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Review

Sepsis and septic shock: New definitions, new diagnostic and therapeutic approaches

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ABSTRACT

Sepsis and septic shock are common life-threatening pathologies associated with high mortality and substantial costs for healthcare system. Clinical guidelines and bundles for the management of patients with sepsis have recently been updated. Herein, we review the history of sepsis and related conditions definitions from the first consensus conference in 1991 to nowadays, the epidemiologic data resulting from worldwide studies on incidence and mortality, the diagnostic approaches including the microbiological assessment of infection and the use of several prognostic and diagnostic biomarkers and finally we review the main therapeutic measures as the intravenous immunoglobulin therapy and the administration of appropriate antibiotic treatment to provide patients with sepsis a favourable outcome in the antibiotic-resistance era.

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1. Introduction

Sepsis and septic shock are life-threatening conditions caused by a dysregulated immune response to infections, which may lead to tissue and organ injures and finally to death. Despite advances in management, sepsis and septic shock still represent major healthcare problems worldwide leading to a substantial consumption of health-care resources. New guidelines and bundles have recently been published [1–3]. In this study we review the epidemiology, the history of definitions, the diagnostic and therapeutic approaches of sepsis and septic shock.

2. Definitions

2.1. Previous definitions

In 1991, the American College of Chest Physicians (ACCP) and the Society of Critical Care Medicine (SCCM) held a consensus conference whose result was the development of a new set of terms and definitions, such as "systemic inflammatory response syndrome", "sepsis" and "septic shock" based on clinical and laboratory parameters. These definitions were agreed and widely used by theinternational scientific community. The phrase ***Systemic inflammatory response syndrome*** (SIRS) was referred to the inflammatory process, regardless of the type of causative insult and presence of infection. SIRS was defined as the presence of two or more of the following criteria: temperature more than 38 °C or less than 36 °C; heart-rate more than 90 beats/min; respiratory rate more than 20 breaths/min or $PaCO_2$ less than 32 mmHg; abnormal white blood cell count ($>12 \times 10^3$/mL, $< 4.0 \times 10^3$/mL, or >10% of immature forms). ***Sepsis*** was defined as SIRS in response to an infectious process. ***Severe sepsis*** was defined as sepsis associated with organ dysfunction, hypoperfusion or hypotension (including lactic acidosis, oliguria and acute alteration in mental status). ***Sepsis-induced hypotension*** was the condition of systolic blood pressure <90 mmHg or a reduction of ≥40 mmHg from baseline in the absence of other cause of hypotension. ***Septic shock*** was defined as a persistent sepsis-induced hypotension despite adequate administration of intravenous fluids [1].

In 2001, several European and North American intensive care societies convened in a second consensus conference to revisit these definitions. They expanded the list of diagnostic criteria but the current concepts of sepsis, severe sepsis and septic shock were only slightly revised and they remained the basis for clinical practice and research into sepsis for the following years [2].

2.2. New definitions

In 2014, the European Society of Intensive Care Medicine and the Society of Critical Care Medicine convened a new panel of 19 experts to update definitions of sepsis and septic shock, which were characterized by limited specificity and inadequate sensibility. The most relevant changes were the elimination of the term severe sepsis, considered redundant, and the deleting of the concept of SIRS, which may simply reflect an appropriate host response to several non-infectious diseases (such as pancreatitis and ischemic reperfusion syndromes) [3].

Therefore, the results of the third international consensus conference, published in 2016, allow to define the following conditions: ***Organ dysfunction*** is represented by an increase in the Sequential [Sepsis-related] Organ Failure Assessment (SOFA) score of 2 points or more (Table 1); **Sepsis** is defined as life threatening organ dysfunction caused by a dysregulated host response to infection; **Septic shock** is defined as a subset of sepsis in which circulatory, cellular or metabolic abnormalities are associated to increased risk of mortality. Clinical parameters to identify patients with septic shock are: vasopressor requirement to maintain a mean arterial pressure of 65 mm Hg or greater and serum lactate level greater than 2 mmol/L (>18 mg/dL) in the absence of hypovolemia [3,4].

The same group of experts elaborated a simplified version of the SOFA score, the quick SOFA Score (quick SOFA or qSOFA), incorporating systolic blood pressure of 100 mmHg or less, respirator rate of 22/min or greater and altered mentation (any Glasgow coma scale score different from 15). The qSOFA score is based on clinical criteria but does not require laboratory tests, thus it provides a simple and quick evaluation of patients with suspected infection who are more likely to have poor outcomes [3]. Several recent studies supported the use of SOFA and qSOFA classifications demonstrating that such scores have a greater prognostic value than previous SIRS criteria for the identification of patients with higher risk of mortality among those afferents to emergency departments with suspected infection [5,6]. Although several authors support the usefulness of qSOFA score in predicting Intensive Care Unit (ICU) admission and in-hospital mortality among patients with suspected infection [6,7], there are still doubts about the adequacy of replacing previous early warning scores with qSOFA because of its poor sensitivity for early risk assessment in patients with suspected infection, therefore further clinical researches are needed to better define the screening capacity of this new score [8–10].

Table 1
Sequential [Sepsis-related] Organ Failure Assessment (SOFA) score.

Sequential [Sepsis-related] Organ Failure Assessment Score[a]					
Parameters	Score				
	0	1	2	3	4
PaO_2/FiO_2(mmHg)	≥400	<400	<300	<200	<100
MAP (mmHg) and catecholamine doses[b] need	MAP ≥ 70	MAP < 70	Dopamine <5 or dobutamine (any dose)	Dopamine 5.1–15 or epinephrine ≤0.1 or norepinephrine ≤0.1	Dopamine >15 or epinephrine >0.1 or norepinephrine >0.1
Platelets ($\times 10^3/\mu L$)	≥150	<150	<100	<50	<20
Bilirubin (mg/dL)	<1.2	1.2–1.9	2.0–5.9	6.0–11.9	>12.0
Glasgow coma scale	15	13–14	10–12	6–9	<6
Creatinine (mg/dL)	<1.2	1.2–1.9	2.0–3.4	3.5–4.9	>5.0
Urine output (mL/d)				<500	<200

Abbreviations: PaO_2 = partial pressure of oxygen; FiO_2 = fraction of inspired oxygen; MAP = mean arterial pressure.
[a] Adapted from Singer et al. [3].
[b] Catecholamine doses are calculated as μg/kg/min for at least 1 h.