qSOFA score and LqSOFA score as predictors of outcome in an elderly population with chest infection treated in the Emergency Department. A case series

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Abstract

The objective of this study is to assess the prognostic value regarding 28-day outcome of the quick sequential organ failure assessment (qSOFA) score and the combined score calculated from blood lactate levels + qSOFA (LqSOFA) score in elderly patients initially treated in the Emergency Department (ED) for sepsis due to pneumonia or other chest infections. This is a prospective observational study, conducted at the ED in a Greek University Hospital. Forty-one patients with sepsis due to chest infection were enrolled in the study. All patients were treated in the Resuscitation Room of the ED according to the international treatment protocols for sepsis. The qSOFA score was calculated on admission for all patients, and one point was added in the calculation of the LqSOFA score in patients with blood lactate levels >2 mmol/L. Both the qSOFA and the LqSOFA scores had high sensitivity and specificity in predicting unfavorable outcome in elderly patients with chest infection and sepsis. In the ongoing debate of early diagnosis of sepsis and identification of prognostic indexes of the syndrome, qSOFA score alone or in combination with lactate levels could serve as a reliable predictor of outcome. Large prospective studies are needed to further evaluate the role and prognostic validity of these scores in the ED.

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Introduction

Sepsis remains one of the leading causes of death worldwide.[1] Based on the latest 2016 definition, sepsis is now diagnosed as a *life-threatening organ dysfunction caused by a dysregulated host response to an infection.*[2] The necessity of new definitions for sepsis and septic shock was due to the complex underlying pathophysiology, however, a diagnostic *gold standard* still does not exist. Among several commonly used biomarkers and prognostic scores, quick sequential organ failure assessment (qSOFA) score is increasingly used in the evaluation of patients with suspected sepsis in medical settings like the Emergency Department (ED). After the introduction of the qSOFA in 2016 by the Task force, its utility as a prognostic tool remains a matter of debate,[3,4] We present a case series of 41 elderly patients suffering from chest infection who were initially treated in the Resuscitation Room of the Emergency Department in a Greek tertiary care University Medical Center. qSOFA score and a score calculated by the combination of qSOFA and blood lactate levels (LqSOFA score) at admission time were used as predictors for the 28-day outcome.

Materials and Methods

Study population and design

We enrolled in the study 41 consecutive patients who presented in the ED of the University Hospital of Patras, Greece with diagnosis of sepsis due to chest infection and received initial treatment in the Acute Care Area of the ED between January 01, 2018 and June 30, 2018. Inclusion criteria were age >18 years and diagnosis of pneumonia confirmed by clinical examination, arterial blood gas analysis and radiographic findings (chest X-ray) performed in the ED. Exclusion criteria were known liver or renal disease, acute renal failure with creatinine clearance <50 mL/min/1.73 m^2), metformin use and cardiovascular instability requiring use of intravenous vasoactive agents on admission.

The diagnosis of sepsis was based on the international criteria and sepsis-3 definitions.[2] All patients were initially treated for respiratory distress, as defined by increased respiratory rate (RR>30), and abnormal values in partial oxygen pressure (PaO_2) and/or carbon dioxide partial oxygen pressure ($PaCO_2$) in arterial blood gas analysis. Patients received oxygen therapy via a Venturi mask or received support with forced oxygenation using Continuous Positive Airway Pressure. All appropriate treatment was provided in accordance with the Surviving Sepsis Guidelines.[5] After stabilization, all patients were admitted to the Internal Medicine Department of the Hospital for further evaluation and treatment.

The study protocol was approved by the Ethics Committee of the University Hospital and all patients (or their legal guardian or power of attorney) gave written informed consent for participation in the study. All data collected for the purposes of this study were anonymized and stored in an encrypted electronic database. The medical team involved in the study included University of Patras Faculty physicians, resident physicians rotating through the ED and outside consultants.

Data collection

Collected data included demographic information, a detailed history of present illness, pre-existing co-morbidities and related medications, social history and surgical history. Clinical records for each patient consisted of detailed physical examination and radiological data (chest X-ray images). Blood laboratory data were obtained immediately on admission to the ED after analyzing 10 mL of peripherally collected blood samples, blood gas analysis also was obtained in order to measure lactate levels and monitor respiratory status. For each patient, the qSOFA score was calculated based on the following variables: i) systolic blood pressure ≤100 mmHg; ii) RR≥22 breaths/min; and iii) altered mental status. One point was added for every abnormal value from above parameters in order to calculate the score.[6]

Serial serum lactate measurements were obtained in the ED at the time of initial assessment and were repeated at the discretion of the physician team in order to monitor response to treatment. The first serum lactate value was used to calculate the LqSOFA score by adding 1 point to the qSOFA score for lactate levels >2 mmol/L. Patient demographic data, major laboratory findings, qSOFA score and LqSOFA scores (based on the aggregation of qSOFA score + lactate blood levels) are presented in Table 1. Patient survival to hospital discharge was the primary endpoint of the study.

Statistical analysis

Data were analyzed with descriptive and inferential statistics. Continuous variables were summarized as mean (±SD) and differences between groups were evaluated using the Student's t-test or Mann–Whitney U test as appropriate. Frequency of comorbidities in survivors *vs* non-survivors was compared using the Chi-square test. Variables which differed significantly between survivors and non-survivors in univariate analysis (age, dementia, qSOFA and LqSOFA) were then evaluated as independent predictors of outcome using logistic regression analysis. However, because of collinearity, dementia could not be entered in the regression model and only one of the qSOFA or LqSOFA variables (but not both) could be entered in each regression analysis.

The discriminating ability of qSOFA and LqSOFA for predicting mortality was expressed as the area under the receiver operating characteristic curve (ROC).

All tests were two-tailed, and P<0.05 were considered statistically significant. All data were analyzed using the IBM SPSS Statistics software (version 25) and the MedCalc Statistical Software version 19.0.7 (MedCalc Software bvba, Ostend, Belgium).

Results

The study enrolled 41 patients (24 women, 17 men) with age

Table 1. Demographic, basic laboratory data, clinical data and calculated severity scores in survivors *vs* non-survivors. Values are presented as Mean (SD) or as number of patients.

	Survivors (N=19)	Non-survivors (N=22)	P-value
Gender (M/F)	9/10	8/14	ns
Age	74 (12)	83.5 (7.3)	0.027
WBC	17400 (9000)	15500 (7000)	ns
CRP	12.5 (10)	15.2 (10)	ns
Central Line in ED	8	17	0.021
Vasopressors in ED	0	4	ns
Dementia	3	13	0.001
Stroke	1	3	ns
COPD	3	2	ns
Serum lactate level	2.7 (1.1)	3 (1.16)	ns
qSOFA	1.06 (0.64)	1.9 (0.5)	<0.001
LqSOFA	1.72 (0.83)	3 (0.66)	<0.001

WBC, white blood cells; CRP, C-reactive protein; ED, Emergency Department; COPD, chronic obstructive pulmonary disease; qSOFA, quick SOFA; LqSOFA, lactate qSOFA; ns, not significant.

range 55 to 98 years. The primary diagnosis on arrival to the ED was pneumonia confirmed by clinical signs (increased respiratory ratio, dyspnea, fever, respiratory distress) and radiologic findings on chest X-ray in all patients. In addition, detailed evaluation also revealed the presence of Cholecystitis in 7 patients, Diverticulitis in 1 patient, Cellulitis in 3 patients, Glomerulonephritis in 2 patients, Osteomyelitis in 1 patient, Pyelonephritis in 1 patient and Urinary Tract Infection in 3 patients. Demographic data, laboratory data and calculated qSOFA and LqSOFA scores are summarized in Table 1. Non-survivors were significantly older, required central line significantly more often, had significantly higher frequency of dementia and had significantly higher qSOFA and LqSOFA scores compared to survivors.

Furthermore, in order to better understand the impact of qSOFA score and of Lactate values on mortality, we divided patients in four subgroups based on whether they had qSOFA score <2 *vs* ≥2, and Lactate values ≤2 *vs* >2, and calculated mortality for these subgroups. The data are summarized in Table 2. Chi-square analysis of these subgroups showed that differences in mortality were highly significant (P<0.00001).

ROC analysis was used to distinguish patients who survived from patients who did not survive and showed that the qSOFA score area under the curve (AUC) was 0.849 (95% CI 0.703-0.942; P<0.0001; Figure 1). qSOFA ≥2 had 90.9% sensitivity and 78.9% specificity in predicting unfavorable outcome. Similarly, the LqSOFA score >2 AUC was 0.830 (95% CI 0.679-0.929; P<0.0001; Figure 2), and LqSOFA >2 had 81.8% sensitivity and 84.2% specificity in predicting unfavorable outcome.

Multivariate logistic regression analysis showed that age was not a significant predictor of mortality, whereas qSOFA ≥2 and LqSOFA>2 were both significant predictors: patients with qSOFA score ≥2 or LqSOFA score >2 had significantly higher risk of mortality (OR 32.15, 95% CI 4.971 to 207.919, P<0.001 and OR 25.213, 95% CI 4.239 to 149.978, P<0.001 respectively Tables 3 and 4).

Discussion and Conclusions

In this study, we assessed the predictive value of the qSOFA and the calculated LqSOFA score in a prospective case series of sepsis patients with chest infection. Although several scores (SOFA, APACHE II, SAPS II) and serum biomarkers (white blood cell count, C-reactive protein, Procalcitonin) have been used by clinicians for assessment of patients with suspected or proven sepsis, a *gold standard* for diagnosis and monitoring of the sepsis syndrome has not been established, and the sensitivity and specificity of these scores and biomarkers for prediction of outcome vary.[7,8] The qSOFA score is easy to calculate using three bedside parameters and has been recently proposed as a rapid test for detection of sepsis in early stages. Although the majority of publications show that qSOFA score has better accuracy than SIRS criteria for predicting mortality in the non-intensive care unit (ICU) environment,[9,10] there is ongoing debate regarding its usefulness because of poor sensitivity.[11] A meta-analysis published by Jiang *et al.* in 2018 attempted to compare the qSOFA score with the SIRS criteria and determine the accuracy of the qSOFA score in predicting mortality in ED patients with infections and showed that although qSOFA score≥2 and SIRS score≥2 were both strongly

Table 2. Mortality in patient sub-groups, based on combination of qSOFA and Lactate values. The observed differences in mortality between the four sub-groups are highly significant (P<0.00001).

Sub-Group Definition		Number of patients	Deaths	Mortality
qSOFA≤1	Lactate≤2	6	0	0%
qSOFA=1	Lactate>2	11	2	18.2%
qSOFA≥2	Lactate≤2	3	2	66.6%
qSOFA≥2	Lactate>2	21	18	85.7%
Total		41	22	-

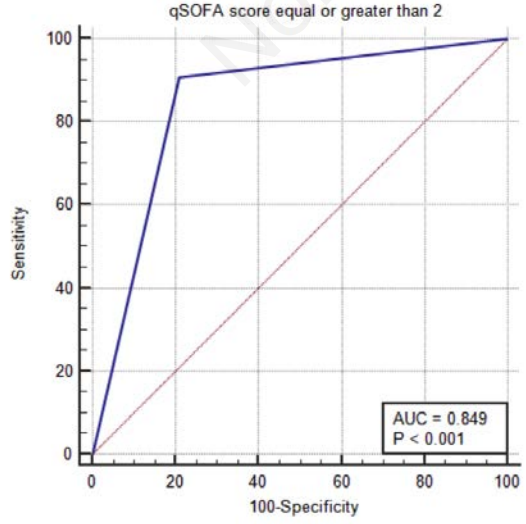

Figure 1. ROC curve evaluating the ability of qSOFA≥2 to predict mortality. Area under the curve (AUC)=0.849, P<0.001.

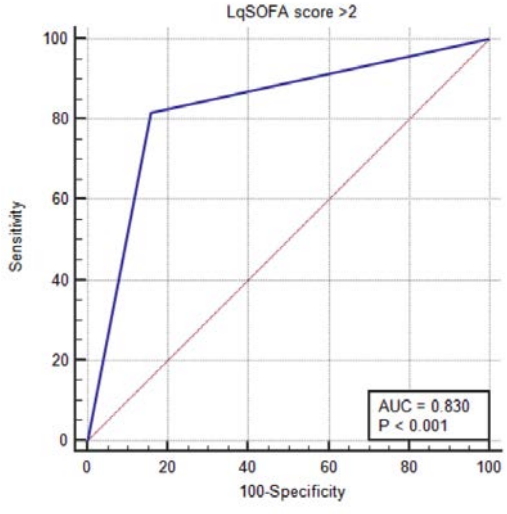

Figure 2. ROC curve evaluating the ability of LqSOFA>2 to predict mortality. Area under the curve (AUC)=0.830, P<0.001.

Table 3. Logistic regression analysis evaluating qSOFA≥2 as predictor of risk of death in septic patients. qSOFA≥2 is significant predictor of mortality both in univariate and in multivariate analysis.

	Univariate Analysis			Multivariate Analysis		
	OR	95% CI	P-value	OR	95% CI	P-value
Age	1.082	1.008 to 1.161	0.03	1.059	0.969 to 1.158	0.208
qSOFA≥2	37.5	6.048 to 232.518	<0.001	32.150	4.971 to 207.919	<0.001

OR, odds ratio; CI, confidence interval.

Table 4. Logistic regression analysis evaluating LqSOFA> 2 as predictor of risk of death in septic patients. LqSOFA>2 is significant predictor of mortality both in univariate and in multivariate analysis.

	Univariate Analysis			Multivariate Analysis		
	OR	95% CI	P-value	OR	95% CI	P-value
Age	1.082	1.008 to 1.161	0.03	1.084	0.992 to 1.186	0.075
LqSOFA >2	24	4.649 to 123.904	<0.001	25.213	4.239 to 149.978	<0.001

OR, odds ratio; CI, confidence interval.

associated with mortality, the qSOFA cannot completely replace the use of SIRS in the ED due to its low sensitivity.[12]

Septic shock is defined, according to the new definitions as a subset of sepsis in which the patient has profound hypoperfusion. Septic shock is characterized by underlying circulatory and metabolic abnormalities resulting in tissue hypoperfusion with serum lactate level ≥2 mmol/L despite adequate volume resuscitation and hypotension that requires vasopressors in order to maintain mean arterial pressure ≥65 mmHg. Increased serum lactate levels can be identified in early stages of the sepsis syndrome due to abnormal tissue perfusion. During the process of the sepsis syndrome, insufficient circulation fails to maintain adequate tissue metabolism. Elevated blood lactate levels most commonly indicate impaired oxidative phosphorylation secondary to decreased oxygen availability to the tissue cells (hypoxic hypoxia) and/or tissue hypoperfusion. This complex pathophysiology leads finally to tissue hypoxia, and lactate overproduction due to increased anaerobic glycolysis.[13,14] However, there is evidence supporting the view that, in addition to tissue hypoxia and anaerobic glycolysis, other mechanisms are also involved in sepsis-related hyperlactatemia. Experimental and human studies all consistently support that elevated lactate levels in sepsis are explained by increased aerobic glycolysis secondary to activation of the stress response (adrenergic stimulation) in order to facilitate a bioenergetic efficiency.[15]

Literature search revealed a few earlier publications related to lactate measurements and qSOFA score evaluation in the Emergency Department: A multi-center retrospective cohort study from US hospitals enrolled 3743 patients assessed in the ED and revealed that qSOFA criteria performed as well or better compared to SIRS criteria, severe sepsis criteria and lactate levels in predicting critical illness.[16] A retrospective cohort study from Shetty *et al*. included 12555 patients with suspected infection in Australia and the Netherlands and showed that the lactate ≥2 mmol/L threshold-based LqSOFA score performs better than qSOFA alone in identifying the risk of adverse outcomes (defined as mortality and/or ICU stay ≥72 h) in ED patients.[6] A retrospective study published in 2018 by Jung included 457 surgical patients with complicated intra-abdominal infection and concluded that the LqSOFA score, which is derived from the qSOFA and serum lactate levels had better predictive performance and higher sensitivity regarding mortality than the qSOFA alone and had predictive performance comparable the full SOFA score.[17]

Our results suggest that both the qSOFA and the LqSOFA scores calculated on admission to the Emergency Department had high sensitivity and specificity in predicting mortality in patients with chest infection and sepsis. However, comparison of the two scores as predictors of outcome shows that qSOFA has higher sensitivity (90.9% *vs* 81.8%), whereas LqSOFA has higher specificity (84.2% *vs* 78.9%). Because there is a need for effective reliable instruments to detect sepsis in the Emergency Department, where treatment in the *golden hour*[18] remains the cornerstone of therapy, use of additional modified indexes as means to improve sensitivity or specificity of detecting patients at risk for adverse outcome could be helpful.

Limitations of our study include the small sample size and the fact that it only includes data from elderly patients treated for respiratory failure in the Resuscitation room of the Emergency Department. The dynamic nature of the sepsis syndrome can make detection of sepsis difficult in the ED setting, and the qSOFA score alone has limitations in predicting outcome due to low sensitivity. The combination of qSOFA score with other clinical parameters and laboratory measurements could possibly identify more patients with sepsis who may benefit from further assessment and interventions in the ED. This clinical study suggests that serum lactate level, a sensitive finding reflecting anaerobic metabolism has comparable validity when added to qSOFA score, and its use in the calculation of prognostic scores already in use could be beneficial in clinical practice by improving specificity of predicting a bad outcome. However, because of the significant limitations of our study, further large prospective clinical studies are warranted to confirm and validate our findings.

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