New Sepsis and Septic Shock Definitions

Clinical Implications and Controversies

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KEYWORDS

• Sepsis • Septic shock • Clinical diagnosis • SOFA • qSOFA • SIRS

KEY POINTS

- The new sepsis definitions shift emphasis from the systemic inflammatory response syndrome (SIRS) to organ dysfunction. They use the Sequential Organ Failure Assessment (SOFA) score as a simple, tested method of quantifying organ dysfunction, and require vasopressor-dependent hypotension and increased lactate levels in the absence of hypovolemia to diagnose septic shock.
- The new sepsis definitions also propose Quick SOFA (qSOFA) criteria ($\geq$2 of hypotension, tachypnea, and/or altered mental status) for efficient bedside screening to identify potentially infected patients at risk for poor outcomes in out-of-hospital, emergency department, and general hospital ward settings.
- Although the new sepsis definitions have been endorsed by multiple professional societies, there have been concerns that their emphasis on organ dysfunction may lead to delays in identifying serious infections before they progress to organ dysfunction. Furthermore, the SOFA score has primarily been used as a research tool and is unfamiliar to many clinicians.
- Controversy also exists as to whether or not there is still a role for SIRS criteria, whether or not qSOFA is sufficiently sensitive as a screening tool for sepsis, and what the role of lactate testing is under the new sepsis definitions.
- Despite these controversies, the new definitions should not change the basics of sepsis management. The cornerstone remains early appropriate antibiotic therapy and source control for patients with serious infections, particularly those with signs of organ dysfunction, and rapid fluid resuscitation when hypotension is present.

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INTRODUCTION

Sepsis is a major cause of death, disability, and cost to the health care system. However, despite its clinical significance, sepsis is difficult to define. For more than 2 decades, the sepsis classification framework has been based on identifying infection accompanied by the systemic inflammatory response syndrome (SIRS) (sepsis), and then looking for organ dysfunction (severe sepsis) or refractory hypotension (septic shock).[1] In 2016, the European Society of Intensive Care Medicine (ESICM) and Society of Critical Care Medicine (SCCM) released new consensus definitions (Sepsis-3) defining sepsis as "life-threatening organ dysfunction caused by a dysregulated host response to infection"[2] and eliminating SIRS criteria from the definition. The Sepsis-3 Task Force operationalized the new definition as infection associated with an increase in Sequential Organ Failure Assessment (SOFA) score by 2 or more points from baseline. In addition, a new set of simple clinical criteria were endorsed, called Quick SOFA (qSOFA), which can be easily calculated at the bedside to identify potentially infected patients at high risk for adverse outcomes who might merit additional care. The qSOFA score was also intended to prompt clinicians to consider the possibility of infection if not previously suspected.[3] In addition, septic shock is now defined as sepsis-induced hypotension requiring vasopressors and an increased lactate level in the absence of hypovolemia. Although the new definitions benefit from greater simplicity and clearer association with adverse outcomes, there are concerns that the emphasis on organ dysfunction and qSOFA may delay early identification and intervention in infected patients before they develop organ dysfunction. This article summarizes some of the challenges in defining sepsis, the history of sepsis definitions, the rationale and development of the new definitions, their strengths and weaknesses, and clinical controversies.

SEPSIS BURDEN AND NEW QUALITY MEASURES

Sepsis is the leading cause of death in noncoronary intensive care units (ICUs), the most expensive condition treated in hospitals, and a contributor in 30% to 50% of all hospital deaths.[4–6] Survivors are also at high risk for recurrent sepsis, readmissions, and long-term cognitive and functional impairment.[7,8] Reports based on administrative data have suggested an increase in sepsis cases over the past 2 decades,[9–11] although it is unclear whether this is caused by true increases in disease rates or greater recognition and more complete coding.[12,13] Nonetheless, increasing appreciation of the severe burden that sepsis imposes on society has prompted public education campaigns and quality improvement initiatives in hospitals around the world. In the United States, new regulatory requirements have been implemented, including the Centers for Medicare & Medicaid Services (CMS) SEP-1 measure, which compels hospitals to publicly report their compliance with 3-hour and 6-hour management bundles for patients diagnosed with sepsis.[14]

CHALLENGES IN DEFINING AND TRACKING SEPSIS

Sepsis is an elusive condition to define because it is a complex syndrome without a pathologic gold standard. It is often unclear whether a patient is infected or not, even when assessing the patient's clinical course in retrospect, and microbiological tests and cultures are often unrevealing.[15] Even positive microbiological tests do not always indicate active infection. Most clinicians would agree that a patient with bacteremia and hypotension or multiorgan dysfunction is septic, but blood cultures are positive in only a fraction of septic patients.[16] In addition, the line between normal