Prognostic accuracy of the quick Sequential Organ Failure Assessment (qSOFA)-lactate criteria for mortality in adults with suspected bacterial infection in the emergency department of a hospital with limited resources

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ABSTRACT

Background Routine use of the Sequential Organ Failure Assessment (SOFA) score to prognosticate patients with sepsis is challenged by the requirement to perform numerous laboratory tests. The prognostic accuracy of the quick SOFA (qSOFA) without or with lactate criteria has not been prospectively investigated in low and middle income countries. We assessed the performance of simplified prognosis criteria using qSOFA-lactate criteria in the emergency department of a hospital with limited resources, in comparison with SOFA prognosis criteria and systemic inflammatory response syndrome (SIRS) screening criteria.

Methods This prospective cohort study was conducted between March and December 2017 in adult patients with suspected bacterial infection visiting the emergency department of the Indonesian National Referral Hospital. Variables from sepsis prognosis and screening criteria and venous lactate concentration at enrolment were recorded. Patients were followed up until hospital discharge or death. Prognostic accuracy was measured using area under the receiver operating characteristic curve (AUROC) of each criterion in the prediction of in-hospital mortality.

Results Of 3026 patients screened, 1213 met the inclusion criteria. The AUROC of qSOFA-lactate criteria was 0.74 (95% CI 0.71 to 0.77). The AUROC of qSOFA-lactate was not statistically significantly different to the SOFA score (AUROC 0.75, 95% CI 0.72 to 0.78; p=0.462). The qSOFA-lactate was significantly higher than qSOFA (AUROC 0.70, 95% CI0.67 to 0.74; p=0.006) and SIRS criteria (0.57, 95% CI0.54 to 0.60; p<0.001).

Conclusions The prognostic accuracy of the qSOFA-lactate criteria is as good as the SOFA score in the emergency department of a hospital with limited resources. The performance of the qSOFA criteria is significantly lower than the qSOFA-lactate criteria and SOFA score.

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Key messages

What is already known on this subject

- The Sequential Organ Failure Assessment (SOFA) score has been developed and validated to predict prognosis in patients with sepsis in developed countries.
- The prognostic accuracy of the SOFA score and quick SOFA (qSOFA) criteria in low and middle income countries has not been prospectively assessed.
- The simplified rapid and accurate prognosis criteria using more affordable parameters is not available.

What this study adds

- The prognostic accuracy of the qSOFA is significantly lower than the qSOFA-lactate criteria (defined as two or more qSOFA criteria, and venous lactate concentration >2 mmol/L) and the SOFA score in an emergency department of a hospital with limited resources.
- The qSOFA-lactate criteria may be used as a simplified prognosis criteria in the emergency department of a hospital with limited resources.
- The qSOFA-lactate criteria perform as good as the SOFA score, without the requirement to use numerous routine laboratory tests.

INTRODUCTION

In 2016, the European Society of Intensive Care Medicine and the Society of Critical Care Medicine proposed a new criteria for the diagnosis of sepsis based on predictive validity assessment, that is, sepsis-3 criteria, which highlight the role of organ dysfunction in increasing the risk of mortality in patients with infection. Two prognostic criteria—quick Sequential Organ Failure Assessment (qSOFA) criteria and Sequential Organ Failure Assessment (SOFA) score—were proposed in the application of this updated criteria.[1] The use of the SOFA score is challenged by the complexity of routine laboratory tests (such as blood gas analysis, bilirubin, creatinine, thrombocyte count), which are needed for the fulfilment of criteria, especially in hospitals

with limited resources in low and middle income countries (LMICs), where most of the sepsis burden occurs.[2 3] Although the prognostic accuracy of the SOFA score and qSOFA criteria were previously determined using retrospective patient data from high income countries, such results may differ from those of patients from LMICs with more limited resources.[1] Previous studies on the accuracy of the qSOFA criteria in hospitals with limited resources and in LMICs demonstrated various results.[4–7]

Hyperlactataemia has been extensively studied as a valuable predictor for in-hospital mortality in patients admitted to hospital for a number of reasons, including infection.[8–10] In areas with limited resources, including Indonesia, where delays in seeking medical care are related to a worsening prediction of infection outcome, high lactate concentrations have been identified as independent predictors of mortality in infected patients with diabetic ketoacidosis.[11] Furthermore, as an important predictor of mortality, venous lactate concentrations can easily be measured using an accurate point of care test which helps in identifying patients with poor prognosis.[12]

A previous study which added lactate criteria as the fourth component of the qSOFA criteria revealed no meaningful change in the predictive validity as a balance of complexity and cost alongside the three components of the qSOFA criteria.[13] However, the potential use of lactate criteria in infected patients with a positive qSOFA criteria has not been previously investigated in a prospective cohort study, especially in LMICs. The aim of this study was to investigate the prognostic accuracy of the qSOFA and lactate criteria (defined as two or more qSOFA criteria, and venous lactate concentration higher than the defined cut-off) in an emergency department of a hospital with limited resources, in comparison with established prognosis criteria (ie, SOFA score, qSOFA) and screening criteria (ie, systemic inflammatory response syndrome (SIRS) criteria).

METHODS

Study design, setting and population

This was a prospective cohort study conducted between March and December 2017 in the emergency department of Cipto Mangunkusumo National Hospital, an Indonesian national referral hospital containing 927 beds. Adult patients (≥18 years) with suspected bacterial infection (identified as those who had received oral or parenteral antibiotics and had body fluid cultures) and who were hospitalised were consecutively included in the study after being administered the first dose of antibiotics.

Data collection and endpoints

Each patient's characteristics, vital signs and consciousness levels were recorded upon study enrolment for the included sample. These physical examination data, along with a complete blood count, creatinine, bilirubin, arterial blood gas analysis, and venous lactate measurements were recorded at their worst level during the previous 12 hours before study enrolment if there were more than two measurements provided for each variable. All medical, nursing and laboratory staff in the emergency department received training on how to perform standardised measurements and record data on the above-mentioned variables before study initiation.

Prognosis criteria based on SOFA score were considered positive in the presence of two or more increments of SOFA score when compared with the patient's baseline SOFA score before bacterial infection was suspected.[1] The baseline SOFA score was determined through history-taking, the presence of a past diagnosis, and from clinical and laboratory data (if available) for established patients in the hospital's medical record system. Positive qSOFA criteria were defined as the fulfilment of two or more qSOFA criteria, that is, respiratory rate of 22/min or more, abnormal mental status (Glasgow Coma Scale 14 or less), and systolic blood pressure of 100 mmHg or less.[1] Positive qSOFA-lactate criteria were defined as fulfilment of two or more qSOFA criteria and a venous lactate concentration higher than the determined cut-off. SIRS criteria—which included: respiratory rate >20/min or arterial carbon dioxide pressure ($PaCO_2$) <32 mmHg; temperature >38°C or <36°C; pulse >90 beats/min; white blood cell count >12 000/μL or <4000/mL or >10% bands—were calculated for all patients.[14] Positive SIRS criteria were defined as the fulfilment of two or more SIRS criteria. Patients were classified based on their fulfilment of increments of SOFA score, qSOFA, qSOFA-lactate, and SIRS criteria.

The endpoint was in-hospital mortality within 28 days; thus, patients were followed up until hospital discharge or death. Patients who were still hospitalised after 28 days were considered as failing to meet the endpoint of in-hospital mortality.

Venous lactate measurement using point-of-care test

Venous lactate was measured using the commercially available Accutrend Plus Roche, Roche Diagnostics GmbH, Mannheim and test strip Diagnostics GmbH, Mannheim. A sample of 50 μL of fresh venous blood, collected by venepuncture, was dropped into the test area containing detection reagents.[15] The strips were stored at a temperature of 24°C up to the stated expiration date. Accutrend Plus Roche was regularly calibrated every 6 months by Diagnostic Division Roche Indonesia.

To determine the appropriate cut-off values, the receiving operating characteristic (ROC) curve analysis was used to obtain the best sensitivity and specificity for venous lactate concentration in the prediction of in-hospital mortality. The best cut-off was >2 mmol/L (71% sensitifity and 69.4% specificity) with an area under the receiver operating characteristic curve (AUROC) of venous lactate concentration in the prediction of in-hospital mortality of 0.76 (95% CI 0.73 to 0.79).

Ethics

This study was approved by the Faculty of Medicine Universitas Indonesia, Cipto Mangunkusumo National Hospital Ethics Committee (ID of approval: 0040/UN2.F1/ETIK/2018). Written informed consent was obtained from all patients or their representatives in cases where the patient's mental capacity was lacking. All patients or their representatives were able to provide informed consent.

Stastistical analysis

The sample size for this study was based on an estimated AUROC of the SOFA score 0.80, with $\delta=0.10$, $\alpha=0.05$ and $\beta=0.20$. The required sample size for comparison of AUROC curves was calculated to be 1142 patients.[16]

Non-normally distributed variables were reported as median (IQR). Categorical variables were expressed as numbers and percentages. To assess the performance of qSOFA-lactate criteria to predict the endpoint, an ROC curve was constructed and the corresponding AUROC, sensitivity, specificity, positive and negative predictive values for a determined cut-off were calculated. This AUROC was compared with the AUROC of the SOFA score, qSOFA and SIRS criteria in order to assess the performance of every criteria.

Statistical analyses were performed using the STATA Statistical Software Version 12 (Stata Corp, College Station, TX, USA). All

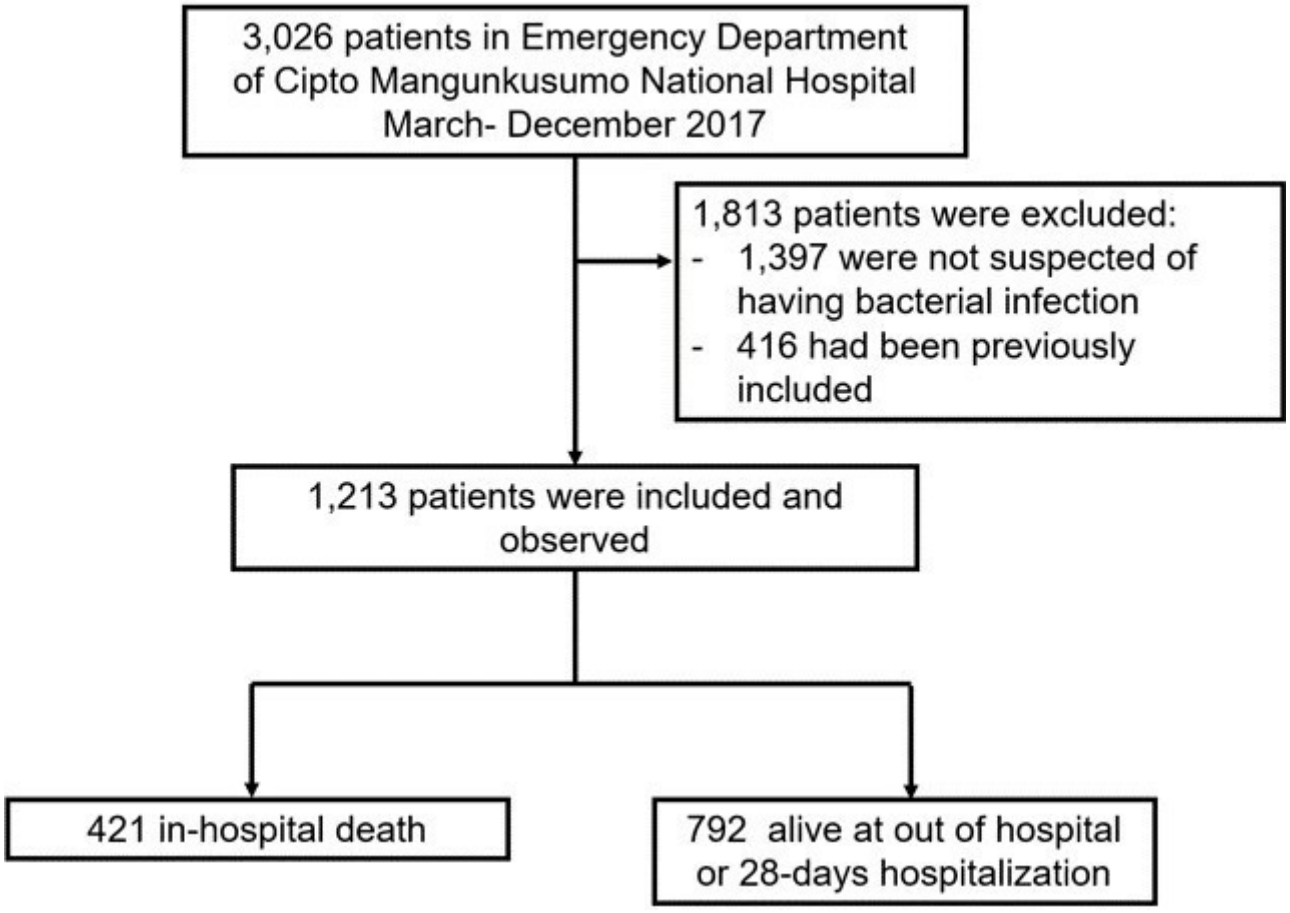

Figure 1 Flow diagram of study.

analyses were two-tailed, and a value of $p<0.05$ was required for statistical significance.

Patient and public involvement

At the beginning of the study the emergency department announcement board was used to inform the public about the research questions and outcome measurements. Patients were not involved in the design of the study. Patients voluntarily participated in the study after patients or their representatives provided informed consent. Results and interpretations of every physical examination, laboratory data and outcome related to this study were explained to patients or their representatives incoordination with the treating physicians. The amount of time required to participate in this study was explained at the beginning of recruitment. The results of the study were disseminated to participants in a short message. Furthermore, dissemination of study results to the public were delivered by a poster attached to the emergency department announcement board.

RESULTS

Patient characteristics

During the recruitment period 3026 patients were screened, and 1813 patients were excluded as they were not suspected to have bacterial infection or had been included the day before. Thus a total of 1213 patients were included and observed for final analysis (figure 1).

The median (IQR) age was 51 (38-60) years and 637 patients (52.5%) were men. The most common findings for comorbidity, site of infection, and organ dysfunction were malignancy (29% of cases), respiratory (66.6% of cases) and renal dysfunction (48.9% of cases), respectively. Baseline characteristics are summarised in table 1. The SIRS criteria were ≥2 in 819 patients (67.5%), the qSOFA criteria were ≥2 in 750 patients (61.8%), and 774 patients (63.8%) had an increment of SOFA score of ≥2. In total 599 patients (49.4%) had a venous lactate concentration >2 mmol/L. Positive qSOFA-lactate criteria (defined as two or more qSOFA criteria and venous lactate concentration >2 mmol/L) were fulfilled by 395 patients (32.1%).

Outcome

The overall in-hospital mortality rate was 34.7% (95% CI 32% to 37.4%). As shown in table 2, in-hospital mortality was increased among patients meeting positive sepsis prognosis criteria compared with those not meeting positive criteria. A SOFA score with an increment of >2 points demonstrated the highest hazard ratio for mortality (HR 8.3, 95% CI 5.9 to 11.6).

Performance of sepsis prognosis criteria

The prognostic performance for each of the criteria are reported in tables 3 and 4. For the prediction of in-hospital mortality, the SOFA score had a sensitivity of 89.3% (95% CI 86.0 to 92.1) and a specificity of 49.8% (95% CI 46.2 to 53.3), while the simplified qSOFA-lactate score had a sensitivity of 72.4% (95% CI 67.9% to 76.6%) and a specificity of 82.1% (95% CI 79.2% to 84.6%).

An ROC curve for the prediction of in-hospital mortality was constructed with the established and proposed sepsis prognosis criteria, namely the SOFA score, qSOFA, qSOFA-lactate, and

Table 1 Patients characteristics

Characteristics	All patients (n=1213)	In-hospital death (n=421)	Alive at out-of-hospital or 28 days hospitalisation (n=792)
Demographic characteristics			
Gender, N (%)			
Men	637 (52.5)	214 (50.8)	423 (53.4)
Women	576 (47.5)	207 (49.2)	369 (46.6)
Age (years), median (IQR)	51 (38–60)	52 (38.5–60.5)	50 (38–60)
Length of hospitalisation (days), median (IQR)	8 (4–15)	4 (2–8)	10 (6–8)
Critical care unit stays of 3 days or longer, N (%)	339 (27.9)	183 (43.5)	156 (19.7)
Clinical characteristics			
Comorbidity, N (%)*			
Chronic heart failure	130 (10.7)	33 (7.8)	97 (12.2)
Chronic obstructive pulmonary disease	21 (1.7)	8 (1.9)	13 (1.6)
Chronic kidney disease	266 (21.9)	102 (24.2)	164 (20.7)
Chronic kidney disease with routine dialysis	56 (4.6)	18 (4.3)	38 (4.8)
Cerebrovascular disease	105 (8.7)	49 (11.6)	56 (7.1)
Liver cirrhosis	71 (5.9)	27 (6.4)	44 (5.6)
Malignancy	352 (29)	163 (38.7)	189 (23.9)
Diabetes mellitus	286 (23.6)	80 (19)	206 (26)
Autoimmune disease	33 (2.7)	13 (3.1)	20 (2.5)
Tuberculosis infection	100 (8.2)	43 (10.2)	57 (7.2)
Site of infection, N (%)†*			
Neurological	61 (5.0)	28 (6.7)	33 (4.2)
Respiratory	808 (66.6)	331 (78.6)	477 (60.2)
Abdominal	210 (17.3)	62 (14.7)	148 (18.7)
Urinary	71 (5.9)	16 (3.8)	55 (6.9)
Skin, soft tissue, bone and joints	247 (20.4)	60 (14.3)	187 (23.6)
Typhoid fever	13 (1.1)	0 (0)	13 (1.6)
Leptospirosis	5 (0.4)	2 (0.5)	3 (0.3)
Source of infection, N (%)‡			
Community	1010 (83.3)	340 (80.8)	670 (84.9)
Nosocomial	213 (16.7)	81 (19.2)	122 (15.1)
Bacterial culture, N (%)§*			
Blood culture	742	206	536
Positive	265 (35.7)	136 (66.0)	129 (24.1)
Negative	477 (64.3)	70 (34.0)	407 (75.9)
Sputum culture	558	263	295
Positive	469 (84.1)	225 (85.6)	244 (82.7)
Negative	89 (15.9)	38 (14.4)	51 (17.3)
Urine culture	69	16	53
Positive	59 (85.5)	14 (87.5)	46 (86.8)
Negative	10 (14.5)	2 (12.5)	7 (13.2)
Wound culture	201	51	150
Positive	174 (86.6)	45 (88.2)	131 (87.3)
Negative	27 (13.4)	6 (11.8)	19 (12.7)
Other (cerebrospinal fluid, pleural fluid, ascites, faeces)	283	93	190
Positive	164 (57.9)	58 (62.4)	106 (55.8)
Negative	119 (42.1)	35 (37.6)	84 (44.2)
SOFA-based organ dysfunction, N (%)*			
Respiration	502 (41,4)	253 (60.1)	249 (31.4)
Liver	225 (18,5)	90 (21.4)	135 (17.0)
Cardiovascular	278 (22.9)	158 (37.5)	120 (15.2)
Central nervous system	415 (34,2)	234 (55.6)	181 (22.9)
Renal	594 (48,9)	227 (54.0)	367 (46.3)
Coagulation	297 (24,5)	111 (26.4)	186 (23.5)
SIRS criteria, median (IQR)	3 (2–4)	3 (2–4)	3 (2–3)
SIRS >2, N (%)	819 (67.5)	358 (85.0)	461 (58.2)
qSOFA criteria, median (IQR)	2 (1–2)	2 (2–3)	2 (1–2)
qSOFA ≥2, N (%)	750 (61.8)	331 (78.6)	419 (52.9)
SOFA score, median (IQR)	4 (1–6)	6 (3–8)	3 (1–5)
Increment SOFA score, median (IQR)	2 (1–5)	4 (3–6)	2 (0–4)
Increment SOFA score ≥2, N (%)	774 (63.8)	376 (89.3)	398 (50.3)
Venous lactate concentration (mmol/L), median (IQR)	1.9 (1.1–3.4)	3.4 (2–5.6)	1.5 (0.8–2.4)
Positive qSOFA-lactate criteria, N (%)	395 (32.5)	235 (55.8)	160 (20.2)

*Patients could be recorded for more than one item in a category.
†Site of infection(s) were determined based on emergency department diagnosis.
‡Patients were categorised as acquiring hospital (nosocomial) infections if patients were transferred to the emergency room from another healthcare facility where he or she was admitted for ≥2 calendar days. Patients who did not fulfil that criteria were categorised as acquiring community infections (including those who were cared for at outpatient clinics).[25]
§Contaminated samples were not included.
qSOFA, quick Sequential Organ Failure Assessment; SIRS, systemic inflammatory response syndrome; SOFA, Sequential Organ Failure Assessment.

SIRS criteria (figure 2 and table 4). The highest AUROC was seen in the SOFA score (0.75, 95% CI 0.72 to 0.78) and the lowest AUROC was seen in the SIRS criteria (0.57, 95% CI 0.54 to 0.6). Addition of lactate criteria to positive qSOFA criteria significantly increased its prognostic performance (p=0.006 compared with qSOFA criteria) to 0.74 (95% CI 0.71 to 0.77). The performance of this new simplified prognosis criteria was statistically similar to sepsis-3 criteria (p=0.462).

DISCUSSION

This was the first study in Indonesia to prospectively determine the performance comparison of the SOFA score and the qSOFA criteria with the addition of lactate criteria to identify adult patients with suspected bacterial infection with higher risk of in-hospital mortality. The recommendation of using an increment of SOFA score is challenged by the routine laboratory tests required; thus, simplified prognosis criteria using more affordable parameters in hospitals with limited resources, that is, physical examination data and lactate measured by point of care test, are warranted. This study demonstrated that when used as a prognosis criterion in an Indonesian emergency department, the simplified criteria using the qSOFA-lactate criteria performs similar to the SOFA score.

Compared with the derivation and validation cohort of sepsis-3 criteria, patients included in our cohort showed a higher degree of infection severity. The median SIRS, qSOFA and SOFA scores in this study were 3, 2 and 4, respectively. These medians are higher than the medians of derivation and validation cohort of sepsis-3 criteria and a validation study reported in an emergency department in Australia.[13 17] The derivation and validation cohort of the sepsis-3 study reported medians of SIRS and SOFA scores in a non-intensive care unit (ICU) population of 1 and 1, respectively, while the ICU population had a median SIRS of 3 and a median SOFA score of 6.[13] In addition, the higher degree of severity was also confirmed by the lactate concentration seen in patients in this study. The median venous lactate concentration was 1.9 mmol/L, referring to nearly 50% of patients having a lactate concentration >2 mmol/L. On the other hand, the derivation and validation cohort of sepsis-3 criteria patients showed a lower percentage of lactate concentration >2 mmol/L, that is, 21% and 2% in ICU and non-ICU patients, respectively.[13] The higher proportion of positive blood cultures in this study when compared with other studies further reflects the higher degree of infection severity in our patients.[18]

In the present study, the SOFA score demonstrated significantly better prognostic performance when compared with qSOFA

Table 2 Mortality according to sepsis prognosis criteria

	SOFA		qSOFA		qSOFA-lactate		SIRS	
Prognosis criteria	**≥2 (n=774)**	**<2 (n=439)**	**≥2 (n=750)**	**<2 (n=463)**	**Yes (n=395)**	**No (n=818)**	**≥2 (n=819)**	**<2 (n=394)**
In-hospital mortality	376 (48.6)	45 (10.3)	331 (44.1)	90 (19.4)	235 (59.5)	186 (22.7)	358 (43.7)	63 (15.9)
Hazard ratio (%) (95% CI)*	8.3 (5.9 to 11.6)		3.3 (2.5 to 4.3)		5.8 (4.4 to 7.5)		2.9 (1.7 to 5.4)	

*Group of patients not meeting positive sepsis prognosis criteria was used as reference.
qSOFA, quick Sequential Organ Failure Assessment; SIRS, systemic inflammatory response syndrome; SOFA, Sequential Organ Failure Assessment.

criteria in the non-ICU population. This finding contrasted with the derivation and validation cohort of the sepsis-3 criteria, and with several other reported validation studies. The derivation and initial external datasets validation cohort showed a significantly better performance of qSOFA criteria compared with SOFA score (0.81, 95% CI 0.80 to 0.82 vs 0.79, 95% CI 0.78 to 0.80) in the non-ICU population.[13 19] The lower performance of qSOFA was similar to results of previous published validation studies in LMICs.[5 7] The higher degree of infection severity may explain this finding. In populations with a higher mortality rate, a more detailed criteria is required for more accurate outcome prediction.[20] In addition, the most common organ dysfunction for patients in this study was renal dysfunction (48.9%), the parameter of which is not covered by the qSOFA criteria. A previous study concluded that renal dysfunction is the second strongest independent predictor of outcome when compared with other organ dysfunctions.[21]

The performance of qSOFA is significantly improved by the addition of venous lactate criteria. This study demonstrated an optimal cut-off for lactate concentration of 2 mmol/L, which is in accordance with data from the derivation cohort of the sepsis-3 criteria.[13] Simplified criteria using the fulfilment of two or more qSOFA criteria and venous lactate concentration >2 mmol/L had an AUROC comparable with criteria using an increment of 2 or higher SOFA score and is also significantly better than SIRS criteria. Lactate is a well-known metabolic indicator of microcirculation and cellular stress, and has shown a strong correlation with mortality level in critically ill patients, including those with sepsis.[8–10] Abnormal liver and kidney function in septic patients contributes to increased lactate levels; thus, indirectly, lactate can also be used as a coarse indicator of organ dysfunction.[22] Venous lactate has no significant difference with arterial lactate and is not interfered by the use of a tourniquet.[23] Moreover, the measurement of venous lactate using a point of care portable analyzer has proved to be a simple, rapid and accurate method.[12]

Although qSOFA-lactate criteria showed similar AUROC with SOFA score, they demonstrated lower sensitivity and better specificity (table 3). As a prognosis criteria, better specificity is a desirable property, although in diseases with high rates of mortality such as sepsis, sensitivity is considered important as well.[24] As can be seen in the present study, mortality was predicted in only 31.1% of patients by the qSOFA-lactate criteria, compared with 63.8% of patients by the SOFA score. The smaller population categorised as a group with a higher risk of mortality will potentially lead to an increase in more focused intensive clinical care in this population.

Contrary to the derivation and validation cohort of the sepsis-3 criteria study, the present study has several strengths. First, this study was carried out prospectively in an emergency department, thus enabling the measurement of venous lactate concentration and SOFA score components universally in every patient to assess the prognostic performance of venous lactate concentration and increment SOFA score without missing values. This study was also the first to report prospective external validation of the prognostic accuracy of SOFA score and qSOFA criteria in an LMIC in Asia and included a large sample size and proportional outcomes, ensuring adequate power. Another strength of this study was the affordable use of point-of-care testing for the measurement of venous lactate concentration, encouraging applicability in a hospital with limited resources.

Table 3 Performance of sepsis prognosis criteria

Prognosis criteria	SOFA	qSOFA	qSOFA-lactate	SIRS
Sensitivity (%) (95% CI)	89.3 (86.0 to 92.1)	78.6 (74.4 to 82.4)	55.8 (50.9 to 60.6)	92.6 (89.7 to 94.9)
Specificity (%) (95% CI)	49.8 (46.2 to 53.3)	47.1 (43.6 to 50.6)	82.1 (79.2 to 84.6)	11.9 (9.7 to 14.3)
PPV (%) (95% CI)	48.6 (45 to 52.2)	44.1 (40.6 to 47.7)	62.3 (57.2 to 67.2)	35.9 (35.0 to 36.7)
NPV (%) (95% CI)	89.7 (86.4 to 92.3)	80.6 (76.6 to 84)	77.5 (74.7 to 80.5)	75.2 (67.3 to 81.7)

NPV, negative predictive value; PPV, positive predictive value; qSOFA, quick Sequential Organ Failure Assessment; SIRS, systemic inflammatory response syndrome; SOFA, Sequential Organ Failure Assessment.

Table 4 Area under the receiver operating characteristic curve (95% CI) for in-hospital mortality of sepsis prognosis criteria

	SOFA	qSOFA	qSOFA-lactate	SIRS
SOFA	0.75 (0.72 to 0.78)	0.05 (0.02 to 0.08)	0.01 (0.01 to 0.02)	0.18 (0.14 to 0.22)
qSOFA	0.002	0.70 (0.67 to 0.74)	0.04 (0.01 to 0.07)	0.13 (0.09 to 0.17)
qSOFA-lactate	0.462	0.006	0.74 (0.71 to 0.77)	0.17 (0.13 to 0.21)
SIRS	<0.001	<0.001	<0.001	0.57 (0.54 to 0.60)

The data in the dark grey-shaded diagonal cells indicate the AUROC (95% CI) for each diagnosis criteria. Below the AUROC data cells are p values for comparisons between criteria, while above the AUROC data cells are AUROC differences (95% CI).
AUROC, area under the receiver operating characteristic curve; qSOFA, quick Sequential Organ Failure Assessment; SIRS, systemic inflammatory response syndrome; SOFA, Sequential Organ Failure Assessment.

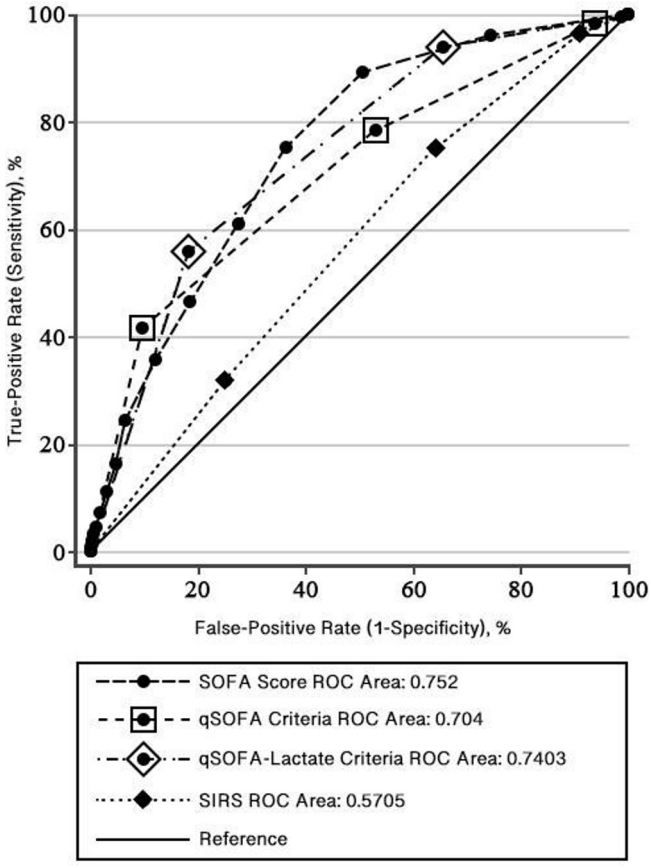

Figure 2 Receiver operating characteristic curve for in-hospital mortality of sepsis prognosis criteria. ROC, receiving operating characteristic; SIRS, systemic inflammatory response syndrome; SOFA, Sequential Organ Failure Assessment; qSOFA, quick Sequential Organ Failure Assessment.

This study had some limitations. First, we included patients with suspected infection and did not follow the final diagnosis of infection. Second, the increment of the SOFA score was determined based on subtraction of the current SOFA score from the baseline SOFA score derived from history-taking, past diagnosis, and clinical and laboratory data (if available) for patients found in the hospital's medical record system. Unknown past medical history and laboratory data could potentially lead to bias in the increment of SOFA score calculation. However, these two limitations are some of the real-life problems which are faced by physicians in daily practice, therefore making the results of this study applicable to daily clinical practice in hospital emergency departments of LMICs.

Thirdly, although this study was conducted in Indonesia, which is a tropical country, rates of the tropical infectious diseases which were included were low (1.1% typhoid fever and 0.4% leptospirosis). Furthermore, the two major tropical non-bacterial infections that are treated without antibiotic use, dengue infection and malaria, did not meet the inclusion criteria and hence were not included in the present study. The study was conducted in a national referral hospital in Indonesia. According to Indonesian regulations, restricted referral to our hospital was indicated in complicated cases or in the presence of multi-organ failure requiring comprehensive care and consultations from sub-specialties. Patients with uncomplicated tropical infectious diseases should be managed in city or provincial hospitals. Thus, the result of our study is more applicable for potential generalisation in non-tropical infectious diseases. Further similar studies in various tropical infection patients are needed for potential generalisation in emergency departments of LMIC country hospitals mainly managing tropical infections. In addition, this study included adult patients only and therefore did not evaluate the prognostic accuracy of sepsis diagnosis criteria in paediatrics. Future multicentre research on the impact of the use of this simplified sepsis prognosis criteria in hospitals with limited resources is warranted.

CONCLUSIONS

When used as sepsis prognosis criteria in emergency departments of hospitals with limited resources, the simplified qSOFA-lactate criteria perform as well as the SOFA score. The prognostic performance of the qSOFA is significantly lower than the qSOFA-lactate criteria and SOFA score.

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