Original Article

Accuracy of qSOFA for the diagnosis of sepsis-3: a secondary analysis of a population-based cohort study

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Background: We aimed to evaluate the accuracy of quick Sequential (sepsis-related) Organ Failure Assessment (qSOFA) for the diagnosis of sepsis-3, and to analyze the prognosis of infected patients in wards over-diagnosed with qSOFA but missed by sepsis-3, and those missed by qSOFA but in accordance with sepsis-3 criteria. We also intended to validate the performance of qSOFA as one predictor of outcome in patients with suspicion of infection.

Methods: We reviewed the medical records of 1,716 adult patients with infection who were hospitalized from July 1st, 2012 to June 30th, 2014 in the Yuetan subdistrict of Beijing, China. Based on the sepsis-3 criteria and qSOFA score proposed by the Third International Consensus Definitions for Sepsis and Septic Shock, these patients were categorized into four groups: qSOFA(–)sepsis(–), qSOFA(+)sepsis(–), qSOFA(–)sepsis(+), and qSOFA(+)sepsis(+). Multivariate logistic regression analysis was used to determine the independent risk factors for in-hospital mortality. The area under the receiver operating characteristic curves (AUROCs) of the qSOFA(+) group were compared with the sepsis(+) group for in-hospital mortality, ICU admission, and invasive ventilation.

Results: Among the 1,716 patients with infection, there were 935 patients (54.5%) with sepsis, and 640 patients (37.3%) with qSOFA ≥2. There were 610 patients in the qSOFA(–)sepsis(–) group, 171 in the qSOFA(+)sepsis(–) group, 466 in the qSOFA(–)sepsis(+) group, and 469 in the qSOFA(+)sepsis(+) group. In the logistic regression analysis, increasing age, bedridden status, and malignancy were all independent risk factors of hospital mortality. Sepsis and qSOFA ≥2 were also independent risk factors of hospital mortality, with an adjusted OR of 3.85 (95% CI: 2.70–5.50) and 13.92 (95% CI: 9.87–16.93) respectively. qSOFA had a sensitivity of 50.2% and a specificity of 78.1% for sepsis-3. The false-positive [qSOFA(+)sepsis(–)] group had 38 patients (22.2%) die during hospitalization, and an adjusted OR of 9.20 (95% CI: 4.86–17.38). In addition, the false-negative [qSOFA(–)sepsis(+)] group had a hospital mortality rate of 7.3% (34/466) and an adjusted OR of 2.59 (95% CI: 1.39–4.83). In comparison, patients meeting neither qSOFA nor sepsis criteria had the lowest hospital mortality [2.6% (16/610)], whereas patients with both qSOFA ≥2 and sepsis had the highest hospital mortality [56.5% (265/469)], with an adjusted OR of 42.02 (95% CI: 24.31–72.64). The discrimination of in-hospital mortality using qSOFA (AUROC, 0.846; 95% CI, 0.824–0.868) was greater compared with sepsis-3 criteria (AUROC, 0.834; 95% CI, 0.805–0.863; P<0.001).

Conclusions: In our analysis, the sensitivity(Se) of qSOFA for the diagnosis of sepsis was lower, and qSOFA score ≥2 might identify a group of patients at a higher risk of mortality, regardless of being septic or not.

Keywords: Sequential (sepsis-related) Organ Failure Assessment (SOFA); quick Sequential Organ Failure Assessment (qSOFA) score; sepsis-3; mortality; the area under the receiver operating characteristic curves (AUROCs)

Submitted Jan 09, 2019. Accepted for publication Apr 17, 2019.
doi: 10.21037/jtd.2019.04.90
View this article at: http://dx.doi.org/10.21037/jtd.2019.04.90

Introduction

In 1991, sepsis was defined as systemic inflammatory response syndrome (SIRS) induced by infection (1). After more than two decades of widespread use in clinical practice and research, it is now well understood that both pro- and anti-inflammatory responses are involved in the pathogenesis of sepsis (2). Moreover, SIRS criteria are too sensitive and insufficiently specific to identify some severely infected patients (3,4). In 2001, the definitions of sepsis and septic shock were revised (5), incorporating the concept and diagnostic criteria of organ damage. However, owing to its complexity, the 2001 definition of sepsis has not been widely applied in clinical practice. In 2016, the Third International Consensus Definitions for Sepsis and Septic Shock Task Force (Sepsis-3) redefined sepsis as a "life-threatening organ dysfunction caused by a dysregulated host response to infection" (6). Organ dysfunction was defined as an acute increase in total Sequential (sepsis-related) Organ Failure Assessment (SOFA) score ≥2 points consequent to the infection. Because the components of SOFA were too complex and required multiple laboratory tests that might be impractical in daily clinical practice, the Task Force proposed a quick SOFA (qSOFA) score to facilitate easier identification of patients who were potentially at risk of dying from sepsis (6). The qSOFA score consists of only three criteria: Glasgow Coma Scale (GCS) <15, systolic blood pressure ≤ 100 mmHg, and respiratory rate ≥22/min. A qSOFA score of 2 or more points indicates organ dysfunction with predictive validity similar to that of the full SOFA score outside the intensive care unit (ICU) (7).

Since the definition of the new criteria was published, there have been controversies over the predictive values of qSOFA criteria in the diagnosis of sepsis-3 (8-13). Both retrospective studies and meta-analyses have demonstrated low sensitivity and high specificity of qSOFA score in the diagnosis of sepsis-3 (13-17). However, data concerning the prognosis of infected patients misdiagnosed by qSOFA score are still lacking (18). Based on a secondary analysis of a database of all hospitalized patients living in a subdistrict of Beijing, we performed the current study to investigate the predictive value of qSOFA score for sepsis-3, the clinical outcome of septic patients who are missed by the qSOFA score (false-negatives), and the clinical outcome of nonseptic patients who are misdiagnosed as sepsis-3 by the qSOFA score (false-positives).

Methods

The methodology of the current study has been previously reported in detail (19). In brief, this was a retrospective cohort study of all adult (≥18 years) residents of the Yuetan subdistrict of Beijing, China, who were hospitalized from July 1st, 2012, to June 30th, 2014. These patients were identified with the use of the hospital discharge database of the Beijing Public Health Information System. All available medical records of enrolled patients were manually reviewed independently by any two of three investigators, all who had more than 5 years of working experience in the ICU. Any disagreement was resolved by discussion among the three investigators, and then among the steering committee (XM, YA, and BD) if consensus could not be reached.

Retrieved data included demographic data, admission category (medical, elective surgery or emergency surgery), comorbidities (20), and in-hospital mortality. Derived from the above data, the severity of underlying illness was assessed by McCabe and Jackson classification (21), while chronic organ dysfunction or immunosuppression was defined based on the criteria from the Acute Physiology and Chronic Health Evaluation (APACHE) II score (22). In addition, body mass index (BMI) was calculated based on the height and weight on hospital admission.

For patients with infection, we collected data about the

source of infection, relevant microbiological information, ICU admission, ICU length of stay, and all data necessary for the calculation of SOFA and qSOFA scores (6,23). For the purpose of this study, infection was diagnosed based on clinical manifestations, laboratory tests, and radiographic findings, including microbiologically documented (with definite positive results of microbial culture of body fluids or blood) and clinically documented (with no definite positive culture results but with imaging or pathological evidence of clinical infection) infections (24). Regardless of admission or discharge diagnoses, we identified cases with infection based on manual review of clinical manifestations, in addition to laboratory, imaging, and microbiologic parameters.

For patients with infection, we calculated maximum SOFA and qSOFA scores based on retrieved clinical data until 72 hours after hospital admission (for those who were admitted due to infection) or onset of infection (for those who developed infection during hospitalization). Sepsis was diagnosed as an acute change in total SOFA score ≥2 points consequent to the infection, according to the Third International Consensus Definitions for Sepsis and Septic Shock [6]. In addition, a patient meeting at least 2 of the 3 criteria of qSOFA score was deemed as qSOFA(+) [6].

Univariate and multivariate logistic regression analyses were used to identify independent risk factors associated with in-hospital mortality, such as age and chronic comorbidities. All potential risk factors were added into the model using stepwise conditional backward entry, if $P<0.1$ in univariate analysis. Age was categorized in three categories (18–64, 65–84, and ≥85 years) (25,26), because the assumption of linearity would be violated if age was included in the model as a continuous variable. The prognostic value of qSOFA and sepsis was also assessed by the area under the receiver operating characteristic curve (AUROC).

In order to delineate the performance of qSOFA for the diagnosis of sepsis, we calculated sensitivity and specificity. Moreover, clinical outcomes of those patients misdiagnosed by qSOFA score, including overdiagnosis (false-positives) and underdiagnosis (false-negatives), were also compared with adjusted odds ratio (OR).

Continuous variables were presented as median and interquartile range (IQR). Categorical variables were presented as a percentage of the group from which they were derived, and compared by the use of chi-square test or Fisher's exact test. All comparisons were unpaired and all tests of significance were two-tailed. A P value <0.05 was considered as statistically significant.

Ethical approval

This study was approved by the ethics committee of Peking Union Medical College Hospital and informed consent was waived. This study was registered at ClinicalTrials.gov, with registration number NCT02285257.

Results

Patient enrollment

During the 2-year study period, a total of 22,552 adult residents in the Yuetan subdistrict were hospitalized, among whom 21,191 had their medical records manually reviewed. We were not able to review the medical records of the other 1,361 patients due to missing records (n=277), and refusal by the hospitals (n=1,084).

Out of the 21,191 adult patients, 1,716 infected patients with complete results of physical examination and laboratory examination required for the diagnosis of sepsis and calculation of qSOFA score were enrolled in this study.

Patient characteristics

Among 1,716 patients with infection, there were 935 patients (54.5%) with sepsis, 640 patients (37.3%) with qSOFA ≥2, and 610 patients (35.5%) meeting neither of the above criteria. Compared with patients without sepsis, patients with sepsis were older, more likely to be male, and had more comorbidities and chronic organ dysfunction. In addition, patients with sepsis were more likely to have lower respiratory tract infections, with more severe acute illness (as shown by more ICU admissions, more acute organ failures including septic shock and respiratory failure, higher mortality, and longer length of stay). Similar findings were also reported when patients with qSOFA ≥2 were compared with those with qSOFA <2 (*Table 1*).

Performance of qSOFA for the diagnosis of sepsis

Among the 935 patients with sepsis, 469 (50.2%) met qSOFA criteria (qSOFA ≥2), whereas 171 (21.9%) out of 781 patients without sepsis also had qSOFA ≥2 (*Table 2*). As a result, for the diagnosis of sepsis, qSOFA criteria had a sensitivity of 50.2%, specificity of 78.1%, positive predictive value of 73.3%, and a negative predictive value of 56.7%.

Table 1 Characteristics of patients with infection, categorized by the presence or absence of qSOFA and sepsis criteria

Characteristics	qSOFA(–) (n=1,076)	qSOFA(+) (n=640)	Sepsis(–) (n=781)	Sepsis(+) (n=935)
Age, year, median [IQR]	79 [61–85]	82 [74–86]**	78 [57–84]	81 [74–86]‡
Male sex, n (%)	613 (57.0)	375 (58.6)	414 (53.0)	574 (61.4)‡
Body mass index (BMI), kg/m^2, median [IQR]	24 [21–26]	22 [19–25]**	24 [21–26]	23 [20–26]†
Type of hospital admission, n (%)				
Medical	970 (90.1)	583 (91.1)	691 (88.5)	862 (92.2)‡
Elective surgery	93 (8.6)	35 (5.5)*	75 (9.6)	53 (5.7)‡
Emergency surgery	13 (1.2)	22 (3.4)**	15 (1.9)	20 (2.1)†
McCabe and Jackson classification, n (%)				
Nonfatal	762 (70.8)	448 (70.0)	524 (67.1)	686 (73.4)‡
Ultimately fatal	164 (15.2)	125 (19.5)*	112 (14.3)	177 (18.9)†
Rapidly fatal	17 (1.6)	28 (4.4)**	22 (2.8)	23 (2.5)
Charlson comorbidity index, median [IQR]	1 [1–3]	2 [1–3]**	1 [0–3]	2 [1–3]‡
Comorbidities, n (%)				
None	176 (16.4)	68 (10.6)*	162 (20.7)	82 (8.8)‡
Hypertension	579 (53.8)	371 (58.0)	395 (50.6)	555 (59.4)‡
Diabetes	256 (23.8)	198 (30.9)**	206 (26.4)	248 (26.5)
Malignancy	188 (17.5)	86 (13.4)*	124 (15.9)	150 (16.0)
Cerebrovascular disease	394 (36.6)	237 (37.0)	273 (35.0)	358 (38.3)‡
Coronary heart disease	315 (29.3)	235 (36.7)**	206 (26.4)	344 (36.8)‡
Chronic lung disease	235 (21.8)	150 (23.4)	150 (19.2)	235 (25.1)‡
Peptic ulcer	112 (10.4)	36 (5.6)**	87 (11.1)	61 (6.5)‡
Rheumatic disease	43 (4.0)	23 (3.6)	19 (2.4)	47 (5.0)‡
Hematologic malignancy	18 (1.7)	14 (2.2)	7 (0.9)	25 (2.7)‡
Dementia	81 (7.5)	42 (6.6)	33 (4.2)	90 (9.6)‡
Chronic organ dysfunction, n (%)				
None	889 (82.6)	477 (74.5)**	659 (84.4)	707 (75.6)‡
Cardiovascular	13 (1.2)	24 (3.8)**	8 (1.0)	29 (3.1)‡
Liver	23 (2.1)	9 (1.4)	13 (1.7)	19 (2.0)
Respiratory	42 (3.9)	65 (10.2)**	42 (5.4)	65 (7.0)
Renal	36 (3.3)	19 (3.0)	10 (1.3)	45 (4.8)‡
Immunosuppression	86 (8.0)	65 (10.2)	62 (7.9)	89 (9.5)
Site of infection, n (%)				
Lower respiratory tract infection	724 (67.3)	524 (81.9)**	518 (66.3)	730 (78.1)‡
Urogenital tract infection	104 (9.7)	49 (7.7)	102 (13.1)	51 (5.5)‡
Intra-abdominal infection	83 (7.7)	52 (8.1)	55 (7.0)	80 (8.6)
Upper respiratory infection	51 (4.7)	5 (0.8)**	32 (4.1)	24 (2.6)
Gastroenteritis	50 (4.6)	18 (2.8)	38 (4.9)	30 (3.2)
Skin and soft tissue infection	29 (2.7)	3 (0.5)**	26 (3.3)	6 (0.6)‡
Bacteremia	42 (3.9)	42 (6.6)*	36 (4.6)	48 (5.1)
Other	44 (4.1)	20 (3.1)	31 (4.0)	33 (3.5)

Table 1 (*continued*)

Table 1 (*continued*)

Characteristics	qSOFA(–) (n=1,076)	qSOFA(+) (n=640)	Sepsis(–) (n=781)	Sepsis(+) (n=935)
Positive cultures, n (%)	286 (26.6)	343 (53.6)**	250 (32.0)	379 (40.5)‡
Invasive ventilation, n (%)	26 (2.4)	203 (31.7)**	17 (2.2)	212 (22.7)‡
ICU admission, n (%)	44 (4.1)	184 (28.8)**	5 (0.6)	223 (23.9)‡
Septic shock, n (%)	56 (5.2)	261(40.8)**	0 (0.0)	317 (33.9)‡
Hospital length of stay, median [IQR]	16 [9–28]	25 [12–43]**	17 [9–29]	20 [11–38]
In-hospital mortality, n (%)	50 (4.6)	303 (47.3)**	54 (6.0)	299 (32.0)‡

*P<0.05, **P<0.01, compared with qSOFA(–); †P<0.05, ‡P<0.01, compared with sepsis(–).

Clinical outcome of patients with infection stratified by sepsis and qSOFA criteria

A total of 353 patients (20.6%) died before hospital discharge. In logistic regression analysis, increasing age, bedridden status, and malignancy were all independent risk factors of hospital mortality. Including age as a continuous variable or intertertile range in the logistic regression model did not change the results (*Tables S1*,*S2*). Moreover, sepsis and qSOFA ≥2 were also independent risk factors of hospital mortality, with an adjusted OR of 3.85 (95% CI: 2.70–5.50) and 13.92 (95% CI: 9.87–19.63) respectively (*Table 3*). The qSOFA and sepsis criteria had similar prognostic value, with an AUROC of 0.846 (95% CI, 0.824–0.868) and 0.834 (95% CI, 0.805–0.863) respectively (*Table 4*).

The false-positive group comprised 171 patients (SOFA ≥2) among whom 38 (22.2%) died during hospitalization, and had an adjusted OR of 9.20 (95% CI: 4.86–17.38). In addition, the false-negative group comprised 466 patients (qSOFA <2, met sepsis criteria), with a hospital mortality rate of 7.3% (34/466), and an adjusted OR of 2.59 (95% CI: 1.39–4.83). In comparison, patients meeting neither qSOFA nor sepsis criteria had the lowest hospital mortality [2.6% (16/610)], whereas patients with both qSOFA ≥2 and sepsis had the highest hospital mortality [56.5% (265/469)], with adjusted OR of 42.02 (95% CI: 24.31–72.64) (*Table 3*).

Discussion

When qSOFA score was used as a screening tool in the non-ICU setting, it had a sensitivity of 50.2%, and a specificity of 78.1% for the diagnosis of sepsis-3. In addition, both nonseptic patients with qSOFA ≥2 [false positives, or qSOFA(+)sepsis(–) group in our study] and septic patients with qSOFA <2 [false negatives, or qSOFA(–)sepsis(+) group in our study] had a significantly higher mortality than patients meeting neither criteria.

Previous studies reported an even lower sensitivity of qSOFA score to detect sepsis (13-15). For example, both Guirgis and Szakmany collected vital signs and laboratory data during the first 24 hours of admission to calculate SOFA and qSOFA scores, and reported a sensitivity of 16% and 18.4% respectively (13,15). Likewise, Williams and colleagues recorded the most abnormal values in the emergency department, and found that qSOFA score had poor sensitivity (29.7%) for organ dysfunction, i.e., sepsis (13). In comparison, we used the maximum qSOFA score within 72 hours after onset of infection, and also reported an unsatisfactory, albeit higher, sensitivity of 50.2%, which was consistent with those in the two recent meta-analyses (14,17). The low sensitivity of qSOFA score in the diagnosis of sepsis might raise serious concerns. The validity of qSOFA score as a screening tool for sepsis should be re-evaluated (16), because a high sensitivity should be a prerequisite for any screening tool, which would trigger extensive workup to search for evidence of infection-induced organ dysfunction, i.e., sepsis. In fact, such a low sensitivity of qSOFA suggests that it would miss about half of the patients with sepsis (false-negatives), precluding detection of these patients who are at higher risk of death (adjusted OR 2.59) until development of overt organ failure.

In the meanwhile, those patients fulfilling qSOFA but not sepsis criteria (false positives) also had a significantly higher mortality (adjusted OR 9.20). Previous studies reported the presence of shock and multiple organ failure (including altered mental status) as independent risk factors for mortality in cohorts of patients with sepsis (27,28). As a result, for any patients with infection and qSOFA score ≥2, regardless of sepsis diagnosis or not, clinicians should start supportive therapy as soon as possible, as well as further investigation of sepsis or other etiologies.

Table 2 Characteristics of patients with infection categorized by qSOFA and sepsis

Characteristics	qSOFA(–)Sepsis(–) (n=610)	qSOFA(+)Sepsis(–) (n=171)	qSOFA(–)Sepsis(+) (n=466)	qSOFA(+)Sepsis(+) (n=469)
Age, year, median [IQR]	76.5 [56–84]	81 [68.5–85]**,‡	81 [73–85]**,†	82 [75–87]**
Male sex, n (%)	326 (53.4)	88 (51.5)†	287 (61.6)**	287 (61.2)*
Body mass index (BMI), kg/m^2, median [IQR]	24 [21–27]	21 [19–24]**	23 [21–26]	23 [19–25]**
Type of hospital admission, n (%)				
Medical	533 (87.4)	158 (92.4)	437 (93.8)**	425 (90.6)
Elective surgery	68 (11.1)	7 (4.1)**	25 (5.4)**	28 (6.0)**
Emergency surgery	9 (1.5)	6 (3.5)	4 (0.9)‡	16 (3.4)*
McCabe and Jackson classification, n (%)				
Nonfatal	405 (66.4)	119 (69.6)	357 (76.6)**,†	329 (70.1)
Ultimately fatal	91 (14.9)	21 (12.3)‡	73 (15.7)†	104 (22.2)**
Rapidly fatal	10 (1.6)	12 (7.0)**,†	7 (1.5)	16 (3.4)
Charlson comorbidity index, median [IQR]	1 [0–3]	2 [1–3]*	2 [1–3]*,†	2 [1–3]**
Comorbidities, n (%)				
None	139 (22.8)	23 (13.5)**	37 (7.9)**	45 (9.7)**
Hypertension	305 (50.0)	90 (52.6)	274 (58.4)**	281 (60.3)**
Diabetes	159 (26.1)	47 (27.5)	97 (20.7)*,‡	151 (32.4)*
Malignancy	93 (15.2)	31 (18.1)†	95 (20.3)*,‡	55 (11.8)
Cerebrovascular disease	196 (32.1)	77 (45.0)**,†	198 (42.2)**,‡	160 (34.3)
Coronary heart disease	144 (23.6)	62 (36.3)**	171 (36.5)**	173 (37.1)**
Chronic lung disease	117 (19.2)	33 (19.3)	118 (25.2)*	117 (25.1)*
Peptic ulcer	71 (11.6)	16 (9.4)†	41 (8.7)‡	20 (4.3)**
Rheumatic disease	17 (2.8)	2 (1.2)†	26 (5.5)*	21 (4.5)
Hematologic malignancy	7 (1.1)	0 (0)†	11 (2.3)	14 (3.0)*
Dementia	32 (5.2)	1 (0.6)**,‡	49 (10.4)**	41 (8.8)*
Chronic organ dysfunction, n (%)				
None	525 (86.1)	134 (78.4)	364 (78.1)	343 (73.1)**
Cardiovascular	4 (0.7)	4 (2.3)	9 (1.9)†	20 (4.3)**
Liver	11 (1.8)	2 (1.2)	12 (2.6)	7 (1.5)
Respiratory	22 (3.6)	20 (11.7)**,‡	20 (4.3)‡	45 (9.6)**
Renal	10 (1.6)	0 (0)	26 (5.6)**	19 (4.1)*
Immunosuppression	45 (7.4)	17 (10.0)	41 (8.8)	48 (10.2)
Site of infection, n (%)				
Lower respiratory tract infection	382 (62.6)	136 (79.5)**	342 (73.4)**,‡	388 (82.7)**
Urogenital tract infection	72 (11.8)	30 (17.5)*,‡	32 (6.9)**	19 (4.1)**
Intra-abdominal infection	44 (7.2)	11 (6.4)	39 (8.4)	41 (8.7)
Upper respiratory infection	29 (4.8)	3 (1.8)	22 (4.7)‡	2 (0.4)**
Gastroenteritis	36 (5.9)	2 (1.2)*	14 (3.0)	16 (3.4)
Skin and soft tissue infection	24 (3.9)	2 (1.2)	5 (1.1)**	1 (0.2)**
Bacteremia	30 (4.9)	6 (3.5)	12 (2.6)*,‡	36 (7.7)
Other	25 (4.6)	6 (3.5)	19 (4.1)	14 (3.0)

Table 2 (*continued*)

Table 2 (*continued*)

Characteristics	qSOFA(–)Sepsis(–) (n=610)	qSOFA(+)Sepsis(–) (n=171)	qSOFA(–)Sepsis(+) (n=466)	qSOFA(+)Sepsis(+) (n=469)
Positive cultures, n (%)	168 (27.5)	82 (48.0)**	118 (25.3)‡	261 (55.7)**
Invasive ventilation, n (%)	8 (1.3)	9 (5.3)**,‡	18 (3.9)**,‡	194 (41.4)**
ICU admission, n (%)	4 (0.7)	1 (0.6)‡	40 (8.6)**,‡	183 (39.0)**
Septic shock, n (%)	0 (0)	0 (0)	56 (12.0)‡	261 (55.7)
Hospital length of stay, median [IQR]	16 [9–27]	27 [15–40]	17 [10–29]	24 [12–45]*
In-hospital mortality, n (%)	16 (2.6)	38 (22.2)**,‡	34 (7.3)**,‡	265 (56.5)**

*P<0.05, **P<0.01, compared with qSOFA(–)sepsis(–); †P<0.05, ‡P<0.01, compared with qSOFA(+)sepsis(+).

Table 3 Risk factors of in-hospital mortality in patients with infection, by univariate and multivariate regression analysis

Variables	Control	Case	Model 1		Model 2	
			Crude OR (95% CI)	Adjusted OR[a] (95% CI)	Crude OR (95% CI)	Adjusted OR[a] (95% CI)
Age groups (years), n						
18–64	381	25	1.00 (ref)	1.00 (ref)	1.00 (Ref)	1.00 (Ref)
65–84	633	189	4.55 (2.94–7.04)	3.21 (1.91–5.40)	4.55 (2.94–7.04)	3.22 (1.91–5.43)
≥85	349	139	6.07 (3.87–9.52)	3.86 (2.22–6.71)	6.07 (3.87–9.52)	3.86 (2.21–6.71)
BMI (kg/m^2), n						
18.5–24.9	390	56	1.00 (ref)	1.00 (ref)	1.00 (ref)	1.00 (ref)
<18.5	90	29	2.24 (1.36–3.71)	1.72 (0.91–3.25)	2.24 (1.36–3.71)	1.76 (0.93–3.34)
>24.9	229	32	0.97 (0.61–1.55)	1.29 (0.72–2.30)	0.97 (0.61–1.55)	1.28 (0.71–2.28)
Bedridden[b]	654	236	2.51 (1.83–3.45)	1.63 (1.08–2.45)	2.51 (1.83–3.45)	1.65 (1.10–2.49)
Comorbidities, n						
Hypertension	730	220	1.43 (1.13–1.82)			
Chronic heart disease	409	141	1.44 (1.14–1.83)		1.44 (1.14–1.83)	
Chronic kidney disease	53	25	1.88 (1.15–3.08)		1.88 (1.15–3.08)	
Malignancy	175	99	2.65 (2.00–3.51)	3.72 (2.55–5.45)	2.65 (2.00–3.51)	3.71 (2.53–5.42)
Groups, n						
Sepsis (*vs.* nonsepsis)	636	299	6.33 (4.65–8.62)	3.85 (2.70–5.50)		
qSOFA (*vs.* qSOFA <2)	337	303	18.45 (13.35–25.50)	13.92 (9.87–19.63)		
qSOFA(–)sepsis(–)	594	16			1.00 (ref)	1.00 (ref)
qSOFA(–)sepsis(+)	432	34			2.71 (1.48–4.97)	2.59 (1.39–4.83)
qSOFA(+)sepsis(–)	133	38			10.61 (5.74–19.59)	9.20 (4.86–17.38)
qSOFA(+)sepsis(+)	204	265			48.23 (28.41–81.85)	42.02 (24.31–72.64)

[a], adjusted for gender, age in age categories (15–64, 65–84, and ≥85 years), comorbidities such as malignancy, and the disease-related groups; [b], BMI could not be calculated because these patients were bedridden. CI, confidence interval; OR, odds ratio; SOFA, sequential organ failure assessment.

Table 4 Comparison of the area under the receiver operating characteristic curves of qSOFA and Sepsis-3 criteria for in-hospital mortality, ICU admission, and invasive ventilation

Variable	qSOFA	Sepsis
In-hospital mortality	0.846 (0.824–0.868)	0.834 (0.805–0.863)
ICU admission	0.805 (0.775–0.835)	0.884 (0.863–0.906)
Invasive mechanical ventilation	0.842 (0.816–0.869)	0.875 (0.848–0.901)

Our study had some strengths. This study was based on a secondary analysis of all hospitalized patients in a subdistrict of Beijing (19). Clinical and laboratory data from all enrolled patients in this study were collected through manual review of medical records by two independent investigators. Moreover, although many studies have been published to compare the prognostic performance of qSOFA with that of SOFA score in patients with infection, no studies had yet investigated the clinical outcomes of those septic patients missed by qSOFA score <2 (false-negatives) and those nonseptic patients with qSOFA score ≥2 (false-positives).

Our study was also subject to some limitations. First, this study was based on a secondary analysis of a database not originally designed for this purpose. Second, maximum qSOFA score was not necessarily obtained before onset of sepsis. However, this approach was still valid because the laboratory results required for SOFA score were not available every day in general wards. Therefore, qSOFA might still serve as a prompt of pending or unrecognized sepsis. Third, we only included patients with confirmed infection in our cohort. In clinical practice, patients with unconfirmed but suspected infection might also be screened for the presence of organ dysfunction, therefore compromising the specificity of qSOFA score for the diagnosis of sepsis, even if the sensitivity remained unchanged. Furthermore, by including patients without infection (regardless of meeting qSOFA criteria or not), the high mortality rate of septic patients not identified by qSOFA score [i.e., sepsis(+)qSOFA(–)] are unlikely to be affected, but whether the mortality rate of nonseptic patients meeting qSOFA criteria [i.e., sepsis(–)qSOFA(+)] will change remains uncertain. Last, the difference between crude and adjusted ORs was significant, indicating the possibility of including inappropriate covariates in the multivariate model.

In conclusion, the results of our study confirmed the low sensitivity of qSOFA score in the diagnosis of sepsis, therefore questioning its value as a screening tool. In addition, qSOFA score ≥2 might identify a group of patients at higher risk of mortality, regardless of being septic or not. Further prospective cohort studies are needed to confirm our findings and to evaluate the predictive value of qSOFA score in different settings.

Acknowledgments

Funding: The study was supported, in part, by the Capital Clinical Application Research Grant (Z131107002213112) from the Science and Technology Commission of Beijing, and the Chinese Academy of Medical Sciences (CAMS) Innovation Fund for Medical Sciences (CIFMS) 2016-I2M-1–014. The funders had no role in the study design, data collection and analysis, decision to publish, or preparation of the article

Footnote

Conflicts of Interest: The authors have no conflicts of interest to declare.

Ethical Statement: The study was approved by the ethics committee of Peking Union Medical College Hospital and informed consent was waived.

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Cite this article as: Tian H, Zhou J, Weng L, Hu X, Peng J, Wang C, Jiang W, Du X, Xi X, An Y, Duan M, Du B; for China Critical Care Clinical Trials Group (CCCCTG). Accuracy of qSOFA for the diagnosis of sepsis-3: a secondary analysis of a population-based cohort study. J Thorac Dis 2019;11(5):2034-2042. doi: 10.21037/jtd.2019.04.90

Supplementary

Table S1 Risk factors of in-hospital mortality in patients with infection, by univariate and multivariate regression analysis

Variables	Control	Case	Model 1		Model 2	
			Crude OR (95% CI)	Adjusted OR[a] (95% CI)	Crude OR (95% CI)	Adjusted OR[a] (95% CI)
Age groups (years), n						
18–74	518	59	1.00 (ref)	1.00 (ref)	1.00 (ref)	1.00 (ref)
75–83	427	134	2.76 (1.98–3.84)	2.21 (1.47–3.32)	2.76 (1.98–3.84)	2.22 (1.48–3.34)
84	418	160	3.36 (2.43–4.65)	2.62 (1.73–3.97)	3.36 (2.43–4.65)	2.64 (1.74–4.00)
BMI (kg/m^2), n						
18.5–24.9	390	56	1.00 (ref)	1.00 (ref)	1.00 (ref)	1.00 (ref)
<18.5	90	29	2.24 (1.36–3.71)	1.86 (0.99–3.49)	2.24 (1.36–3.71)	1.90 (1.01–3.57)
>24.9	229	32	0.97 (0.61–1.55)	1.41 (0.79–2.51)	0.97 (0.61–1.55)	1.39 (0.78–2.48)
Bedridden[b]	654	236	2.51 (1.83–3.45)	1.72 (1.15– 2.58)	2.51 (1.83–3.45)	1.75 (1.16–2.62)
Comorbidities, n						
Hypertension	730	220	1.43 (1.13–1.82)			
Chronic heart disease	409	141	1.44 (1.14–1.83)		1.44 (1.14–1.83)	
Chronic kidney disease	53	25	1.88 (1.15–3.08)		1.88 (1.15–3.08)	
Malignancy	175	99	2.65 (2.00–3.51)	3.67 (2.51–5.36)	2.65 (2.00–3.51)	3.66 (2.50–5.34)
Groups, n						
Sepsis (*vs.* nonsepsis)	636	299	6.33 (4.65–8.62)	3.95 (2.76–5.63)		
qSOFA ≥2 (*vs.* qSOFA <2)	337	303	18.45 (13.35–25.50)	14.34 (10.17–20.23)		
qSOFA(–)Sepsis(–)	594	16			1.00 (ref)	1.00 (ref)
qSOFA(–)Sepsis(+)	432	34			2.71 (1.48–4.97)	2.60 (1.39–4.83)
qSOFA(+)Sepsis(–)	133	38			10.61 (5.74–19.59)	9.26 (4.90–17.50)
qSOFA(+)Sepsis(+)	204	265			48.23 (28.41–81.85)	43.72 (25.30–75.53)

[a], adjusted for gender, age in age categories (18–74, 75–83 and ≥84 years), comorbidities such as malignancy and the disease related groups; [b], BMI could not be calculated because these patients were bedridden. CI, confidence interval; OR, odds ratio; SOFA, sequential organ failure assessment.

Table S2 Risk factors of in-hospital mortality in patients with infection, by univariate and multivariate regression analysis

Variables	Control	Case	Model 1		Model 2	
			Crude OR (95% CI)	Adjusted OR[a] (95% CI)	Crude OR (95% CI)	Adjusted OR[a] (95% CI)
Age groups (years), n	1,363	353	1.05 (1.03–1.06)	1.04 (1.02–1.05)	1.05 (1.03–1.06)	1.04 (1.02–1.05)
BMI (kg/m^2), n						
18.5–24.9	390	56	1.00 (ref)	1.00 (ref)	1.00 (ref)	1.00 (ref)
<18.5	90	29	2.24 (1.36–3.71)	1.80 (0.96–3.41)	2.24 (1.36–3.71)	1.84 (0.97–3.50)
>24.9	229	32	0.97 (0.61–1.55)	1.39 (0.78–2.48)	0.97 (0.61–1.55)	1.37 (0.77–2.46)
Bedridden[b]	654	236	2.51 (1.83–3.45)	1.62 (1.08–2.43)	2.51 (1.83–3.45)	1.64 (1.09–2.47)
Comorbidities, n						
Hypertension	730	220	1.43 (1.13–1.82)		1.43 (1.13–1.82)	
Chronic heart disease	409	141	1.44 (1.14–1.83)		1.44 (1.14–1.83)	
Chronic kidney disease	53	25	1.88 (1.15–3.08)		1.88 (1.15–3.08)	
Malignancy	175	99	2.65 (2.00–3.51)	3.52 (2.42–5.13)	2.65 (2.00–3.51)	3.59 (2.46–5.23)
Groups, n						
Sepsis (*vs.* nonsepsis)	636	299	6.33 (4.65–8.62)	3.83 (2.68–5.47)		
qSOFA ≥2 (*vs.* qSOFA <2)	337	303	18.45 (13.35–25.50)	14.06 (9.97–19.83)		
qSOFA(–)Sepsis(–)	594	16			1.00 (ref)	1.00 (ref)
qSOFA(–)Sepsis(+)	432	34			2.71 (1.48–4.97)	2.55 (1.37–4.75)
qSOFA(+)Sepsis(–)	133	38			10.61 (5.74–19.59)	9.20 (4.86–17.40)
qSOFA(+)Sepsis(+)	204	265			48.23 (28.41–81.85)	41.89 (24.22–72.44)

[a], adjusted for gender, age in age categories (18–74, 75–83 and ≥84 years), comorbidities such as malignancy and the disease related groups; [b], BMI could not be calculated because these patients were bedridden. CI, confidence interval; OR, odds ratio; SOFA, sequential organ failure assessment.