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RESEARCH ARTICLE

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Contributions of individual qSOFA elements to assessment of severity and for prediction of mortality

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ABSTRACT

Background: The quick sequential [sepsis-related] organ failure assessment (qSOFA) acts as a prompt to consider possible sepsis. The contributions of individual qSOFA elements to assessment of severity and for prediction of mortality remain unknown.

Methods: A total of 3974 patients with community-acquired pneumonia were recruited to an observational prospective cohort study. The area under the receiver operating characteristic curve (AUROC), odds ratio, relative risk and Youden's index were employed to assess discrimination.

Results: Respiratory rate ≥22/min demonstrated the most superior diagnostic value, indicated by largest odds ratio, relative risk and AUROC, and maximum Youden's index for mortality. However, the indices for altered mentation and systolic blood pressure (SBP) ≤100 mm Hg decreased notably in turn. The predictive validities of respiratory rate ≥22/min, altered mentation and SBP ≤100 mm Hg were good, adequate and poor for mortality, indicated by AUROC (0.837, 0.734 and 0.671, respectively). Respiratory rate ≥22/min showed the strongest associations with SOFA scores, pneumonia severity index, hospital length of stay and costs. However, SBP ≤100 mm Hg was most weakly correlated with the indices.

Conclusions: Respiratory rate ≥22/min made the greatest contribution to parsimonious qSOFA to assess severity and predict mortality. However, the contributions of altered mentation and SBP ≤100 mm Hg decreased strikingly in turn. It is the first known prospective evidence of the contributions of individual qSOFA elements to assessment of severity and for prediction of mortality, which might have implications for more accurate clinical triage decisions.

KEY MESSAGES

- Respiratory rate ≥22/min demonstrated the most superior diagnostic value.
- Respiratory rate ≥22/min showed the strongest association with severity.
- Respiratory rate ≥22/min, altered mentation and SBP ≤100 mm Hg predicted mortality well, adequately and poorly, respectively.

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qSOFA; community-acquired pneumonia; sepsis; contribution; triage; severity; mortality

Introduction

Sepsis is a common syndrome associated with high morbidity and mortality and thus is regarded as an important global health problem [1–3]. An international task force of experts redefined this syndrome as a life-threatening organ dysfunction due to a dysregulated host response to infection in the Third International Consensus Definitions for Sepsis and Septic Shock (Sepsis-3), and organ dysfunction can be identified as an acute change in total sequential [sepsis-related] organ failure assessment (SOFA) score ≥2 points consequent to the infection. They recommend a new clinical

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score termed quick SOFA (qSOFA), which incorporates respiratory rate of 22/min or greater, altered mentation, and systolic blood pressure (SBP) of 100 mm Hg or less (range: 0–3; 1 point for each of the criteria), to rapidly identify adult patients with suspected infection who are likely to have poor outcomes. The task force strongly encourages prospective validation in multiple health care settings to confirm its robustness [4,5]. The qSOFA has merits according to its proponents [6,7]. However, the contributions of individual qSOFA elements to predictive validity are unclear [5]. It might further facilitate the rationalization of clinical triage decision-making and then reduce mortality much more was the unequal weight of individual qSOFA elements elucidated.

Pneumonia is the top communicable cause of death worldwide. Community-acquired pneumonia (CAP) results in great mortality and morbidity and high costs worldwide and its usual complication is sepsis [8,9]. Therefore, it is important to assess the outcome prediction ability of qSOFA in patients with pneumonia. Ranzani et al. [10] corroborated qSOFA presented better clinical usefulness for patients with CAP in the emergency department. Hence, an observational prospective cohort study of patients with CAP was conducted to determine the contributions of individual qSOFA elements to assessment of severity and for prediction of mortality.

Material and methods

Design and setting

A total of 3974 patients with CAP were recruited to an observational prospective cohort study in the Departments of Pulmonary and Critical Care Medicine in two Chinese tertiary hospitals of two universities from 1 January 2016 to 31 December 2021. The database used for the three articles published partly overlapped the current database [11–13].

Criteria for enrolment

CAP was defined as an acute infection of the pulmonary parenchyma associated with an acute infiltrate on the chest radiograph with two or more symptoms including fever (>38 °C), hypothermia (<36 °C), rigours, sweats, new cough or change in colour of respiratory secretions, chest discomfort or dyspnoea [14]. Patients younger than 18 years, recruited during the 28 days before the study, presented severe immunosuppression, active tuberculosis, or end-stage diseases, showing a written 'do not resuscitate' order, having COVID-19, or being unconscious before suffering from pneumonia were excluded.

Clinical management

The study was conducted based on the principles of human experimentation guidelines of the United States Department of Health and Human Services. The report followed the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) guidelines. Respiratory physicians attended patients with CAP according to the Infectious Disease Society of America/American Thoracic Society guidelines [8] and the Surviving Sepsis Campaign guidelines [15,16]. qSOFA score of 2 or higher indicated a transfer to respiratory intensive care unit (ICU). Antibiotic regimens for the empirical treatment were adherence to the guidelines and then adjusted in the light of subsequently cultured pathogens. All patients who reached clinical stability and became afebrile were discharged home.

Approval of study design

The study was approved by the Institutional Review Boards (Review Board of Sun Yat-sen University and Review Board of Peking University, No. 20152958 and No. 20153043, respectively). All procedures included in the study involving human participants were in line with the 1964 Helsinki Declaration and its later amendments.

Sample size calculation

Unit-level design prevalence, cluster-level design prevalence, test sensitivity, target cluster sensitivity, and target system sensitivity were 12%, 1%, 0.9, 0.5, and 0.95, respectively. The total number of clusters to be sampled was 598, and the maximum number of samples was 4186.

Outcomes

The primary outcome was in-hospital mortality. Secondary outcomes incorporated SOFA scores, pneumonia severity index (PSI), hospital length of stay (LOS) and costs.

Data collection

A total of 4032 patients with CAP were recruited consecutively and 58 cases were excluded due to exclusion criteria. Chest radiography and/or computer tomography scans were performed in all patients. Two

senior radiologists (LHL and QZZ) classified independently the frontal and lateral chest radiographic findings and computer tomography scan images. Clinical and diagnostic data and radiological features were gathered. qSOFA and SOFA scores and PSI on admission were calculated. Laboratory variables were determined by the hospital clinical laboratories. The statistician was blinded to the study.

Statistical analysis

All statistical analyses were performed with Statistical Package for the Social Science for Windows version 16.0 (SPSS, Chicago, IL, USA) and MedCalc version 19.6.1 (Mariakerke, Belgium). Categorical variables and continuous variables with normal distribution were reported as the percentages and the mean ± standard deviation (SD), respectively. Chi-square test, Spearman rank correlation, unpaired Student's *t*-test and univariate logistic regression were applied. Odds ratio (OR) and relative risk (RR) for mortality were reckoned. The receiver operating characteristic (ROC) curves were designed and the corresponding areas under the ROC curves (AUROCs) with the 95% confidence interval (CI) were computed to estimate the performances of qSOFA and its individual elements to predict mortality. AUROCs were regarded as poor at 0.6–0.7, adequate at 0.7–0.8, good at 0.8–0.9, and excellent at 0.9 or higher [17]. The sensitivities, specificities, positive predictive values (PPVs), negative predictive values (NPVs), and Youden's index were also calculated to appraise robustness of the variables. All tests were two-sided. *p* Values less than 0.05 were taken as statistically significant.

Results

Patient characteristics

Baseline characteristics are summarized in Table 1. In total, 3408 (85.7%) patients had qSOFA scores of 0 or 1. In total, 1602 (40.3%) patients had concurrent sepsis. The mortality rates increased sharply as qSOFA scores raised ($p < 0.001$). Mortality in CAP patients with sepsis was notably higher compared with those without sepsis. The etiology of pneumonia was not detected in every patient. Table 2 describes the data.

Performances of individual qSOFA elements for the prediction of mortality

Prognostic performances of individual qSOFA elements are reported in Table 3. Respiratory rate ≥22/min demonstrated the most superior diagnostic value, indicated by largest OR, RR and AUROC, and maximum Youden's index for mortality. However, the indices for altered mentation and SBP ≤100 mm Hg decreased notably in turn.

The predictive validities of respiratory rate ≥22/min, altered mentation and SBP ≤100 mm Hg were good, adequate and poor for mortality, indicated by AUROC (0.837, 0.734 and 0.671, respectively; Table 3 and Figure 1). The predictive validity of qSOFA was good for mortality (AUROC, 0.875; 95% CI, 0.857–0.886; Figure 1).

Table 1. Baseline characteristics of study cohort (mean ± SD, $n = 3974$).

Characteristic	Value
Age (years)	51.7 ± 22.9
Sex, No. (%)	
Men	1940 (48.8)
Women	2034 (51.2)
Comorbidities, No. (%)	
Hypertension	1168 (29.4)
Coronary heart disease	358 (9.0)
Heart failure	139 (3.5)
NYHA class IV	68 (1.7)
COPD	270 (6.8)
GOLD 3 and 4	159 (4.0)
Diabetes mellitus	306 (7.7)
Chronic renal insufficiency	171 (4.3)
Dialysis	87 (2.2)
Liver disease	227 (5.7)
Nervous system disease	163 (4.1)
Tumour	282 (7.1)
Alcohol abuse, No. (%)	151 (3.8)
Smoking, No. (%)	755 (19.0)
qSOFA score, No. (%)[a, b]	
0/died	2139 (53.8)/7 (0.3)
1/died	1269 (31.9)/114 (9.0)
2/died	464 (11.7)/61 (13.1)
3/died	102 (2.6)/92 (90.2)
Outcomes, No. (%)	
Ventilated patients	274 (6.9)
Patients received catecholamines	393 (9.9)
Sepsis[c]	1602 (40.3)
In-hospital mortality	274 (6.9)
Mortality from sepsis	220 (13.7)
Mortality not from sepsis	54 (2.3)

COPD: chronic obstructive pulmonary disease; GOLD: global initiative for chronic obstructive lung disease; NYHA: New York Heart Association; qSOFA: quick sequential [sepsis-related] organ failure assessment; SBP: systolic blood pressure; SOFA: sequential [sepsis-related] organ failure assessment; LOS: length of stay.

[a] Score ranges from 0 to 3 [4,5], with higher scores indicating greater likelihood of having severe CAP.

[b] $p < 0.001$.

[c] Sepsis is defined as life-threatening organ dysfunction caused by a dysregulated host response to infection. Organ dysfunction can be identified as an acute change in total SOFA score ≥2 points consequent to the infection [4].

Table 2. Most common etiologies of CAP ($n = 3974$).

Etiology	Patient (%)
Streptococcus pneumoniae	1112 (28.0)
Mycoplasma pneumoniae	759 (19.1)
Haemophilus influenzae	428 (10.8)
Respiratory viruses	261 (6.6)
Staphylococcus aureus	173 (4.4)
Legionella species	130 (3.3)
Gram-negative bacilli	93 (2.3)

CAP: community-acquired pneumonia.

Table 3. Performance of the individual criteria for the prediction of mortality among patients with CAP ($n = 3974$).

Variable		Respiratory rate ≥22/min	Altered mentation	SBP ≤100 mm Hg
Patients alive (%)	Yes	1144 (81.1)	262 (64.2)	560 (80.9)
	No	267 (18.9)	146 (35.8)	132 (19.1)
	χ^2	255.317	249.391	107.394
	p Value	<0.0001	<0.0001	<0.0001
RR (95% CI)		63.508	8.753	4.758
p Value		(24.394–169.261)	(6.462–11.957)	(3.426–6.492)
		<0.0001	<0.0001	<0.0001
OR (95% CI)		75.915	12.632	5.671
p Value		(28.627–207.293)	(8.417–17.839)	(3.916–7.915)
		<0.0001	<0.0001	<0.0001
Sensitivity, % (95% CI)		97.4	53.3	48.2
		(92.8–99.5)	(46.8–63.5)	(39.4–56.9)
Specificity, % (95% CI)		69.1	92.9	84.9
		(67.1–71.3)	(91.4–94.2)	(83.2–86.4)
PPV, % (95% CI)		18.9	35.8	19.1
		(17.2–19.5)	(30.7–39.8)	(16.0–21.8)
NPV, % (95% CI)		99.7	96.4	95.7
		(99.3–99.9)	(95.7–97.0)	(95.1–96.3)
Youden's index		0.67	0.46	0.33
AUROC (95% CI)		0.837	0.734	0.671
		(0.820–0.849)	(0.702–0.765)	(0.653–0.692)

CAP: community-acquired pneumonia; SBP: systolic blood pressure; RR: relative risk; CI: confidence interval; OR: odds ratio; PPV: positive predictive value; NPV: negative predictive value; AUROC: the area under the receiver operating characteristic curve.

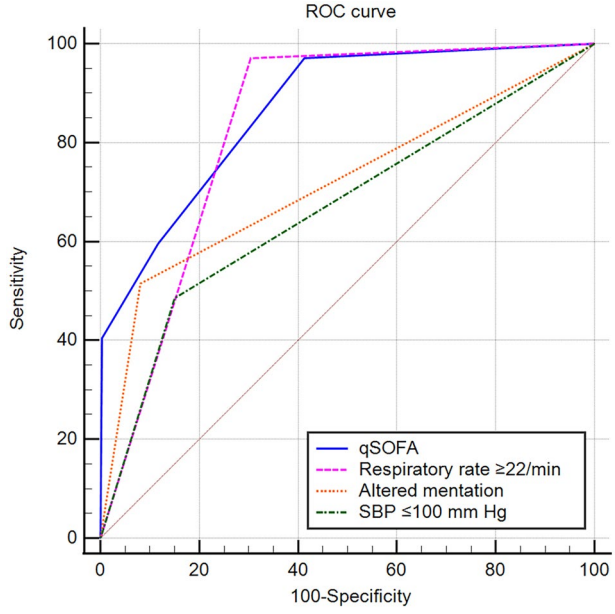

Figure 1. ROC curves for mortality prediction by qSOFA and its individual elements.
ROC: the receiver operating characteristic; qSOFA: quick sequential [sepsis-related] organ failure assessment; SBP: systolic blood pressure.

The association of individual qSOFA elements with SOFA scores

The differences in SOFA scores between the patients meeting an individual qSOFA element and those without the criterion and their associations are shown in Table 4. Respiratory rate ≥22/min demonstrated the strongest association with SOFA scores. However, SBP ≤100 mm Hg showed the weakest correlation with the index.

The contributions of individual qSOFA elements to PSI

The patients with an individual qSOFA element demonstrated higher PSI compared with those without the criterion (Table 4). The association of respiratory rate ≥22/min with PSI was closest, and then SBP ≤100 mm Hg presented the weakest association.

The contributions of individual qSOFA elements to hospital LOS and costs

The patients meeting an individual qSOFA element stayed in the hospital longer and cost much more compared with those without the criterion (Table 4). Respiratory rate ≥22/min was most strongly associated with hospital LOS and costs. On the other hand, SBP ≤100 mm Hg was most weakly correlated with the indices.

Discussion

This observational prospective cohort study involving 3974 patients with CAP showed that respiratory rate ≥22/min demonstrated the most superior diagnostic value, indicated by largest OR, RR, Youden's index and AUROC for mortality from CAP, and the indices for altered mentation and SBP ≤100 mm Hg decreased

Table 4. Associations of the individual criteria with SOFA scores, PSI, hospital LOS and costs (mean ± SD, $n = 3974$).

Criteria	SOFA score/PSI/hospital LOS (days)/cost ($)	*t* Value	*p* Value	r_s Value	*p* Value
Respiratory rate ≥22/min	3.59 ± 1.58 vs. 0.73 ± 1.49	12.739	<0.001	0.675	<0.001
	117.46 ± 6.25 vs. 58.71 ± 3.93	11.361	<0.001	0.604	<0.001
	15.3 ± 7.3 vs. 10.5 ± 4.2	4.847	<0.001	0.316	<0.001
	2015.56 ± 937.35 vs. 766.43 ± 316.74	9.305	<0.001	0.492	<0.001
Altered mentation	5.24 ± 1.37 vs. 1.34 ± 1.82	11.694	<0.001	0.618	<0.001
	130.98 ± 9.14 vs. 73.69 ± 5.27	10.703	<0.001	0.539	<0.001
	16.9 ± 8.1 vs. 11.7 ± 6.3	4.312	<0.001	0.298	<0.001
	1512.08 ± 813.71 vs. 1175.38 ± 651.08	5.493	<0.001	0.292	<0.001
SBP ≤100 mm Hg	2.64 ± 1.79 vs. 1.56 ± 1.92	4.613	<0.001	0.309	<0.001
	96.49 ± 6.01 vs. 76.00 ± 5.04	3.279	<0.001	0.204	<0.001
	14.3 ± 8.35 vs. 11.8 ± 1.17	3.295	<0.001	0.217	<0.001
	1412.98 ± 605.11 vs. 1167.13 ± 573.19	3.014	<0.001	0.195	<0.001

SOFA: sequential organ failure assessment; PSI: pneumonia severity index; LOS: length of stay; r_s: rank correlation coefficient; SBP: systolic blood pressure.
The data in longest cells indicated SOFA scores, PSI, hospital LOS and costs, respectively.

notablely in turn. We first found that the predictive validities of respiratory rate ≥22/min, altered mentation and SBP ≤100 mm Hg were good, adequate and poor for mortality, respectively, and that respiratory rate ≥22/min presented the strongest associations with SOFA scores, PSI, hospital LOS and costs, and then SBP ≤100 mm Hg was most weakly correlated with the indices.

Risk prediction models are key components of treatment algorithms adopted in a wide range of medical fields. All individual qSOFA elements made contributions to mortality prediction in the current study, but respiratory rate ≥22/min predicted best, which is new evidence. Which mechanisms might be envisaged to interpret the phenomena? Enough oxygen is essential for cells, tissues and organs. Tachypnoea indicates hypoxia. Therefore, tachypnoea demonstrated the strongest association with mortality. Higher prevalence of systolic hypertension and higher systolic arterial pressure are undoubted in recent years [13]. As a result, systolic arterial pressures of many patients might not drop to <100 mm Hg, which might be the causation of worst prognostic performance of SBP ≤100 mm Hg. Although CAP is a major source of sepsis, future prospective multicentre cohort studies of patients with sepsis including suspected infection else are warranted to better understand potential generalizability.

SOFA score is an excellent operationalization of disease severity of adult patients with hospitalized CAP [18]. Since the establishment of PSI, it is a good predictor of mortality in CAP, even including SARS-CoV-2 CAP [19–23]. Respiratory rate ≥22/min demonstrated the strongest associations with SOFA scores and PSI, and then similar patterns with hospital LOS and costs. However, SBP ≤100 mm Hg showed the weakest correlations with the indices. The above-mentioned mechanisms (essential role of oxygen and hypoxia indicated by tachypnoea) might be envisaged to explicate the different associations of individual qSOFA elements with severity. Guo et al. [24] previously reported that confusion and respiratory rate ≥30/min showed similar paradigms with SOFA scores, hospital LOS and costs based on a retrospective analysis, but hypotension (SBP <90 mm Hg or diastolic blood pressure ≤60 mm Hg) did not. It is the first known prospective evidence of the associations of respiratory rate ≥22/min with these indices. However, these findings might require external validation.

Severe sepsis (The term has been left behind after 2016 Sepsis-3 guidelines), defined as new-onset acute organ dysfunction in the cohort of patients hospitalized for CAP, developed in one-half of the patients ($n = 639$, 48%) [8]. The percentage of concurrent sepsis discovered in the current study was very similar to the above-mentioned. Mortality in patients with CAP and fulfilling sepsis increased sharply compared with those without sepsis. These findings might be envisaged to interpret the causation of why CAP results in great mortality and morbidity and high costs worldwide.

The current findings might have implications for more accurate clinical triage decisions. It is a major challenge in the management of CAP to identify patients who might rapidly develop adverse medical outcomes among those without obvious reasons for immediate ICU admission [25]. Only 2.6% of patients with CAP met qSOFA score of 3. Among the patients with CAP and fulfilling qSOFA score of 2, the patients who breathe

22/min or more might be more severely ill, demonstrate a higher mortality rate and then have the priority for treatment and intensive care where ICU resources are limited. Most importantly, the patients with qSOFA score of <2 but fulfilling respiratory rate ≥22/min might be prioritized and even should be transferred to ICU. The current findings also have direct clinical implications regarding prompt recognition and resuscitation at the emergency department. As Guo et al. previously reported in the application of the Infectious Disease Society of America/the American Thoracic Society minor criteria for severe CAP: The individual minor criteria for severe CAP were of unequal weight in predicting hospital mortality, SOFA scores, hospital LOS, and costs [24]. The combination of arterial oxygen pressure/fraction inspired oxygen ≤250 mm Hg, confusion and uraemia predicted more severity and higher mortality compared with others, suggesting the former patients should have a higher priority for treatment in ICU and might benefit more from ICU admission [26]. The patients with non-severe CAP fulfilling the predictive findings most strongly associated with mortality (arterial oxygen pressure/fraction inspired oxygen ≤250 mm Hg, confusion and uraemia) demonstrated higher SOFA and PSI scores and mortality rates and might have the priority for treatment and intensive care [25]. Furthermore, the predictive validity of qSOFA might be better were the contributions of individual qSOFA elements accompanied by additional biomarkers. Adami et al. [27] discovered combining qSOFA 1 with the biomarker soluble urokinase plasminogen activator receptor improves its prognostic performance for unfavourable outcome and can help decisions for earlier treatment. Bolanaki et al. [28] reported biomarkers of infection and organ dysfunction, most notably procalcitonin, substantially improve early prediction of sepsis with added value to qSOFA alone as a simple screening tool on emergency department admission.

Limitations

Several limitations of this study deserve comment. First, the prospective cohort was derived from two centres in a city, but not multicentre settings located in different cities in different countries. Popularization of the findings should be cautious. Second, this study tested the questions in patients with CAP. However, its applicability to patients with suspected infection of other parts of the body might not be determined by this study. Third, the samples were relatively small. Had the scale been larger, the results might have been more powerful. Finally, many medications can influence the patient's respiratory rate (e.g. opioids, sedative drugs, etc.).

Conclusions

Respiratory rate ≥22/min made the greatest contribution to parsimonious qSOFA to assess severity and predict mortality. However, the contributions of altered mentation and SBP ≤100 mm Hg decreased strikingly in turn. It provides new prospective evidence of the contributions of individual qSOFA elements to assessment of severity and for prediction of mortality, which might have implications for more accurate clinical triage decisions.

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Authors contributions

QG was in charge of funding acquisition and project administration. QG and HYL made substantial contributions to conception and design and were in charge of data collection and curation, and the writing of the manuscript. LHL and QZZ read the chest radiographs and computer tomography scans. WDS, ML, XKC, HL, HLP, HQY, NL, YHL, ZDL, LHL and QZZ made substantial contributions to acquisition, analysis, and interpretation of data. MJ was in charge of statistical analysis. Each author has participated in the writing of the manuscript or revising it critically for important intellectual content, been involved in the analysis of the data, and seen and approved the submitted version.

Ethical statement

Ethical approval from the regulation committee (Ethical Committee of Shenzhen, No. 201510673) was granted for the study protocol.

Consent form

Written informed consent was obtained from the patient prior to enrolment. The patients with confusion were asked afterwards and before enrolment, a first-degree relative gave assumed consent. They were notified the content of the study on admission and then signed the documents if they approved.

Disclosure statement

All authors report no conflict of interest.

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Data availability statement

The datasets used and/or analysed during the current study are available from the corresponding author upon reasonable request.

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