



Association of Quick Sofa and Systemic Inflammatory Response Syndrome with mortality in septic patients

Associação do Quick Sofa e da Síndrome da Resposta Inflamatória Sistêmica com a mortalidade em pacientes sépticos
Asociación de Quick Sofa y Síndrome de Respuesta Inflamatoria Sistémica con mortalidad en pacientes sépticos

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ABSTRACT

Background and Objectives: sepsis, a life-threatening condition, requires early identification. The Quick Sofa score may contribute to identifying the risk of sepsis in patients admitted to the emergency department. However, these scores and criteria need extensive testing before being implemented in clinical practice. This study aimed to evaluate the association between the Quick Sofa score and the Systemic Inflammatory Response Syndrome criteria with mortality in critically ill septic patients from a university hospital. **Methods:** a retrospective observational study including 614 patients aged over 18 years, admitted to the intensive care unit due to sepsis or septic shock. **Results:** no statistically significant differences were observed in the Quick Sofa or the Systemic Inflammatory Response Syndrome between survivors and non-survivors. Patients with a Quick Sofa score ≥ 2 were associated with the development of septic shock ($p=0.00$). Patients scoring ≥ 2 on Systemic Inflammatory Response Syndrome criteria showed a significant association with intensive care unit stays longer than 72 hours ($p=0.013$). **Conclusion:** the scores and criteria evaluated were not associated with mortality in septic patients. High mortality rates and the incidence of septic shock highlight the need for more effective tools for early diagnosis of sepsis.

Keywords: Sepsis. Mortality. Organ Dysfunction Scores. Systemic Inflammatory Response Syndrome. Critical Care.

RESUMO

Justificativa e Objetivos: a sepse, uma condição ameaçadora à vida, deve ser identificada precocemente. A escala QuickSofa pode contribuir para a identificação do risco de sepse em pacientes admitidos na emergência. No entanto, estes escores e critérios devem ser amplamente testados antes de serem inseridos na prática assistencial. O objetivo do estudo foi avaliar a associação entre o escore Quick Sofa e os critérios da Síndrome da Resposta Inflamatória Sistêmica com a mortalidade de pacientes sépticos críticos de um hospital universitário. **Método:** estudo observacional retrospectivo que incluiu 614 pacientes maiores de 18 anos, internados na unidade de terapia intensiva por sepse ou choque séptico. **Resultados:** não houve diferença estatisticamente significativa entre as pontuações do escore Quick Sofa ou dos critérios da Síndrome da Resposta Inflamatória Sistêmica entre sobreviventes e não sobreviventes. Pacientes com escore Quick Sofa ≥ 2 apresentaram associação com o desenvolvimento de choque séptico ($p=0,00$). Pacientes com pontuação ≥ 2 nos critérios da Síndrome da Resposta Inflamatória Sistêmica tiveram associação estatisticamente significativa com a permanência na unidade de terapia intensiva por mais de 72h ($p=0,013$). **Conclusão:** os escores e critérios avaliados não foram associados à mortalidade de pacientes sépticos. A alta mortalidade e a incidência de choque séptico reforçam a necessidade de ferramentas mais eficazes para o diagnóstico precoce da sepse.

Descritores: Sepse. Mortalidade. Escores de Disfunção Orgânica. Síndrome da Resposta Inflamatória Sistêmica. Cuidado Intensivo.

RESUMEN

Justificación y Objetivos: la sepsis, una condición que pone en riesgo la vida, requiere identificación temprana. La escala Quick Sofa puede contribuir a identificar el riesgo de sepsis en pacientes admitidos en el servicio de emergencias. Sin embargo, estos puntajes y criterios necesitan ser ampliamente evaluados antes de implementarse en la práctica clínica. Este estudio tuvo como objetivo evaluar la asociación entre el puntaje Quick Sofa y los criterios del Síndrome de Respuesta Inflamatoria Sistémica con la mortalidad en pacientes sépticos críticos de un hospital universitario. **Métodos:** estudio observacional retrospectivo que incluyó a 614 pacientes mayores de 18 años ingresados en la unidad de cuidados intensivos debido a sepsis o shock séptico. **Resultados:** no se observaron diferencias estadísticamente significativas entre las puntuaciones de Quick Sofa o Síndrome de Respuesta Inflamatoria Sistémica entre los sobrevivientes y los no sobrevivientes. Los pacientes con un puntaje Quick Sofa ≥ 2 presentaron asociación con el desarrollo de shock séptico ($p=0,00$). Los pacientes con una puntuación ≥ 2 en los criterios de Síndrome de Respuesta Inflamatoria Sistémica mostraron una asociación estadísticamente significativa con una estancia en la unidad de cuidados intensivos por más de 72 horas ($p=0,013$). **Conclusión:** los puntajes y criterios evaluados no se asociaron con la mortalidad en pacientes sépticos. Las altas tasas de mortalidad y la incidencia de shock séptico destacan la necesidad de herramientas más eficaces para el diagnóstico temprano de sepsis.

Palabras Clave: Sepsis. Mortalidad. Puntuaciones en la Disfunción de Órganos. Síndrome de Respuesta Inflamatoria Sistémica. Cuidados Críticos.

INTRODUCTION

Sepsis is a life-threatening condition, and its early identification and diagnostic criteria are challenging for health care professionals.¹ The Global Burden of Disease study has estimated 48.9 million cases of sepsis worldwide, with more than 11 million deaths, representing 19.7% of all global deaths, being considered a public health problem.^{2,3}

In low- and middle-income countries, such as Brazil, the incidence and mortality by sepsis are considerably higher, ranging from 30 to 70%, however, epidemiologic data about sepsis are still scarce in those locations.^{2,4} In Brazil, it is estimated that 30% of the Intensive Care Unit (ICU) beds are occupied by patients with sepsis or septic shock, and that the mortality surpasses 50%.⁵

In 2016, the Third International Consensus Sepsis-3 brought updated definitions of the disease, proposing that suspected infection together with organ dysfunction define the presence of sepsis.¹ The organ dysfunction, which was very dependent on the criteria of the Systemic Inflammatory Response Syndrome (SIRS), has been associated with the Sequential Organ Failure Assessment (SOFA) score in the ICU.¹ And for the identification of suspected cases of sepsis in the emergency departments and general hospital ward settings, where SIRS was also used, it was proposed the use of a score termed quickSOFA (qSOFA), a simplified form of SOFA for the identification of patients with a higher risk for sepsis.¹

SIRS was devalued by the consensus Sepsis-3 as a screening tool because it is considered unspecific since it can precede organ dysfunction in conditions such as infection, trauma, pancreatitis and burns.¹ However, the qSOFA score, which was introduced in the same consensus, has been considered ineffective for the early identification of sepsis. Although qSOFA has high specificity, its sensitivity is low.¹ A meta-analysis showed a sensitivity of just 51.2% for the qSOFA criteria, while SIRS, despite less specific, has a superior sensitivity of 88.1%.⁶ Thus, although qSOFA has increased the diagnostic specificity, it happened at the expense of a significant reduction in the sensitivity, which limits its efficacy for screening in populations of patients with less severity.⁶

In more resourceful settings, the consensus Sepsis-3 definitions have the potential to improve the identification of sepsis.⁷ However, this is not the reality of developing countries with limited resources, such as Brazil, where the rapid identification of the disease is sought, prioritization of assistance to septic patients and the reduction in waiting times for admission to the ICU.⁸ In these unfavorable scenarios, it is paramount that those scores and criteria are broadly validated before their insertion into the assistance routines.⁸

Even though low- and middle-income countries concentrate a significant proportion of the sepsis cases and deaths, the majority of the studies were carried out in high-income countries, where the resources and the epidemiologic characteristics differ substantially.² This disparity hinders the extrapolation of the findings due to the impact of the regional variations in prevalent pathogens, associated chronic diseases, and healthcare infrastructure.^{9,10}

The applicability of qSOFA or SIRS in low- and middle-income countries, such as Brazil, is still not well researched, representing a significant gap in the knowledge.⁸ This lack of data limits the development of effective diagnostic strategies, aligned with the local specificities. In limited resources settings, the early detection of sepsis should be the main focus of any initiative aiming to improve the quality and safety of assistance.^{8,10}

In view of that, the objective of our study was to evaluate the association of the qSOFA score and the SIRS criteria with the mortality of critical septic patients in a university hospital in Brazil, adding to the assessment of these tools in a limited resources setting.

METHODS

Retrospective observational study carried out in a public, tertiary, university hospital located in Southern Brazil. It is an 860-bed hospital, from which 46 are for the emergency service and 60 are ICU. Patients aged 18 years or older, admitted to the ICU with a diagnosis of sepsis or septic shock were included in the study. Patients were followed up from the identification of organ dysfunction related to sepsis up until the hospital discharge or death. Data was collected from 2016 to 2017. Patients with incomplete records in the institution system were excluded from the study.

Information collected included sociodemographic data, comorbidities history, and clinical variables, such as the values of SAPS 3 (Simplified Acute Physiology Score 3). The outcomes analyzed were stay in the ICU over 72h, evolution to septic shock, and death. The organ dysfunction was identified in different wards such as general wards, emergency and ICU.

qSOFA score and SIRS criteria were evaluated from the signs and clinical symptoms recorded at the time of the first organ dysfunction related to sepsis. qSOFA allocates one point for each of the following clinical signs: systolic blood pressure <100 mmHg, respiratory rate > 22 rpm, and altered mental status (Glasgow Coma Scale ≤ 14). On the other hand, SIRS criteria allocate one point to: temperature > 38.3°C or < 36°C, heart rate > 90 bpm, and respiratory rate > 20 rpm. Only the criteria possible to assess at the bedside were considered. Both scores were considered positive if ≥ 2.

This study included all eligible patients assisted from 2016 to 2017, with no previous sample calculation. This approach was taken to ensure the enrolment of as many patients as possible due to the retrospective nature of the study and the availability of data in the institution.

Statistical analyses were performed using the software Statistical Package for Social Sciences (SPSS), version 21.0. Categorical variables were described using absolute and relative frequencies, while continuous variables were presented as the mean and standard deviation, or the median and interquartile range (25–75), depending on the normality assessed by the Kolmogorov-Smirnov test. For the association analyses, the chi-squared test was used for categorical variables, Student's t test for the continuous variables with normal distribution, and Wilcoxon-Mann-Whitney for non-normal distributions. The discrimination performance was evaluated by the ROC curve (Receiver Operating Characteristic). The significance level was set at 5% ($p < 0.05$).

The study was conducted in accordance with the resolutions nº 466/2012, nº 510/2016, and nº 580/2018 from the Brazilian National Health Council, which regulate research involving human subjects. The project was approved by the institutional Research Ethics Committee under the number nº 16-0317, and by the Research Commission from the *Escola de Enfermagem da Universidade Federal do Rio Grande do Sul*. The project was inserted into Plataforma Brasil on August 17th, 2016, under CAAE 57326316300005327.

RESULTS

Six-hundred and fourteen patients diagnosed with sepsis were included in the study. They were predominantly young, with a high disease severity profile. The main infectious sites were the respiratory tract and abdomen. More than half of the patients had a community-acquired infection (Table 1).

Table 1. Sample characterization: sociodemographic aspects, clinical variables at the time of the diagnosis of sepsis, and times assessed. Data presented as mean and standard deviation, or median and interquartile interval (P25-P75), and absolute numbers and frequency, Porto Alegre, Rio Grande do Sul, 2016-2017.

Variables	
Age (years) mean±SD	60.7 ±15.5
Female n (%)	279 (45.4)
SAPS 3 mean±SD	67.8 ±14
Comorbidities n (%)	
Arterial Hypertension	297 (48.4)
Diabetes Mellitus	179 (29.2)
Neoplasia	133 (21.7)
Heart failure	116 (18.9)
Main infectious site n (%)	
Respiratory	314 (51.1)
Abdominal	131 (21.3)
Urinary	60 (9.8)
Others	109 (17.8)
Type of Infection n (%)	
Community-acquired	371 (60.4)
Ward of origin (organ dysfunction) n (%)	
Emergency	304 (49.5)
ICU	75 (12.2)
General wards	235 (38.2)
Time (days or minutes) Median (IQR)	
Total ICU stay	7.6 (3.8-14.0)
Total length of hospital stay	24.2 (12.9-43.0)
Length of time for the identification of sepsis (min)	30 (0-360.4)
Time interval between sepsis diagnosis and death	10.9 (5.1-23.0)

Abbreviations: Abbreviations: min= minutes; SD= standard deviation; N= absolute number; IQR= interquartile range.

Approximately 70% of the patients need mechanical ventilation in the first 24 hours after the diagnosis, and 27.2% needed infusion of vasopressor drugs. In the qSOFA score, the most frequent alteration was the respiratory, yet by SIRS criteria, heart rate alterations were more common.

Sepsis evaluation criteria and severity of disease were assessed in this sample (Table 2). An ICU stay longer than 72h occurred for 483 (78.7%) patients, and 283 (46%) presented septic shock. General mortality was 46.6% (286 patients), from which 48.8% (n=138) was in patients with septic shock.

Table 2. Scores and severity of septic patients admitted to the ICU of a public university hospital, Porto Alegre, Rio Grande do Sul, 2016-2017.

qSOFA score	
Median total (IQR)	1.0 (1-2)
Type of alteration n (%)	
Respiratory	326 (53.1)
Blood pressure	246 (40.1)
Neurologic	210 (34.2)
SIRS Criteria	
Type of Alteration n (%)	
Axillary temperature	252 (41)
Heart rate	432 (70.4)
Respiratory rate	361 (59)
Outcome n (%)	
Need ICU >72h	483 (78.7)
Septic shock	283 (46)
Death	286 (46.6)

Abbreviations: SD= standard deviation; n= Absolute number; IQR= interquartile range.

qSOFA score and SIRS criteria discrimination for mortality is represented by the ROC curve (Figure 1).

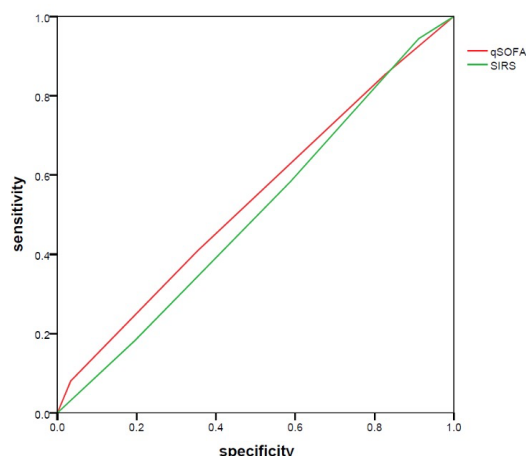


Figure 1. qSOFA score and SIRS criteria ROC curve for mortality.
 qSOFA score (AUC ROC = 0.53, CI95%= 0.49-0.58, p-value= 0.09).
 SIRS criteria (AUC ROC= 0.50, CI95% 0.45-0.54, p-value = 0.96).

From 614 patients evaluated, 328 (53.4%) survived. When we compared the points for qSOFA score and SIRS criteria of the survivors and non-survivors, there was no statistically significant difference (Figure 2).

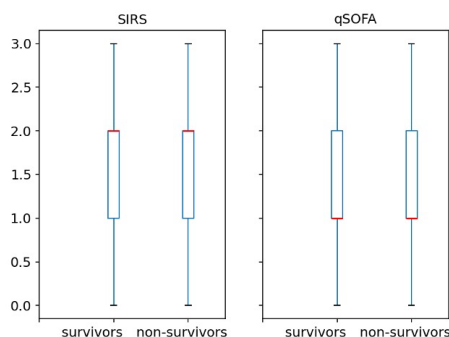


Figure 2. Evaluation of qSOFA and SIRS scores between survivors and non-survivors.
 Score Box-Plot, survivors/non-survivors: median qSOFA; (IQR): survivors 1.0 (1-2); non-survivors 1.00 (1-2); p-value* 0.073. Median SIRS;(IQR): survivors 2.0 (1-2); non-survivors 2 (1-2); p-value* 0.958. * Mann-Whitney test used to calculate significance.

qSOFA score and SIRS criteria, according to Sepsis-3 guidelines, were analyzed and presented to evaluate the association of the scores with survivors and non-survivors (Table 3).

Table 3. Association of qSOFA score and SIRS criteria with survivors and non-survivors.

Scores vs Non-survivors	Survivors	Non-survivors	Total	P-value*
qSOFA < 2 n (%)	212 (55.6)	169 (44.4)	381 (100)	0.184
≥ 2 n (%)	116 (49.8)	117 (50.2)	233 (100)	
SIRS < 2 n (%)	135 (53.1)	119 (46.9)	254 (100)	0.975
≥ 2 n (%)	193 (53.6)	167 (46.4)	360 (100)	

Evaluation of the association between qSOFA and SIRS ≥ 2 vs < 2 points with the outcome non-survivor. P-value*= chi-squared test used to calculate significance. The percentage of each outcome is presented under the total number.

Patients with qSOFA ≥ 2 points presented association with the development of septic shock (p=0.00), but not with length of stay in the ICU (p=0.647). On the other hand, patients who had ≥ 2 points in SIRS criteria

needed to stay for over 72h in the ICU (p=0.013), but there was no association with the development of septic shock (p=0.681) when compared with those patients with < 2 points.

DISCUSSION

The findings of the present study revealed that there was no association between qSOFA and SIRS criteria with the mortality of critical septic patients. Likewise, there was no statistically significant difference in the mortality of patients with qSOFA score or SIRS criteria < 2 e ≥ 2 points. However, SIRS ≥ 2 was associated with a longer ICU stay (p=0.013), while qSOFA ≥ 2 was associated with the development of septic shock (p=0.00). These results are in accordance with previous studies which pointed out the limitations of both scores in the prediction of mortality in severe septic patients.^{11,12}

Multicentric studies, such as the ones conducted in Australia and New Zealand, had already showed those limitations.¹¹ Besides that, a systematic review revealed that qSOFA score has a high specificity (0.75), but a low sensitivity (0.41). On the other hand, SIRS criteria have a higher sensitivity (0.87), but the specificity is reduced. Such characteristics indicate that qSOFA is more effective to identify patients with higher risk of mortality, while SIRS can be more useful as a tool for an initial screening.¹²

Our study reinforces that, although both the score and criteria have limited clinical usefulness in the identification of septic patients with a high risk of death (AUC ROC < 0.55), the sole use of qSOFA as a criterium for the early identification can delay even more the diagnosis in those patients.

In our findings, about 60% of the patients presented ≥ 2 points in SIRS, while only 38% scored ≥ 2 points in qSOFA, highlighting qSOFA's limitation for the early identification of sepsis cases in this population. Although qSOFA is useful to predict outcomes such as death and organic dysfunction in some locations, its low sensitivity reduces its effectiveness as a bedside screening tool.¹³ Alternatives such as score qSOFA ≥ 1 or the addition of lactate in the evaluation have been suggested to improve the sensitivity in resource-limited settings.^{14,15}

In low- and middle-income countries such as Brazil, where the access to ICU beds is limited and the demand for assistance is high, the early identification of sepsis is crucial, especially due to its high lethality.¹⁶ Studies show that, in high-income countries, sepsis mortality ranges from 17 to 26%.⁴ However, in Brazil, those rates are significantly higher, being as high as 41.6% in public hospitals.¹⁷

In our sample, mortality was 46.6% (n=286), being even higher among the patients with septic shock (48.8%, n=138). These numbers strongly contrast with the high-income countries and reinforce the obstacles encountered in Brazil, such as diagnostic delays and in the transfer to the ICU, which ideally should happen in up to six hours after the identification of sepsis.^{4,16} They compromise the identification and the timely management of patients with a higher risk of death.¹⁷

Another relevant finding of the study is the ward of origin of patients at the time of organic dysfunction identification. Nearly half of the patients were diagnosed in the emergency department, which reinforces the need for screening tools that allow the early identification at the bedside. Currently, these patients get to the ICU in critical condition, with a mean SAPS 3 of 67.8±14 for survivors, and 71.7±14.3 for non-survivors, demonstrating high severity and mortality risk at the time of diagnosis.

Literature suggests that physiological alterations precede sepsis formal diagnosis in up to 8 hours and that the patient's survival depends on the team's ability to identify those alterations early and act quickly.^{18,19} In this context, the role of the multidisciplinary team is crucial in the early identification of clinical deterioration signs and in the implementation of effective interventions.²⁰

The 2021 Surviving Sepsis Campaign (SSC) recommends avoiding the sole use of qSOFA as a screening tool for sepsis or septic shock, giving preference to scores such as NEWS (National Early Warning Score) or MEWS (Modified Early Warning Score), which presented higher accuracy in different scenarios.²¹ Nevertheless, qSOFA as well as SIRS are still widely used, and their validation in low- and middle-income countries is yet a hiatus that requires further studies.²¹

The study limitations are related to the data collection, which was done retrospectively. Another limitation is related to the patient's severity, since 88% of patients needed to be transferred to the ICU after the diagnosis of sepsis, which occurred initially at the general wards or emergency department. Future research about how to improve these models and increase the standardization of clinical protocols are paramount to make progress in the treatment of sepsis and its complications.

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AUTHORS' CONTRIBUTIONS

Vanessa Frighetto Bonatto contributed to the literature review, writing of the abstract, introduction, methods, discussion, results interpretation and description, tables elaboration, conclusions, review and statistical analysis. **Karina de Oliveira Azzolin** contributed to the writing of the abstract, methods, results interpretation, conclusions, review and statistical analysis. **Jaqueline Sangiogo Haas** contributed to the project management, literature review, writing of the abstract, introduction, methods, discussion, results interpretation and description, conclusions, review and statistical analysis. **Miriane Melo Silveira Moretti** contributed to the project management, literature review, writing of the abstract, introduction, methods, discussion, results interpretation and description, conclusions, review and statistical analysis. **Arianne dos Santos Gomes** contributed to the writing of the abstract, article review and submission. **Rafael Barberena Moraes** contributed to the writing of the abstract, methods, results interpretation, conclusions, review and statistical analysis. **Gilberto Friedman** contributed to the writing of the abstract, methods, results interpretation, conclusions, review and statistical analysis.

All authors approved the final version of the article to be published, and are responsible for all aspects of the work, including the assurance of its precision and integrity.

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