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CE - EDITORIAL

Using scores in septic patients

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Since rivers' landmark study published in 2001 [1], sepsis has been considered a time-dependent condition, as demonstrated by a significant amount of pathophysiological and clinical data. Given that, attention has been devoted to implement early diagnosis of sepsis. Indeed, if we were able to identify in advance patients at a higher risk of complications, we could follow them more closely and treat them more aggressively, hopefully achieving a better outcome.

One line of research has investigated sensitivity and specificity of biological markers produced by the inflammatory, immunologic, and coagulative phenomena typical of the septic syndrome. Although interesting results have been produced, the overall conclusion is that no single marker can predict with sufficient precision either the presence of sepsis or the risk of a negative outcome.

A second line of research, of which the two meta-analyses published in this issue of IAEM [2, 3] are an example, sets its focus on the potential use of clinical scores. Time-honored scores, such as SIRS and SOFA, have been evaluated together with the more recent such as qSOFA.

For over 25 years, the presence of an SIRS (systemic inflammatory reaction syndrome) has been a fundamental element for the recognition of sepsis. Sepsis diagnosis was made in presence of a suspected infection associated with at least two abnormal values among body temperature, heart rate, respiratory rate, and the number of leukocytes. Although SIRS criteria are a reasonably sensible index of sepsis, they are not specific, since they may be present in many non-infectious conditions.

The Sepsis-Oriented Organ Failure Assessment (SOFA) score was created to describe quantitatively, and as objectively as possible, the degree of organ dysfunction/failure over time in groups of patients or even in individual patients. Calculating an SOFA is time consuming, since it requires a number of clinical and laboratory parameters that reflect the dysfunction of several organs. For this reason, it is used in the ICU rather than in the ED.

Quick SOFA (qSOFA) was recently introduced by the third international consensus on sepsis (Sepsis-3) with the aim to offer a handy score to identify patients at high risk of a negative outcome in the ED (death or transfer to ICU). One point is counted for each of three items: altered consciousness (Glasgow Coma Score ≤ 13); systolic arterial pressure ≤ 100 mmHg; and respiratory rate ≥ 22/min.

High values of SOFA and qSOFA are associated with high mortality; however, they both identify patients, whose severity is already clinically evident, while they do not facilitate early identification of patients at high risk when signs and symptoms of sepsis are more nuanced.

The two meta-analyses published in this issue of IAEM compare SIRS and qSOFA in septic patients outside intensive care units. More specifically, Franchini and colleagues present a thorough revision of 12 observational studies that enroll a total of 80,941 patients, to compare the performance of SIRS and qSOFA in predicting in-hospital mortality of septic patients. Moreover, taking into account their results, the authors critically reappraise the clinical impact of the Sepsis-3 study that introduced for the first time the qSOFA score. This analysis showed that, in the non-intensive setting, the best rule-out clinical tool for mortality was the SIRS criteria, while the qSOFA score provided the highest specificity and LR+.

The authors suggest that SIRS and qSOFA should not be deemed mutually exclusive and that a two-step approach should be preferred. An SIRS-based screening, followed by repeated sequential qSOFA assessments for prognostication, is proposed as a strategy that could optimize the use of these two tools.

The second meta-analysis, by Liu et al., offers a more complex approach to the use of qSOFA outside the ICU. While confirming the better sensitivity of SIRS and the higher specificity of qSOFA, data show also, counter-intuitively, the equivalent diagnostic accuracy of the two scores.

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In both meta-analyses, the results are difficult to interpret due to the high heterogeneity between the studies, mainly due to a wide range of mortality (between 3% and 20–27%).

Both meta-analyses, as well as most of the studies in the field, seem to somehow confuse the diagnostic and the prognostic levels. When approaching the differential diagnosis of a highly lethal syndrome such as sepsis, clinicians would benefit from a sensitive tool that rules out this condition. On the contrary, once the presence of sepsis has been recognized, they would be happy to use a highly specific tool, that could identify patients at high risk of negative outcome, to monitor and treat them more aggressively. Rather than comparing two different scores such as SIRS and qSOFA, it would probably be more appropriate to apply each of them for their specific purpose, using them in sequence, as Franchini et al. suggest, investigating this approach with ad hoc studies. It is important to remember that the SIRS criteria were used for many years in the Survival Sepsis Campaign, which helped to improve the prognosis of sepsis. Therefore, before replacing an indicator that has proven effective over time, more solid evidence is required.

The recent Sepsis-3 definition [4], de facto proposes to identify as sepsis a clinical condition that, up to the year 2016, had been called "severe sepsis". As a consequence, diagnostic attention is today focused on more severe patients who have at least one organ failure and that in most cases appear clinically compromised from the beginning, with no need of a score to help. Moreover, the new definition, which shifts the diagnosis of sepsis on more serious patients, somehow removes attention from those who, although not yet severe, are at high risk of developing, within hours or days, a dysregulated host response to the infection. Of note, half of patients with septic shock and one-third of those with sepsis, complain initially just about vague symptoms and do not have a fever nor other evident signs of infection. Most likely, in these cases, indicators will lose any value if, first of all, we do not develop the habit of "thinking sepsis", actively searching our patients for a possible source of infection. SIRS and qSOFA criteria might help as clinically valuable, but imperfect markers of sepsis [5].

The major limitation of the two meta-analyses is the heterogeneity of the included studies that could significantly affect the interpretation of the results; thus, we even wonder if it was worthwhile to engage in the meta-analytic effort. This should be considered as an incentive to searching a new way for designing the trials that make them easier to compare to each other and to meta-analyze.

It is clear, though, that the heterogeneity of studies is also due to the complexity of sepsis as a research topic. Sepsis is a syndrome, possibly even a set of syndromes, whose clinical manifestations and evolution depend on uncountable factors. Thus, it would not be reasonable to expect that a single laboratory value or a single clinical score can give us an easy "yes or no" answer. The proposal to compare scores and laboratory indicators with shear clinical gestalt, as it was done in the case of syncope and of pulmonary embolism, should not sound as a provocation.

In conclusion, we must recognize that a huge gap still divides research and clinical practice on sepsis. The world of ever-changing clinical definitions and that of real life are still far apart. If we were the patient, we would not probably care whether our risk to die for a respiratory sepsis is 10% or 20%. We would rather wish to receive prompt diagnosis, appropriate and personalized therapy, and careful monitoring.

Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

Statements on human and animal rights All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. This article does not contain any studies with animals performed by any of the author.

Informed consent For this type of study formal consent is not required.

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