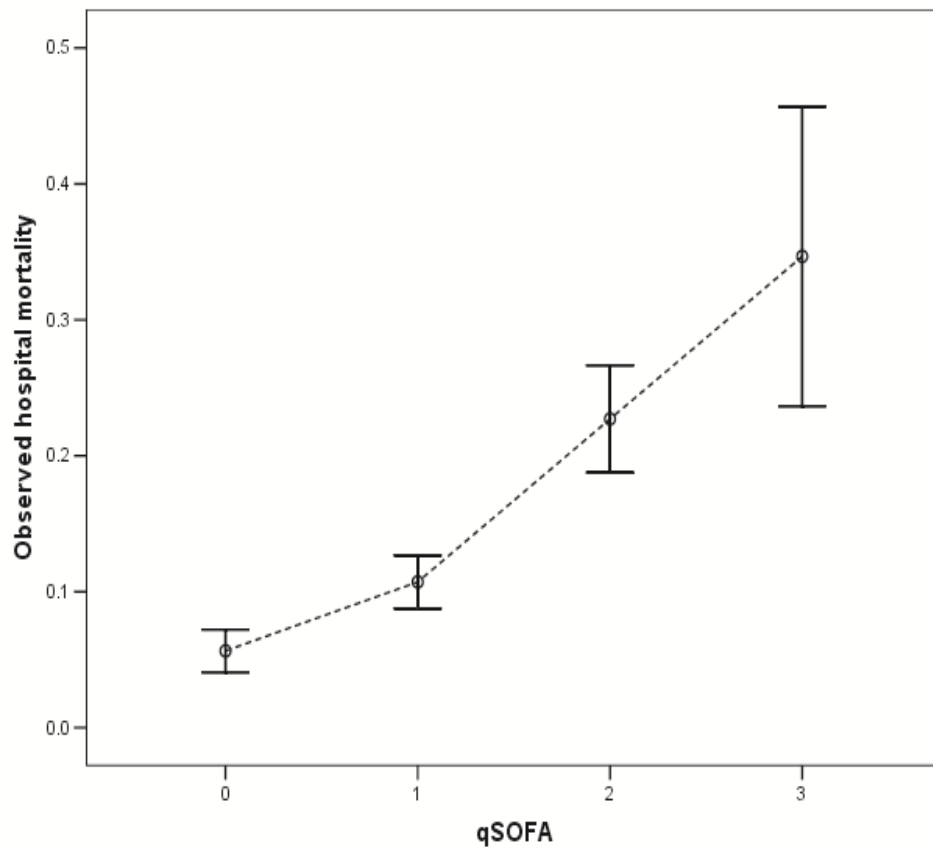
Figure 2

Figure 3
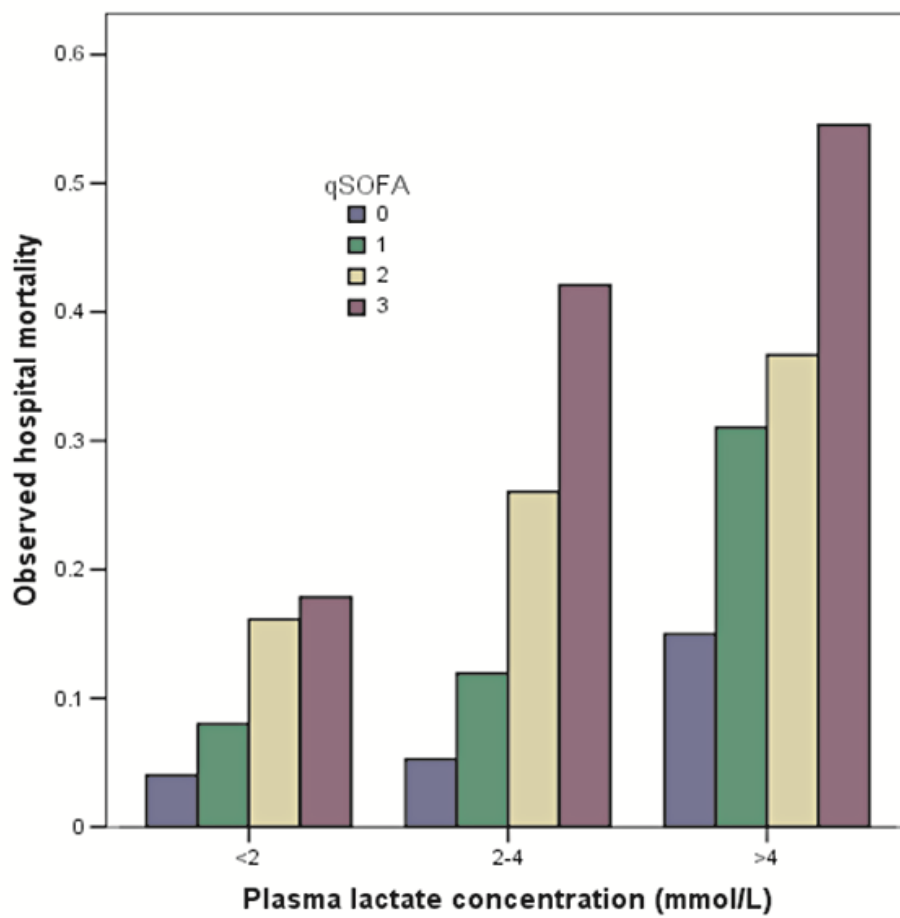
Table 1. Characteristics of the study cohort (N=2322).

Variable	Total cohort (N=2322)	Survivors (n=2043)	Non-survivors (n=279, 12.0%)	P value[#]
Age, years (IQR)	57.1 (41-70)	55.9 (39-69)	60.1 (54-78)	0.001
Male, no. (%)	1423 (61)	1245 (61)	178 (64)	0.394
ICU Admission source, no. (%)				0.001
- Operating theatre	676 (29)	647 (32)	29 (10)	
- Emergency Department	663 (29)	595 (29)	68 (24)	
- Ward	689 (30)	546 (27)	143 (52)	
- CCU/HDU	108 (5)	87 (4)	21 (8)	
- Other hospital	165 (7)	149 (7)	16 (6)	
- Other hospital ICU	21 (1)	19 (1)	2 (0.7)	
Elective surgery, no. (%)	453 (19.5)	433 (21)	20 (7)	0.001
Ward stay before ICU, days (IQR)	4 (2-11)	4 (1-10)	5 (2-15)	0.003
Admission APACHE II score (IQR)	12.0 (8-18)	11.0 (7-17)	20 (15-24)	0.001
Worst 24-hr APACHE II score (IQR)	17.0 (12-23)	16 (11-21)	26 (19-30)	0.001
SAPS III score (IQR)	41 (32-50)	39 (30-48)	54 (46-62)	0.001
SAPS III predicted risk, % (IQR)	6.3 (2-16)	4.9 (1-13)	22.0 (11-37)	0.001
MPM_0 III predicted risk, % (IQR)	9.4 (4-18)	8.5 (4-16)	19.2 (11-31)	0.001
Adm. qSOFA score, (IQR) 1 (0-1)	0 (0-1)	1 (1-2)	0.001	
Adm. qSOFA predicted risk, % (IQR)	11.2 (6-11)	11.2 (6-11)	11.2 (11-22)	0.001
Adm. SOFA score, (IQR)	4 (2-6)	4 (2-6)	6 (4-8)	0.001
Adm. SOFA predicted risk, % (IQR)	10.2 (6-17)	10.2 (6-17)	17.4 (10-28)	0.001
ICU stay, days (IQR)	3 (2-5)	3 (2-5)	4 (2-8)	0.001
Hospital stay, days (IQR)	14 (7-28)	14 (8-28)	13 (4-28)	0.007
Chronic medical conditions (%): *				
- Respiratory	132 (6)	107 (5)	25 (9)	0.018
- Cardiovascular	196 (8)	156 (8)	40 (14)	0.001
- Liver	92 (4)	72 (4)	20 (7)	0.008
- Renal	227 (10)	185 (9)	42 (15)	0.003
- Immune disease	48 (2)	35 (2)	13 (5)	0.005
- Immune treatment	166 (7)	129 (6)	37 13)	0.001
- Metastatic cancer	30 (1)	27 (1)	3 (1)	0.999
- Lymphoma	22 (1)	11 (0.5)	11 (4)	0.001
- Leukaemia / myeloma	75 (3)	58 (3)	17 (6)	0.010
- AIDS	5 (0.2)	2 (0.1)	3 (1)	0.014
Major admission diagnoses, no. (%):				
Cardiac or respiratory arrest	8 (0.3)	7 (0.3)	1 (0.4)	0.999
Pneumonia	186 (8)	159 (8)	27 (10)	0.289
Septic shock	422 (18)	326 (16)	96 (34)	0.001
Multiple trauma	142 (6)	133 (7)	9 (3)	0.032
Isolated head trauma	33 (1)	32 (2)	1 (0.4)	0.171
Intracranial haemorrhage	37 (2)	31 (2)	6 (2)	0.440
Drug overdoses	41 (2)	40 (2)	1 (0.4)	0.053
Congestive heart failure, ischaemic heart disease, or cardiogenic shock	107 (5)	78 (4)	29 (10)	0.001
Peripheral vascular disease or aortic aneurysm	97 (4)	93 (5)	4 (1)	0.010
GI obstruction or perforation	24 (1)	24 (1)	0 (0)	0.105
Aspiration pneumonia	32 (1)	30 (2)	2 (0.7)	0.419
Obstructive airway disease	73 (3)	69 (3)	4 (1)	0.098
Acute lung injury or ARDS	25 (1)	21 (1)	4 (1)	0.532
Gastrointestinal bleeding	56 (2)	50 (2)	6 (2)	0.999
Pulmonary embolism	18 (0.8)	15 (0.7)	3 (1)	0.469

All values are median and interquartile range (IQR) in parenthesis unless stated otherwise. GI, Gastrointestinal. APACHE, Acute Physiology and Chronic Health Evaluation. ARDS, Acute Respiratory Distress Syndrome. CCU, Coronary Care Unit. HDU, High Dependency Unit. ICU, intensive care unit. MPM_0, Mortality Prediction Model on admission. qSOFA, Quick Sequential Organ Failure Assessment. SAPS, Simplified Acute Physiology Score. *According to the definitions by the APACHE model. [#]P values generated by either Mann-Whitney or Chi-square test.

Table 2. Performance of the admission Quick Sequential Organ Failure Assessment (qSOFA), Mortality Prediction Model on admission (MPM$_0$ III), Simplified Acute Physiology Score (SAPS III), and admission and worst first 24-hr Acute Physiology and Chronic Health Evaluation (APACHE II) predicted risks in predicting mortality of critically ill patients who did not require an endotracheal tube on admission to the intensive care unit. AUROC, area under the receiver-operating-characteristic curve. CI, Confidence Interval.

All patients (N=2322)	AUROC (95%CI)	Hosmer-Lemeshow χ^2 (p value)	Brier Score
qSOFA	0.672 (0.638-0.707)	2.7 (0.103)	0.099
Combining qSOFA with lactate[#]	0.730 (0.694-0.765)	1.0 (0.966)	0.097
SOFA	0.727 (0.695-0.759)	8.7 (0.273)	0.105
MPM$_0$ III	0.749 (0.719-0.779)	23.0 (0.003)	0.096
SAPS III	0.806 (0.781-0.831)	35.0 (0.001)	0.089
APACHE II (admission)	0.793 (0.766-0.820)	24.6 (0.002)	0.096
APACHE II (worst first 24-hr)	0.803 (0.777-0.829)	15.5 (0.050)	0.119

Non-infective diagnosis (n=1658)	AUROC (95%CI)	Hosmer-Lemeshow χ^2 (p value)	Brier Score
qSOFA	0.685 (0.637-0.732)	0.1 (0.865)	0.081
Combining qSOFA with lactate[#]	0.728 (0.682-0.774)	2.1 (0.733)	0.080
SOFA	0.733 (0.692-0.774)	8.2 (0.226)	0.087
MPM$_0$ III	0.757 (0.715-0.800)	25.8 (0.001)	0.078
SAPS III	0.819 (0.784-0.854)	24.4 (0.002)	0.071
APACHE II (admission)	0.814 (0.776-0.851)	20.7 (0.008)	0.076
APACHE II (worst first 24-hr)	0.829 (0.794-0.864)	15.9 (0.044)	0.090

Septic shock* (n=422)	AUROC (95%CI)	Hosmer-Lemeshow χ^2 (p value)	Brier Score
qSOFA	0.637 (0.573-0.701)	3.7 (0.157)	0.174
Combining qSOFA with lactate[#]	0.701 (0.630-0.771)	4.6 (0.602)	0.158
SOFA	0.684 (0.619-0.749)	3.5 (0.835)	0.163
MPM$_0$ III	0.708 (0.650-0.766)	7.1 (0.531)	0.162
SAPS III	0.723 (0.665-0.780)	5.0 (0.754)	0.155
APACHE II (admission)	0.717 (0.659-0.775)	3.8 (0.874)	0.167
APACHE II (worst first 24-hr)	0.726 (0.666-0.787)	8.5 (0.387)	0.212

Sepsis** (n=242)	AUROC (95%CI)	Hosmer-Lemeshow χ^2 (p value)	Brier Score
qSOFA	0.600 (0.483-0.717)	0.1 (0.866)	0.101
Combining qSOFA with lactate[#]	0.654 (0.523-0.785)	4.2 (0.241)	0.099
SOFA	0.619 (0.505-0.733)	8.5 (0.207)	0.111
MPM$_0$ III	0.657 (0.543-0.771)	7.6 (0.473)	0.103
SAPS III	0.692 (0.593-0.791)	6.8 (0.455)	0.102
APACHE II (admission)	0.732 (0.632-0.832)	9.6 (0.293)	0.110
APACHE II (worst first 24-hr)	0.702 (0.598-0.806)	10.8 (0.211)	0.156

[#]Plasma lactate grouped into three categories: <2mmol/L, 2-4mmol/L and >4mmol/L. * Septic shock was defined as sepsis with cardiovascular failure requiring inotropic support as per APACHE II definition. ** Including patients with pneumonia, aspiration and bowel perforation. The odds ratio (OR) for mortality per increment of qSOFA was 2.0 (95%CI 1.7-2.4), and ORs for lactate: 2-4mmol/L and lactate>4mmol/L were 1.7 (95%CI 1.2-2.4) and 4.1 (2.9-6.0), respectively. An interaction term between lactate and qSOFA was not significant (p=0.685) in predicting mortality, suggesting that qSOFA and plasma lactate concentration had an additive, but not synergistic, prognostic significance.

Highlights

- Quick Sequential Organ Failure Assessment (qSOFA) score has been shown to predict the risk of mortality in patients with suspected infection.

- This study extended the utility of qSOFA, and showed that it also had a modest ability to predict the requirement of invasive mechanical ventilation, prolonged ICU stay, and mortality in all critically ill patients, including those with a non-infective diagnosis.

- The qSOFA's ability to predict mortality was further enhanced when combined with lactate concentration.

- Combining qSOFA score with plasma lactate concentration represents a simple, and yet reasonably sensitive, tool to identify both septic and non-septic patients who are risk of subsequent deterioration and mortality.