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Research Article

Prognostic Accuracy of SOFA, qSOFA, SIRS Criteria and Lactate Level in Infected Patients Admitted in ICU

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Received: June 26, 2019; **Published:** July 15, 2019

Abstract

Background: Sepsis is identified according to the Sepsis-3 consensus as an increase of at least 2 points in the Sepsis-related Organ Failure Assessment (SOFA) score in patients who presented infection. The quick SOFA or qSOFA is considered as a predictive tool of sepsis and mortality when it is equal to 2 points or more. Systemic Inflammatory Response Syndrome (SIRS) criteria are of limited utility because of their low sensitivity. Hyperlactatemia, as known is a determinant of tissue hypoperfusion. Our objective was to evaluate the prognostic performance of SOFA > 2, SIRS > 2, qSOFA > 2 and lactate level > 2 mmol/l in infected patients.

Methods: 9-month prospective cohort study. Patients aged 18 years or older who had a proven or suspected infection were included. SOFA scores, SRIS criteria, SOFA q and lactate levels were determined within the first 24 hours of infection. The primary endpoint was hospital mortality at 30 days. The predictive power of the studied parameters was determined using using the area under the receiver operating characteristic curve (AUROC).

Results: A cohort of 71 cases was studied with mean age at 49.5 years. Bacterial pneumonia was the most common infection site (66%). In the first 24 hours of onset of infection the medians [IQR 25 - 75] of the SOFA, SRIS, and SOFA scores and lactate levels were respectively 6 [3 - 9], 3 [2 - 3], 1 [1 - 2] and 2.04 [0.65 - 3.4]. The progression to severe septic status was observed in 34 patients (48%) and norepinephrine was introduced in 32 cases. Median length of stay was 11 days [5 - 18] and mortality was 53%. Overall, the accuracy in predicting mortality of the 4 studied parameters was poor. An increase of SOFA score by at least 2 points had greater accuracy with AUROC = 0,762 [0,647 - 0,877], sensitivity = 74% and specificity = 79%.

Conclusion: In infected patients, the SOFA score had greater prognostic accuracy than the SIRS criteria, the qSOFA score or the lactate level. These results suggest that SIRS, qSOFA, and high lactate level may be useful in screening for sepsis, but this utility is limited in predicting mortality.

Keywords: *SOFA; qSOFA; SIRS; Lactate; Sepsis; Mortality; Intensive Care Unit*

Abbreviations

SOFA: Sepsis-related Organ Failure Assessment; q SOFA: Quick SOFA; SIRS: Systemic Inflammatory Response Syndrome; AUROC: Area Under the Receiver Operating Characteristic Curve; ICU: Intensive Care Unit; WBC: white Blood Cells; MAP: Mean Arterial Pressure; SBP: Systolic Blood Pressures; LOS: Length of Stay; APACHE: Acute Physiology and Chronic Health Evaluation; SAPS: Simplified Acute Physiology Score; RRT: Replacement Renal Therapy; SD: Standard Derivation; IQR: Interquartile Range; OR: Odds Ratio; CI: Confidence Interval

Background

Sepsis is a serious clinical condition that represents a patient's response to a severe infection. Normal immune and physiologic responses eradicate pathogens, and the pathophysiology of sepsis is due to the inappropriate regulation of these normal reactions. Overall, sepsis incidence is estimated to 31.5 million cases and has a very high mortality of 5.3 million deaths [1,2].

Sepsis remains difficult to define. The Consensus of 1991 (Sepsis-1) [3] established the systemic inflammatory response syndrome (SIRS) criteria and classified the sepsis gravity into sepsis/severe sepsis and septic shock according to the presence or not of organ failure and to the hemodynamic response to volume expansion [4]. Ten years later, the (Sepsis-2) consensus [5]; describe septic shock as a state of cardiovascular dysfunction associated with infection and unexplained by other causes. However, the recent advances in the pathophysiology of sepsis [6,7] required a revision of all these criteria used to identify it clinically.

On the 2016 (Sepsis-3) update, terminologies of SIRS and severe sepsis were removed. Sepsis is defined as a 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 [2]. A new score has been introduced; the SOFA quick (qSOFA) that is considered as a predictive tool of sepsis and mortality when it is ≥ 2. Hyperlactatemia is a biological indicator of mitochondrial chain dysfunction resulting mainly of tissue hypoperfusion. A serum lactate level > 2 mmol/L is a necessary item in the definition of septic shock with a good prediction of outcome.

Predicting mortality during sepsis based on clinical and biological criteria remains a topic of interest in septic patients admitted in ICU. We aimed in this study to assess the prognostic value in infected patients of SOFA ≥ 2, SIRS ≥ 2, qSOFA ≥ 2 and lactate level ≥ 2 mmol/l measured within the first 24 hours of admission in ICU.

Methods

Study design

A prospective cohort study conducted in the medical ICU of the University Hospital Center of La Rabta over 9 months (January to September 2018). The study was approved by the local ethics committee of our hospital. Given the non-interventional nature, informed consent was not required.

Study population

Patients older than 18 years who had a proven or suspected infection at admission or occurred during hospitalization were included. Patients with pre-existing organ (renal, hepatic, hematologic or chronic respiratory) failure were excluded in order not to bias the association of visceral dysfunction with sepsis.

Definitions:

- The SIRS was defined as the presence of at least 2 of these 4 criteria: temperature > 38°C or < 36°C, tachycardia (heart rate > 90 beats /min), tachypnea (respiratory rate > 20 cycles/min) or hypocapnia ($PaCO_2$ < 32 mmHg) and hyperleukocytosis or leukopenia (WBC > 12000 elts/mm^3 or < 4000 elts/mm^3).
- The SOFA score is composed of 6 items: PaO_2/FiO_2 ratio, Mean arterial pressure (MAP), Glasgow score, bilirubin level, platelet count, blood creatinine level and diuresis. Each item is rated from 0 to 4 depending on the degree of organ dysfunction. The maximum being 24 points.
- Sepsis was defined as an increasing of at least 2 points of the SOFA score during the first 24 hours.
- Septic shock was defined as a persistent hypotension requiring vasopressors to maintain MAP ≥ 65 mmHg and a serum lactate level > 2 mmol/L (18 mg/dl), despite adequate blood volume.
- qSOFA consists of 3 items assessing the respiratory, hemodynamic and neurological status. Each is rated at 0 or 1. At most the score takes 3 points.
- Hyperlactatemia was defined as serum lactate level ≥ 2 mmol/L.

Data collection: For all included patients, were recorded:

- Demographic and clinical characteristics (age, gender, co-morbidities, hospitalization reason, invasine ventilation, vasopressors or hemodialysis during the first 24 hours, ventilator duration, length of stay (LOS) and 30-day mortality.

- Variables of the studied Prognostic Scores, these scores were calculated within 24 hours of the occurrence of infection with extremes of intervals [best-worst] to [0 - 24], [0 - 4] and [0 - 3] respectively for SOFA, SIRS and qSOFA. A threshold of 2 or more was used with each scoring system.
- Details of suspected or documented Infection: localization of infection and results of microbiological sampling.

Outcome's criteria

The primary outcome was hospital mortality at 30 days. The secondary was the ICU-LOS. A prolonged ICU-LOS was defined as a duration exceeding 7 days.

Statistical analyses

Continuous and normally distributed quantitative variables were expressed as mean and standard deviation (SD) and compared using Student's t-test. Quantitative non-Gaussian distribution variables were expressed in median and interquartile (IQR) and compared using the Mann-Whitney U-test. Categorical variables were expressed as percentages and compared using the Chi 2 test or Fisher's exact test as appropriate.

The predictive power of the studied parameters was determined using the ROC curves with comparison of the confidence intervals at 95% of the areas under the curve.

A value of $p < 0.05$ was considered statistically significant. The data analysis was performed using the Statistical Package for Social Sciences (SPSS) version 20 software.

Results

Seventy-one were included among 80 patients; 9 patients were excluded for pre-existing organ dysfunctions. 35 patients (49%) had a SOFA increase of at least 2 points, 61 (86%) had a SIRS ≥ 2 and 34 (48%) a qSOFA ≥ 2. A lactate level ≥ 2 was observed in 51 patients (72%). Severe sepsis occurred in 34 cases with mainly a septic shock in 32 cases (Figure 1). All Clinical Characteristics of the study population are summarized on table 1. Bacterial pneumonia was the most common localization (66%), followed by central nervous system infection (15.5%) and urinary tract infection (7%).

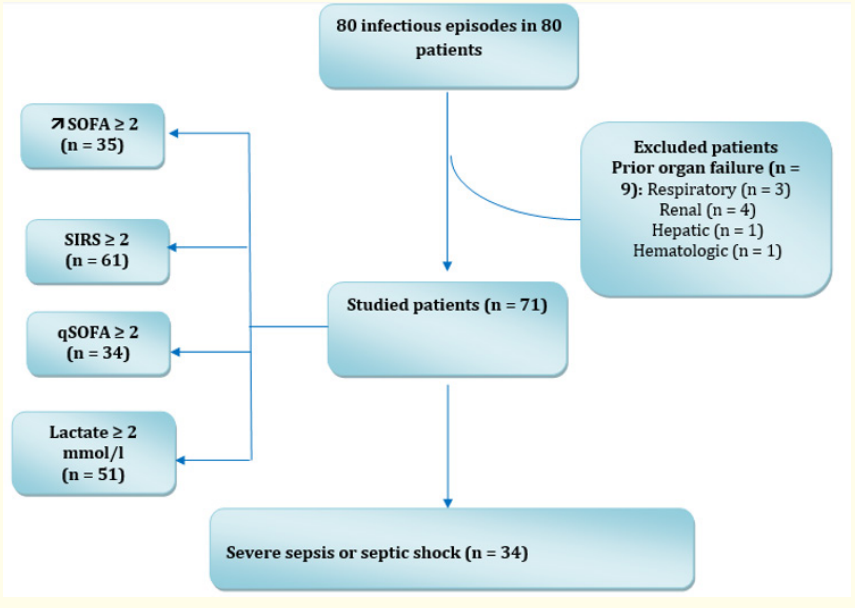

Figure 1: *Study's flow.*

SOFA: Sequential Organ Failure Assessment; qSOFA: quick SOFA; SIRS: Systemic Inflammatory Response Syndrome.

	Studied patients (n = 71)	
Sex Ratio (M /F)	0,97	
Age, years (moy ± SD)	49,5±17	
APACHE II, median [IQR]	12,5 [1-30]	
SAPS II, median [IQR]	29,5 [12-73]	
Co morbidities, n (%):		
• Diabetes	24 (33,8%)	
• Chronic respiratory failure	21 (29,5%)	
• Hypertension	19 (26,8%)	
• Immunocompromised	9 (12,6%)	
Admission mode, n (%):		
• Emergency department	42 (59,2%)	
• Medical	19 (26,8%)	
• Surgical	1 (1,4%)	
• Already hospitalized in ICU	9 (12,7%)	
Admission reason, n (%)		
• Respiratory	35 (49,3%)	
• Neurological	21 (29,6%)	
• Metabolic Disorder	6 (8,5%)	
• Infectious	5 (7%)	
• Hemodynamic	4 (5,6%)	
Scores at admission, median [IQR]		**Scores at H 24 of the onset of infection, median [IQR]**
• SOFA	6 [0 - 18]	6 [3 - 9]
• qSOFA	1 [0 - 3]	3 [2 - 3]
• SIRS	3 [0 - 4]	1 [1 - 2]
• Lactates, mmol/l	2.6 [0.9 - 4]	2.04 [0.65 - 3.4]
Vasopressors during the 1st 24h, n (%)	32 (45,1%)	
Invasive ventilation during the 1st 24h, n (%)	43 (60,6%)	
RRT, n (%)	15 (21,1%)	
Mortality, n (%)	38 (53,5%)	

Table 1: *Patients Baseline characteristics.*

SD: Standard Derivation; SOFA: Sequential Organ Failure Assessment; qSOFA: quick SOFA; SIRS: Systemic Inflammatory Response Syndrome; APACHE: Acute Physiology and Chronic Health Evaluation; SAPS: Simplified Acute Physiology Score; RRT: Replacement Renal Therapy

The table 2 displayed the independent factors related to mortality by logistic regression. Regarding the second outcome (prolonged ICU stay): no factor was found significant; invasive ventilation was near to significance with OR = 8,85, CI 95% [0,77-100], p = 0.07.

	OR, CI 95%,	p
SBP ≤ 100 mmHg	2,43 [0,98 - 6,01]	0,05
Vasopressors during the 1st 24H	2,60 [1,36 - 4,99]	0,002
Invasive ventilation during the 1st 24H	2,08 [1,17 - 3,69]	0,009
SOFA increase ≥ 2 points	3,93 [1,86 - 8,28]	0,001
qSOFA ≥ 2	2,08 [1,17 - 3,69]	0,009

Table 2: *Factors related to mortality by logistic regression.*

SBP: Systolic Blood Pressures; SOFA: Sequential Organ Failure Assessment; qSOFA: quick SOFA.

Overall, the accuracy in predicting mortality of the 4 studied parameters was modest (Figure 2). The SOFA score increase by at least 2 points had the best sensitivity/specificity cross with AUC = 0,762 [0,647 - 0,877], sensitivity = 74% and specificity = 79% (Table 3).

	AUROC	CI 95%	Sensitivity	Specificity
Increase in SOFA score ≥ 2	0,762	[0,647 - 0,877]	73,7%	79%
SIRS ≥ 2	0,538	[0,403 - 0,674]	89,5%	18%
qSOFA ≥ 2	0,664	[0,536 - 0,792]	63,2%	30,3%
Lactates ≥ 2 mmol/l	0,463	[0,328 - 0,598]	68,4%	75,8%

Table 3: *Prognostic accuracy of the studied parameters.*

SOFA: Sequential Organ Failure Assessment; SIRS: Systemic Inflammatory Response Syndrome; qSOFA: quick SOFA; AUROC: area under the ROC curve.

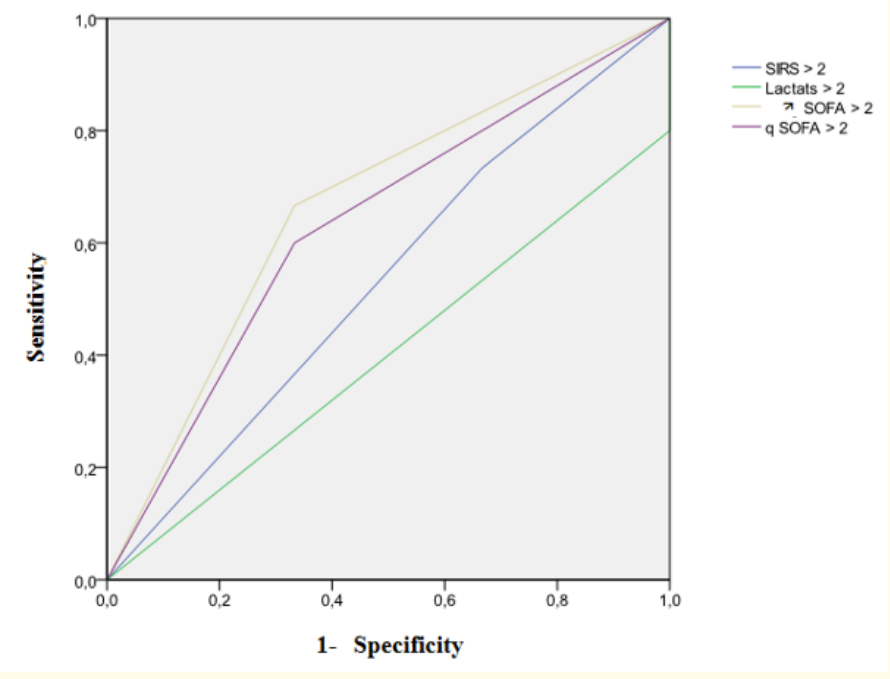

Figure 2: *ROC curves of SOFA, qSOFA, SIRS, lactae level to predict mortality.*

SOFA: Sequential Organ Failure Assessment; qSOFA: quick SOFA; SIRS: Systemic Inflammatory Response Syndrome.

The performance of these scores in the prediction of prolonged LOS was not performed since there was no significant association.

Discussion

Our prospective cohort collected 71 infected patients among them 34 patients (48%) presented sepsis and mortality was at 53%. We demonstrated that a worsening of SOFA score by a minimum of 2 points and a qSOFA ≥ 2 were independently associated with mortality (OR = 3.93, 95% CI [1.86 - 8.28], p = 0.001 and OR = 2.08, 95% CI [1.17 - 3.69], p = 0.009 respectively). The prognostic accuracy of the 4 studied parameters was of a modest contribution in the prediction of mortality. Nevertheless, a SOFA score > 2 at the beginning (or a secondary increase greater than 2), was better contributive (AUROC: 0,762, sensitivity: 74% and specificity: 79%).

The obvious improvement of the clinical diagnosis of sepsis in the sepsis-3 consensus, did not fail to raise criticisms mainly in the early detection of sepsis and the power of scores in the screening of patients at high risk of death. Williams., *et al.* [8] recently conducted a prospective study in Australia (8871 patients) and compared the reliability of SIRS and qSOFA in the occurrence of organ dysfunction. SIRS and qSOFA showed similar discrimination for organ dysfunction (AUROC 0.72 vs. 0.73). qSOFA was specific but weakly sensitive for organ dysfunction (96.1% versus 29.7% respectively).

A large Greek study including 3346 infections outside ICUs and 1058 infections in ICU showed that qSOFA had a low sensitivity for early evaluation of organ failure and mortality [9]. Despite the fact that lactate levels are known to be associated with a severe outcome in patients with sepsis [10-13], there was no added value in associating hyperlactatemia or qSOFA in this study [9]. Moreover, the authors of sepsis-3 did not find an improved value by adding lactates to qSOFA to predict intra-hospital mortality, with a similar AUROC: 0.80 (95% CI, 0.75 - 0.85) for qSOFA and lactate and 0.80 (95% CI, 0.74 - 0.85) for qSOFA alone [2]. Our values were lower at 0.66 (95% CI, 0.53 - 0.79) for qSOFA and 0.46 (95% CI, 0.32 - 0.59) for lactate. The combination of the two did not improve the prognostic performance with AUROC = 0.64 (95% CI, 0.50 - 0.79).

Eamon P., *et al.* [14] conducted a retrospective cohort analysis including 184,875 patients with an infection-diagnosed at admission in Australia and New Zealand from 2000 until 2015 (182 ICUs). the main judgment was intra-hospital mortality and the secondary criterion was secondary was a length of stay of 3 days or more; in agreement with Seymour., *et al* [6].

The predictive performance of intra-hospital mortality was significantly better using SOFA (AUROC, 0.753 [99% CI, 0.750 - 0.757]) than SIRS (AUROC, 0.589 [99% CI, 0.585 - 0.593]) or qSOFA (AUROC, 0.607 [99% CI, 0.603 - 0.611]) with significant differences: SOFA vs qSOFA, 0.146 [99% CI, 0.142 - 0.151]; SOFA vs SIRS, 0.164 [99% CI, 0.159 - 0.169], qSOFA vs SIRS, 0.018 [99% CI, 0.013 - 0.023], with P < .001) [1]. The superiority of SOFA score was also demonstrated in predicting prolonger ICU stay [1].

Our results are similar regarding the superiority of SOFA in predictive performance of mortality while no link was objectified with an extended LOS. Kaukonen., *et al.* [7] had previously shown that SIRS was a poor predictor of mortality in intensive care units [1]. This study confirmed that, qSOFA has a slight additional predictive value compared to that of SIRS and for these authors; the use of qSOFA may be allowed [1,14].

Finally, a SOFA score measured in the first 24 hours of infection, greater than 2 or increased by 2 points may screen patients at high risk of mortality which could benefit of a first-line broad-spectrum antibiotic as early as possible.

Conclusion

Based on our findings and the literature review; it becomes understandable that SIRS, qSOFA and hyperlactatemia, measured at the first 24 hours, have limited utility in predicting mortality in infected patients. Nonetheless, an increase in SOFA score of 2 points or more has a greater prognostic accuracy for intra-hospital mortality.

Declarations

Ethics Approval and Consent to Participate

The study was approved by the local ethics committee of our hospital. Given the non-interventional nature, informed consent was not required.

Consent for Publication

Not applicable.

Availability of Data and Materials

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

Competing Interests

The authors declare that they have no competing interests.

Funding

This research received no external funding.

Author Contributions

AT analyzed, interpreted the data, performed the statistical analysis and drafted the manuscript. CA collected the data and contributed to the written of the manuscript. FD, YT participated in the collection of data and revision of the manuscript. SA and SBL corrected with critical revision of the manuscript.

Acknowledgments

Not applicable.

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Volume 3 Issue 8 August 2019