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Clinical Insights

Sepsis scoring systems: Mindful use in clinical practice

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1. Introduction

Sepsis is a challenging condition: the high prevalence and the complexity of its clinical presentation lead to high morbidity and mortality. The most updated definition of sepsis and septic shock, Sepsis-3 introduced in 2016, changed the previous paradigm and highlighted the importance of the pathophysiological alterations and their prognostic implications. Sepsis is defined as a dysregulated inflammatory response to an infection, which leads to organ dysfunction, while septic shock is defined as a subset of sepsis in which underlying circulatory and cellular metabolism abnormalities are profound enough to substantially increase mortality [1]. This allowed to overcome the Sepsis-2 definition, based on the systemic inflammatory response syndrome (SIRS) criteria, considered poorly specific [2]. With the Sepsis-3 definition, SIRS criteria were sidelined and the sequential organ failure assessment (SOFA) score was introduced for the identification of organ dysfunction. Nevertheless, even the SOFA score presents some drawbacks, mainly related to the fact that it was developed for the ICU setting (e.g. it requires several clinical data and laboratory tests which are not available in the early phase of the diagnostic process). These features precluded its use as a diagnostic tool in the Emergency Department (ED) and led to the introduction of the quick SOFA (qSOFA). Such "quick version" of the SOFA score was developed with the aim of helping clinicians in the early identification of patients at risk of sepsis - especially in the ED – and was validated both retrospectively [3] and prospectively [4]. The goal seemed to be reached: qSOFA, in fact, is simple, does not require lab test and can be easily assessed. Unfortunately, even though it showed an improved specificity compared to SIRS criteria, several limitations have emerged during its use, mainly related to its relatively low sensitivity. As a matter of fact, the latest Surviving Sepsis Campaign guidelines have recommended against its use as a single screening tool [5]. Due to this complexity, many study protocols have been designed to simplify the diagnostic approach and the assessment of sepsis risk through the design and validation of different scores based on both clinical parameters and biomarkers; one study introduced an original diagnostic approach based on a nomogram build with a combination of clinical variables and biomarkers [6]. Therefore, several limitations impair the reliability of these *ad hoc* developed scores, and many authors proposed to recur to the national early warning score (NEWS) and the modified early warning score (MEWS) for the identification of patients with sepsis [7,8]. Even though they are not specifically intended for septic patients, their performance in such population seems encouraging. NEWS, emerged as the best predictor of adverse outcome in a large cohort of patients with different acute conditions, evaluated in the ED, and this result further supports its use in this setting [9].

Here, we aim at concisely reviewing the most used scores in the ED, as well as the information they provide in terms of sepsis identification, clinical deterioration and prognostic value. We would like to provide ED physicians with pragmatic information useful to enhance both knowledge and understanding of the different scores that can be used in the diagnosis of sepsis to promote their proper and aware utilization. In particular, we highlight the usefulness of MEWS and NEWS in identifying and managing patients with sepsis, especially in the ED. Table 1 portrays the scores analysed in this review.

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1.1. Clinical use of the scores

To optimize scoring information, with a pragmatic approach, it is extremely relevant that clinicians pay attention to some fundamental principles: the performances of all the scores depend on the population considered (unselected vs selected based on clinical suspicion) and the timing of data collection (single evaluation vs time course).

The further step aims at focusing which question the score will answer to; facing sepsis, in our opinion, the three most relevant questions can be summarized as follows:

- Does my patient have sepsis?
- Does my patient need intensive care admission or critical care interventions?
- Is my patient with sepsis at risk of death?

1.2. Does my patient have sepsis?

This is the most difficult challenge for physicians since no diagnostic test or biomarker can be considered as a gold standard for the diagnosis of sepsis. Moreover, Sepsis-3 definition is focused on organ dysfunction and often it fails in identifying early manifestations of sepsis [10]. The recognition of sepsis is sometimes made difficult also by the broad spectrum of clinical manifestations related to the source of infection, the etiological agent, the type of organ dysfunction, the time since symptoms onset. Other variables that deserve attention are the setting in which the patient is evaluated (ED vs general ward) as well as the presence of confounders – e.g. organ dysfunction may be caused by non-infectious disease – and the host characteristics (amongst the others immunosuppression, pre-existing conditions, medications taken). Consequently, scores interpretation suffers of the same problems, implying that clinical suspicion still plays a pivotal role in the diagnosis of sepsis. Serafim R et al., published a systematic review and meta-analysis of 7 studies of good quality, comparing qSOFA≥2 and SIRS≥2 in sepsis diagnosis outside the ICU [11]. Despite some limitations, such as the different size of the samples and the lack of homogeneity of the criteria for the diagnosis of sepsis, they found a better sensitivity for SIRS≥2 and a better specificity for qSOFA≥2; considering the Forest plot of sensitivity for the diagnosis of sepsis, SIRS≥2 emerged as the best predictor (risk ratio 1.32). Usman OA et al., conducted a study involving 64,995 unselected ED patients; the most relevant limitations of the study were the use of Sepsis-2 criteria, the retrospective,

Table 1
The table shows the main scores useful in the diagnosis and risk stratification of sepsis and septic shock.

Sistemic inflammatory response syndrome (SIRS)	Temperature > 38 °C or < 36 °C Heart rate > 90 beats/minute Respiratory rate > 20 acts/minute or $paCO_2$ < 32 mm Hg White cell count < 4000 or > 12,000 /μL, or >10 % immature (band) forms							
Sequential organ failure assessment (SOFA)		**0**	**1**	**2**	**3**		**4**	
	paO_2/FiO_2 (mm Hg)	> 400	≤ 400	≤ 300	≤ 200 with respiratory support		≤ 100 with respiratory support	
	Platelets x $10^3/mm^3$	> 150	≤ 150	≤ 100	≤ 50		≤ 20	
	Bilirubin (mg/dL)	< 1.2	1.2–1.9	2.0–5.9	6.0–11.9		≥ 12.0	
	Hypotension	No hypotension	Mean arterial pressure < 70 mmHg	Dopamine ≤ 5 *or* Dobutamine (any dose)	Dopamine > 5 *or* Epinephrine ≤ 0.1 *or* Norepineprhine ≤ 0.1		Dopamine > 15 *or* Epinephrine > 0.1 *or* Norepineprhine > 0.1	
	Glasgow coma score	15	13 – 14	10 – 12	6 – 9		< 6	
	Creatinine (mg/dL) *or* urinary output	< 1.2	1.2 – 1.9	2.0 – 3.4	3.5 – 4.9 or < 500 mL/d		5.0 or < 200 mL/d	
quick SOFA (qSOFA):	Respiratory rate (> 22 acts/min) Mental status (Glasgow coma score < 15) Systolic blood pressure < 100 mm Hg							
National Early Warning Score (NEWS)		**3**	**2**	**1**	**0**	**1**	**2**	**3**
	Respiratory rate (acts/min)	≤ 8		9 – 11	12 – 20		21 – 24	≥ 25
	Oxygen saturation (%)	≤ 91	92 – 93	94 – 95	≥ 96			
	Any supplemental oxygen		Yes		No			
	Temperature (°C)	≤ 35		35.1 – 36.0	36.1 – 38.0	38.1 – 39.0	≥ 39.1	
	Systolic blood pressure (mm Hg)	≤ 90	91 – 100	101 – 110	111 – 219			≥ 220
	Heart rate (beats/min)	≤ 40		41 – 50	51 – 90	91 – 110	111 – 130	≥ 131
	Level of consciousness				Alert			Verbal, Pain or Unresponsive
Modified Early Warning Score (MEWS)		**3**	**2**	**1**	**0**	**1**	**2**	**3**
	Systolic blood pressure (mm Hg)	< 70	71 – 80	81 – 100	101 – 199		≥ 200	
	Heart rate (beats/min)		< 40	41 – 50	51 – 100	101 – 110	111 – 129	≥ 130
	Respiratory rate (acts/min)		< 9		9 – 14	15 – 20	21 – 29	≥ 30
	Temperature (°C)		< 35		35 – 38.4		≥ 38.5	
	Level of consciousness				Alert	Voice	Pain	Unresponsive

single centre design with a predominately African-American population. With these limitations, the authors evaluated the diagnostic performances, in terms of sensitivity and specificity, of SIRS≥2, qSOFA≥2 and NEWS≥4 on 930 patients that were diagnosed by severe sepsis and septic shock at the end of the diagnostic workup. The results confirmed the good sensitivity (86.1 %) and relatively low specificity (79.1 %) of SIRS, the poor sensitivity (28.5 %) and the high specificity (98.9 %) of qSOFA, the good sensitivity and specificity of NEWS (84.2 % and 85 % respectively). The ROC curve analysis demonstrated the better diagnostic performance of NEWS, with an area under the curve (AUC) of 0.91, which was significantly higher than the ones of both SIRS and qSOFA (0.81 and 0.88, respectively, $p < 0.001$ for all comparisons) [12]. Oduncu AF et al., obtained similar results, in a prospective study involving 463 patients with either suspicion or diagnosis of infection in a single Turkish ED [13]. In conclusion, to answer the question, if our ED patient suffers from sepsis, NEWS – despite not specifically designed for sepsis – seems to perform better than both SIRS and qSOFA.

1.3. Does my patient need intensive care admission or critical care interventions?

Moskowitz A et al., introduced the novel outcome of "received critical care intervention" and compared the related predictive performance of both SIRS and qSOFA criteria [14]. This single centre retrospective study involved more than 24,000 patients admitted to the ED with suspected infection. Their results confirmed the poor sensitivity of qSOFA, especially if evaluated early - immediately after ED admission - in predicting the need of critical care intervention (sensitivity 13 %). In the same conditions, the SIRS criteria showed a sensitivity of 66 %. Moreover, 13.4 % of patients with a baseline qSOFA of 0 or 1 received a critical care intervention within 48 h. The main limitation of the study is related to poor sensitivity of the retrospective evaluation of the mental status. Nonetheless, these data demonstrated that qSOFA could not be considered a useful tool in early identification of impelling clinical deterioration of septic patients and it is not suitable to assist clinical decision-making. Churpek et al., conducted a single-centre prospective study demonstrating that both NEWS and MEWS were more accurate compared to SIRS and qSOFA in predicting the composite outcome of either mortality or ICU transfer in a cohort of patients with sepsis outside the ICU, either in the ED or hospital wards [15]. Also, the persistence of NEWS derangement seems to predict both ICU length of stay and mortality: Whebell SF et al., proposed the "score to door" time and demonstrated the significant correlation between this time and hospital mortality (adjusted OR 1.02, 95 % CI 1.0–1.04, $p = 0.026$). Therefore, timely assessment and close reassessment of NEWS are strongly recommended [16]. In addition, one should bear in mind that early identification of clinical derangement is facilitated by the continuous collection of clinical parameters, which may overcome the bias related to a "spot" collection: as soon as the patient worsens, a prompt identification of vitals deterioration allows the clinician to anticipate critical care interventions [17]. In conclusion, NEWS seems to be the most reliable tool for identifying which septic patients may benefit from ICU admission and critical care intervention, whereas both SIRS and qSOFA do not seem suitable for this purpose.

1.4. Is my patient with sepsis at risk of death?

According to the study of Churpek et al. [15], when mortality alone was considered as outcome, NEWS emerged as the best predictor in such specific septic population (AUC 0.77, 95 % CI 0.76–0.79) followed by MEWS (AUC 0.73, 95 % CI 0.71–0.74), qSOFA (AUC 0.69, 95 % CI 0.67–0.7) and SIRS (AUC 0.65, CI 0.63–0.66). Freund et al., evaluated the prognostic accuracy of Sepsis-3 criteria for in-hospital mortality: patients with suspected infection were enrolled in the ED [4]. The AUC analysis confirmed qSOFA≥2 as the most appropriate model for predicting mortality (AUC 0.80) compared both to SIRS≥2 (AUC: 0.65) and SOFA (deterioration ≥ 2 points - AUC: 0.77). The systematic review and meta-analysis published by Song JU et al., based on 23 previously published studies, evaluated sensitivity and specificity of SIRS criteria and qSOFA in predicting mortality in infected patients outside the ICU, mainly in the ED; the study showed a sensitivity of 0.86 *vs* 0.51 and a specificity of 0.29 *vs* 0.83 for SIRS≥2 and qSOFA≥2 respectively [18].

In conclusion, NEWS, MEWS and qSOFA emerged as good predictors of mortality in patients with sepsis, although qSOFA≥2 requires caution due to its low sensitivity. The SIRS criteria showed a worse performance than the other scores mentioned.

2. Discussion

In summary, MEWS and especially NEWS are promising tools for the diagnosis and risk stratification of sepsis in the ED; although not specifically designed for sepsis, they both confirmed good diagnostic and prognostic performances (better than qSOFA and SIRS) in many studies. These scores, designed to identify impelling clinical deterioration in different acute conditions, are more time consuming compared to qSOFA but they emerged as a unique tool for risk stratification of hospitalized patients. These features support their wide diffusion and require the implementation of education programs to increase the competence of physicians and nurses about their proper use [7]. Moreover, the availability of their automated computation within electronic health records can strengthen their advantages, encourage their utilization among the other scores and enable strict monitoring over time. On the other hand, SIRS criteria are sensitive but poorly specific predictors of diagnosis of sepsis and mortality; some of them in fact, are signs of infection and are not necessarily expression of dysregulated host response to the infection. Moreover, many patients with acute conditions other than sepsis may show 2 or more SIRS criteria. qSOFA is an effective predictor of mortality and it is not a diagnostic tool (it is not part of the definition of sepsis) due to its low sensitivity [19]. This implies that a qSOFA≥2 should be considered expression of a severe clinical condition rather than of an «early sepsis»; thus, the use of qSOFA alone may lead to delayed diagnosis and initiation of treatment with negative prognostic impact. For these reasons, also patients with qSOFA=1 should rise concern.

Nowadays we still lack the «ideal» score: machine learning and the combination of scoring systems with biomarkers seem to be the most promising scenarios for next years.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

References

[1] Singer M, Deutschman CS, Seymour CW, Shankar-Hari M, Annane D, Bauer M, Bellomo R, Bernard GR, Chiche JD, Coopersmith CM, Hotchkiss RS, Levy MM, Marshall JC, Martin GS, Opal SM, Rubenfeld GD, van der Poll T, Vincent JL, Angus DC. The third international consensus definitions for sepsis and septic shock (Sepsis-3). JAMA 2016;315(8):801–10. https://doi.org/10.1001/jama.2016.0287. PMID: 26903338; PMCID: PMC4968574.

[2] Churpek MM, Zadravecz FJ, Winslow C, Howell MD, Edelson DP. Incidence and prognostic value of the systemic inflammatory response syndrome and organ dysfunctions in ward patients. Am J Respir Crit Care Med 2015;192(8):958–64. https://doi.org/10.1164/rccm.201502-0275OC. PMID: 26158402; PMCID: PMC4642209.

[3] Seymour CW, Liu VX, Iwashyna TJ, Brunkhorst FM, Rea TD, Scherag A, Rubenfeld G, Kahn JM, Shankar-Hari M, Singer M, Deutschman CS, Escobar GJ, Angus DC. Assessment of clinical criteria for sepsis: for the third international consensus definitions for sepsis and septic shock (Sepsis-3). JAMA 2016;315(8):762–74. https://doi.org/10.1001/jama.2016.0288. Erratum in: JAMA. 2016 May 24-31;315(20):2237. PMID: 26903335; PMCID: PMC5433435.

[4] Freund Y, Lemachatti N, Krastinova E, Van Laer M, Claessens YE, Avondo A, Occelli C, Feral-Pierssens AL, Truchot J, Ortega M, Carneiro B, Pernet J, Claret PG, Dami F, Bloom B, Riou B, Beaune S, French Society of Emergency Medicine Collaborators Group. Prognostic accuracy of sepsis-3 criteria for in-hospital

mortality among patients with suspected infection presenting to the emergency department. JAMA 2017;317(3):301–8. https://doi.org/10.1001/jama.2016.20329. PMID: 28114554.

[5] Evans L, Rhodes A, Alhazzani W, Antonelli M, Coopersmith CM, French C, Machado FR, Mcintyre L, Ostermann M, Prescott HC, Schorr C, Simpson S, Wiersinga WJ, Alshamsi F, Angus DC, Arabi Y, Azevedo L, Beale R, Beilman G, Belley-Cote E, Burry L, Cecconi M, Centofanti J, Coz Yataco A, De Waele J, Dellinger RP, Doi K, Du B, Estenssoro E, Ferrer R, Gomersall C, Hodgson C, Hylander Møller M, Iwashyna T, Jacob S, Kleinpell R, Klompas M, Koh Y, Kumar A, Kwizera A, Lobo S, Masur H, McGloughlin S, Mehta S, Mehta Y, Mer M, Nunnally M, Oczkowski S, Osborn T, Papathanassoglou E, Perner A, Puskarich M, Roberts J, Schweickert W, Seckel M, Sevransky J, Sprung CL, Welte T, Zimmerman J, Levy M. Surviving sepsis campaign: international guidelines for management of sepsis and septic shock 2021. Crit Care Med 2021;49(11):e1063–143. https://doi.org/10.1097/CCM.0000000000005337. PMID: 34605781.

[6] Mearelli F, Fiotti N, Giansante C, Casarsa C, Orso D, De Helmersen M, Altamura N, Ruscio M, Castello LM, Colonetti E, Marino R, Barbati G, Bregnocchi A, Ronco C, Lupia E, Montrucchio G, Muiesan ML, Di Somma S, Avanzi GC, Biolo G. Derivation and validation of a biomarker-based clinical algorithm to rule out sepsis from noninfectious systemic inflammatory response syndrome at emergency department admission: a multicenter prospective study. Crit Care Med 2018;46(9):1421–9. https://doi.org/10.1097/CCM.0000000000003206. PMID: 29742588.

[7] Royal College of Physicians. National early warning score (NEWS): standardising the assessment of acute illness severity in the NHS. report of a working party. London: RCP; 2012.

[8] Subbe CP, Kruger M, Rutherford P, Gemmel L. Validation of a modified early warning score in medical admissions. QJM 2001;94(10):521–6. https://doi.org/10.1093/qjmed/94.10.521. PMID: 11588210.

[9] Covino M, Sandroni C, Della Polla D, De Matteis G, Piccioni A, De Vita A, Russo A, Salini S, Carbone L, Petrucci M, Pennisi M, Gasbarrini A, Franceschi F. Predicting ICU admission and death in the emergency department: a comparison of six early warning scores. Resuscitation 2023;190:109876. https://doi.org/10.1016/j.resuscitation.2023.109876. Epub 2023 Jun 17. PMID: 37331563.

[10] Verboom DM, Frencken JF, Ong DSY, Horn J, van der Poll T, Bonten MJM, Cremer OL, Klein Klouwenberg PMC. Robustness of sepsis-3 criteria in critically ill patients. J Intensive Care 2019;7:46. https://doi.org/10.1186/s40560-019-0400-6. PMID: 31489199; PMCID: PMC671689.

[11] Serafim R, Gomes JA, Salluh J, Póvoa P. A comparison of the quick-SOFA and systemic inflammatory response syndrome criteria for the diagnosis of sepsis and prediction of mortality: a systematic review and meta-analysis. Chest 2018;153(3):646–55. https://doi.org/10.1016/j.chest.2017.12.015. Epub 2017 Dec 28. PMID: 29289687.

[12] Usman OA, Usman AA, Ward MA. Comparison of SIRS, qSOFA, and NEWS for the early identification of sepsis in the Emergency Department. Am J Emerg Med 2019;37(8):1490–7. https://doi.org/10.1016/j.ajem.2018.10.058. Epub 2018 Nov 7. PMID: 30470600.

[13] Oduncu AF, Kıyan GS, Yalçınlı S. Comparison of qSOFA, SIRS, and NEWS scoring systems for diagnosis, mortality, and morbidity of sepsis in emergency department. Am J Emerg Med 2021;48:54–9. https://doi.org/10.1016/j.ajem.2021.04.006. Epub 2021 Apr 6. PMID: 33839632.

[14] Moskowitz A, Patel PV, Grossestreuer AV, Chase M, Shapiro NI, Berg K, Cocchi MN, Holmberg MJ, Donnino MW. Center for resuscitation science. Quick sequential organ failure assessment and systemic inflammatory response syndrome criteria as predictors of critical care intervention among patients with suspected infection. Crit Care Med 2017;45(11):1813–9. https://doi.org/10.1097/CCM.0000000000002622. PMID: 28759474; PMCID: PMC5663290.

[15] Churpek MM, Snyder A, Han X, Sokol S, Pettit N, Howell MD, Edelson DP. Quick sepsis-related organ failure assessment, systemic inflammatory response syndrome, and early warning scores for detecting clinical deterioration in infected patients outside the intensive care unit. Am J Respir Crit Care Med 2017;195(7):906–11. https://doi.org/10.1164/rccm.201604-0854OC. PMID: 27649072; PMCID: PMC5387705.

[16] Whebell SF, Prower EJ, Zhang J, Pontin M, Grant D, Jones AT, Glover GW. Increased time from physiological derangement to critical care admission associates with mortality. Crit Care 2021;25(1):226. https://doi.org/10.1186/s13054-021-03650-1. PMID: 34193243; PMCID: PMC8243047.

[17] Sun L, Joshi M, Khan SN, Ashrafian H, Darzi A. Clinical impact of multi-parameter continuous non-invasive monitoring in hospital wards: a systematic review and meta-analysis. J R Soc Med 2020;113(6):217–24. https://doi.org/10.1177/0141076820925436. PMID: 32521195; PMCID: PMC7439595.

[18] Song JU, Sin CK, Park HK, Shim SR, Lee J. Performance of the quick sequential (sepsis-related) organ failure assessment score as a prognostic tool in infected patients outside the intensive care unit: a systematic review and meta-analysis. Crit Care 2018;22(1):28. https://doi.org/10.1186/s13054-018-1952-x. PMID: 29409518; PMCID: PMC5802050.

[19] Vincent JL, Martin GS, Levy MM. qSOFA does not replace SIRS in the definition of sepsis. Crit Care 2016;20(1):210. https://doi.org/10.1186/s13054-016-1389-z. PMID: 27423462; PMCID: PMC4947518.