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New sepsis criteria: do they replace or complement what is known in the approach to the infectious patient?

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ABSTRACT

There have recently been profound changes in both the definitions of sepsis and septic shock and the diagnostic criteria established for daily clinical practice. In addition, a new screening tool known as qSOFA has been introduced to identify patients at risk of a poor short-term outcome. This score has been accompanied by some controversy due to presenting a lower sensitivity than the systemic inflammatory response criteria previously used to identify such patients. In this article, we shall summarise and analyse the most important recently published studies in relation to these new criteria.

Keywords: sepsis criteria, infection, mortality

Nuevos criterios de sepsis: ¿sustituyen o complementan lo conocido en la aproximación al enfermo infeccioso?

RESUMEN

Recientemente se han producido cambios profundos tanto en las definiciones de sepsis y shock séptico como en los criterios diagnósticos establecidos para la práctica clínica diaria. Además, se ha introducido una nueva herramienta de cribado para la identificación de pacientes con riesgo de malos resultados a corto plazo, el qSOFA. Esta escala se ha acompañado de cierta controversia al presentar una menor sensibilidad que los criterios de respuesta inflamatoria sistémica utilizados previamente para la identificación de estos pacientes. En el presente trabajo resumimos y analizamos los estudios más importantes recientemente publicados en relación con estos nuevos criterios.

Palabras claves: criterios de sepsis, infección, mortalidad

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INTRODUCTION

New criteria have recently been adopted to define sepsis. In this article, we shall review the causes that triggered the need to redefine this syndrome, the reason for the established definitions, and the problems and criticisms which have arisen as a result.

THE PROBLEM OF PREVIOUS DEFINITIONS

From the pathophysiological point of view, sepsis determines alterations in the metabolic pathways and cellular and circulatory alterations, which cause an increase in the mortality of the infected patient[1]. Previous definitions of sepsis were based on and reflected systemic manifestations of infection, which conceptually does not have to imply such pathophysiological alterations or necessarily indicate an abnormal host response to infection. Systemic inflammatory response syndrome (SIRS), used for the diagnosis of sepsis up to now, may simply reflect an adaptive and transient response. In other words, it reflects the host's inflammatory response to infection, but does not necessarily indicate an abnormal response with risk of death[2,3].

Meanwhile, SIRS criteria are present in many hospitalised patients who do not present with infection or poor clinical evolution[4,5]. In short, the problem was that the previous definition of sepsis did not always reflect a risk situation in an infected patient.

THE PROPOSED SOLUTION TO THE PROBLEM

The new definitions state that sepsis is a potentially life-threatening organic dysfunction, caused by an abnormal host response to infection[6]. In this sense, focus is given to the importance of the non-homeopathic host response to infection, the potential lethality, which greatly exceeds that of an

Table 1 **Studies that evaluate the prognosis scores in infected patients.**

Author	Design	Population	Mortality	False Negat. [n(%)]	SIRS	qSOFA	SOFA	Reference
Seymour CW	R	ED	Hosp.	SIRS: 679 (1.6) qSOFA: 849 (1.5) SOFA: 604 (1.4)	SE: 64 SP: 65 PPV: 5 NPV: 98	SE: 55 SP: 84 PPV: 9 NPV: 98	SE: 68 SP: 67 PPV: 6 NPV: 99	JAMA 2016[8]
Williams JM	P	ED	30-day	SIRS: 74 (1.6) qSOFA: 163 (2.0) SOFA: 80 (1.2)	SE: 77 SP: 54 PPV: 6 NPV: 98	SE: 50 SP: 91 PPV: 18 NPV: 98	SE: 76 SP: 78 PPV: 11 NPV: 99	CHEST 2016[11]
Freund Y	P	ED	Hosp.	SIRS: 5 (2.2) qSOFA: 22 (3.3) SOFA: -	SE: 93 SP: 27 PPV: 11 NPV: 98	SE: 70 SP: 79 PPV: 24 NPV: 97	-	JAMA 2017[10]
Seymour CW	R	ICU	Hosp.	SIRS: 117 (9.3) qSOFA: 103 (4.3) SOFA: 26 (3.7)	SE: 91 SP: 17 PPV: 18 NPV: 91	SE: 92 SP: 34 PPV: 21 NPV: 96	SE: 98 SP: 10 PPV: 17 NPV: 96	JAMA 2016[8]
Raith EP	R	ICU	Hosp.	SIRS: 2.387 (9.8) qSOFA: 11.332 (13.6) SOFA: 793 (4.3)	SE: 93 SP: 15 PPV: 20 NPV: 90	SE: 67 SP: 48 PPV: 23 NPV: 86	SE: 98 SP: 12 PPV: 20 NPV: 96	JAMA 2017[9]

False Negat.: false negatives; SIRS: Systemic inflammatory response syndrome; SOFA: Sequential Organ Failure Assessment; R: retrospective; P: prospective; ED: emergency department; ICU: intensive care unit; Hosp: in hospital; SE: sensitivity; SP: specificity; PPV: positive predictive value; NPV: negative predictive value

infection, and the need for urgent identification. The importance of including "life-threatening organic dysfunction" in the definition is consistent with the pathophysiology underlying the syndrome: cell defects, and physiological and biochemical abnormalities within specific organ systems. Septic shock is defined as a subset of patients with sepsis where the underlying abnormalities of cellular and circulatory metabolism are deep enough to substantially increase mortality[6].

In order to establish the diagnostic method which reflects these definitions, extensive databases were retrospectively analysed. Patients were categorised according to different known prognostic scores (SIRS, LODS, SOFA) and the main outcome variable was in-hospital mortality[7]. Thus, it was concluded that SOFA was the most parsimonious score to diagnose sepsis, and that the cut-off point of 2 or more was the one that showed the greatest difference of mortality between the groups once the patients were categorised.

The diagnosis of septic shock was defined as the presence of maintained hypotension despite fluid therapy with the requirement of vasopressors and a lactate > 2 mmol/l. These criteria identify a subgroup of patients with sepsis who in the database analysis presented with a significantly higher mortality than the other patients[8].

Although from the conceptual point of view these new definitions have not been criticised, the problem of the methodology used to establish the diagnostic criteria is that it was carried out by means of retrospective analysis of databases where there is an important loss of data in several variables, which could affect the outcomes obtained.

THE PROBLEM OF THE PROPOSED SOLUTION

The problem of diagnosing sepsis based on the SOFA score is that this scale contains analytical variables, which could determine a delay in diagnosis and in the start of treatment, and also restricts the care level where it can be performed. For this reason, the new definitions are accompanied by a new methodology which is useful for the screening of patients at risk of suffering sepsis, namely qSOFA, and in which specific treatment should be initiated pending the analytical results that enable SOFA to be conducted.

The adoption of variables included in qSOFA (respiratory rate ≥22 rpm, altered level of consciousness and systolic blood pressure ≤100 mmHg) as a screening tool is also a consequence of the retrospective analysis of the same databases[7]. In this way, it was observed that, in terms of in-hospital mortality, the combination of these variables presented the best area under the curve (AUC) as opposed to the other scores evaluated in patients not admitted to critical care units.

Several studies have subsequently evaluated the usefulness of qSOFA to identify patients at risk of in-hospital mortality or at 30 days[9-11]. These studies have confirmed that qSOFA is the

best AUC prognostic score to identify the infected patient at risk of mortality. However, when assessing the sensitivity and specificity of the different scales for established cut-off points (≥2 points), we can see the lower sensitivity and greater specificity of qSOFA versus SIRS for the risk stratification of these patients[9-11]. The problem of SIRS has been its use as a diagnostic tool for sepsis, but we should question whether it could be useful as a screening tool[12,13].

At this point, it is worth asking what the purpose of a screening test should be. When the price of omitting the diagnosis is very high, as occurs in serious but treatable diseases, a sensitive test is particularly useful, since it allows the doctor to exclude the possible disease when its outcome is negative[14]. A screening test has no diagnostic purpose. People with positive or suspected findings can be evaluated with a more specific diagnostic test to define or reject the final diagnosis. High specificity is useful for confirming a diagnosis which has been suggested by other data, providing few false-positive outcomes[15].

However, sensitivity and specificity do not answer these two questions: if the test is positive, what is the probability of the individual having the disease?; If the test is negative, what is the probability of it not appearing? To answer these two questions, which we actually pose in regular clinical practice, it is necessary to know the positive predictive value (PPV) and the negative predictive value (NPV)[16].

In this way, and in relation to a screening test which can rule out the presence of a seriously infected patient, in regular clinical practice we are interested in having a high negative predictive value that prevents a significant number of false negatives.

In table 1, we can see the different recently published studies[9-11], which evaluate the various prognostic scores. It can be observed how qSOFA detects a population in emergencies with a higher risk of death (specificity and higher PPV) without losing NPV with regard to SIRS. Despite the lower qSOFA sensitivity, false negatives occur in a similar percentage with both scores.

When we evaluated the studies performed in patients admitted to critical care units, we observed that the NPV of SIRS and qSOFA decreased and the false negatives increased. This is because the outcomes of predictive values are influenced by the prevalence of the disease, in this case by the prevalence of mortality. Being critical patients, mortality is higher and, therefore, the NPV declines. For this reason, the best outcomes in this population are obtained with SOFA.

CONCLUSION

The new definitions of sepsis are conceptually more appropriate than previous ones. SOFA as a diagnostic tool is also more useful as it better identifies an infected population at risk of poor outcomes than SIRS.

For the screening of sepsis, qSOFA has shown less sensitivity than SIRS in populations treated outside critical care units, but with a similar NPV. As it is a simpler score, which does not require any analytical variable and can therefore be performed at any level of care, qSOFA should replace SIRS as a tool to be used to identify at-risk patients.

However, there are certain limitations which may compromise our knowledge to date. We should not forget that the studies which led to these new definitions are retrospective; that there is a large loss of data in important variables in these databases, and even in later prospective studies; and that the results have not been evaluated in special populations, such as immunosuppressed patients or the elderly.

CONFLICTS OF INTEREST

None to declare

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