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Page: 11 - 20

Sepsis-3 and its Assesment Tools (Sofa and Qsofa): Historical Evolution, Clinical Utility and Criticisms

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ABSTRACT

Sepsis remains a major global health problem with high morbidity and mortality. Over the past three decades, evolving consensus definitions have sought to improve diagnostic accuracy and patient outcomes. The latest definition, Sepsis-3, defines sepsis as life-threatening organ dysfunction caused by a dysregulated host response to infection, with the Sequential Organ Failure Assessment (SOFA) and quick SOFA (qSOFA) as key tools. This review outlines the historical development of sepsis definitions, examines the role of SOFA and qSOFA, and summarizes their strengths and criticisms. Sepsis-3 marked a shift from inflammation-based to organ dysfunction–centered criteria. Evidence shows that SOFA is highly accurate for prognosis in intensive care, while qSOFA is useful for bedside risk stratification outside the ICU. Both outperform systemic inflammatory response syndrome (SIRS) in specificity, though SOFA requires laboratory parameters and qSOFA shows reduced sensitivity. Some authors argue SIRS should not be entirely discarded due to its early recognition value. In conclusion, Sepsis-3 advanced the standardization of sepsis definitions, yet challenges remain, and this article was written to provide a concise overview of its evolution, utility, and ongoing debates.
Keywords: Sepsis-3, SOFA, qSOFA, SIRS, sepsis definitions

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INTRODUCTION

Sepsis remains one of the most significant global health problems. In 2017, it was estimated that there were 48.9 million cases of sepsis and 11 million sepsis-related deaths worldwide (Rudd et al., 2020). According to the WHO, diarrheal infectious diseases are the leading cause of sepsis, accounting for 9.2 to 15 million cases annually. Lower respiratory tract infections rank second, contributing to 1.8 to 2.8 million cases each year. Approximately one-third of sepsis cases—or nearly half of all sepsis-related deaths—are associated with injury or chronic illness [2]. In Indonesia, a study reported 14,076 sepsis cases between 2013 and 2016, with a mortality rate of 58.3% (Rudd et al., 2020). These figures underscore that sepsis remains a major health threat both globally and nationally.

Etymologically, the term sepsis has a long historical background. It was first mentioned in the works of Homer in the 8th century BC with the term sepo, meaning “I rot”

or “I am decomposing.” The term was later adopted as sepsis. In the Corpus Hippocraticum, written around 400 BC, Hippocrates used the term sepidon, meaning “decay of the webs,” to describe an epidemic. Other historical figures such as Aristotle, Plutarch, and Galen also used the term sepsis with similar meanings (Geroulanos & Douka, 2006).

With the advancement of medical knowledge, the understanding of sepsis has undergone major changes. In the 18th century, the Germ Theory emerged, identifying microorganisms as the cause of sepsis. The modern concept of sepsis was first introduced by Hugo Schottmuller in 2014, defining it as a condition in which pathogenic microbes continuously invade the bloodstream, producing symptoms that can be observed both subjectively and objectively. Throughout the 20th century, numerous studies sought to refine the definition of sepsis; however, the diversity of findings made it difficult to establish a universally accepted definition. A milestone in modern sepsis definition occurred in 1991 when Robert Bone and colleagues initiated the first international consensus during the American College of Chest Physicians (ACCP) and Society of Critical Care Medicine (SCCM) Conference. This consensus defined sepsis as a systemic response to infection meeting two or more criteria of the systemic inflammatory response syndrome (SIRS). The second consensus (Sepsis-2) was held in 2002, and the most recent in 2016 resulted in The Third International Consensus Definitions for Sepsis and Septic Shock (Sepsis-3) (Gyawali et al., 2019).

In Sepsis-3, sepsis is defined as a life-threatening condition arising from a dysregulated host immune response to infection, leading to organ dysfunction (Singer et al., 2016). Infections in sepsis can be caused by various pathogenic microorganisms, including bacteria, fungi, viruses, protozoa, and parasites, with Gram-negative bacteria being the most common causative agents (Gauer et al., 2020). This redefinition marked a shift in focus—from merely identifying signs of systemic inflammation to emphasizing the detection of organ dysfunction as the primary diagnostic criterion for sepsis. Understanding the historical background and rationale behind this definitional change is crucial for evaluating its strengths and limitations, especially regarding its application in diverse clinical settings.

RESEARCH METHODS

This narrative literature review examines the evolution of the definition of sepsis, focusing on Sepsis-3, the introduction of the Sequential Organ Failure Assessment (SOFA) and quick SOFA (qSOFA) scores, and their clinical utility in diagnosing and prognosticating sepsis. The review aims to synthesize existing literature from both primary studies and expert consensus

documents to provide a comprehensive understanding of how sepsis definitions have evolved and the strengths and limitations of current diagnostic criteria.

2.1 Literature Search Strategy

The review includes articles from academic journals, clinical guidelines, and expert consensus statements published between 1992 and 2025. A broad search strategy was used, focusing on key terms such as "sepsis," "Sepsis-3," "SOFA score," "qSOFA," "SIRS," and "sepsis diagnosis." Literature was gathered from electronic databases such as PubMed, Google Scholar, and Scopus, as well as direct references from key studies and official guidelines.

2.2 Inclusion and Exclusion Criteria

Articles included in the review were:

- Published in peer-reviewed journals or recognized medical guidelines.
- Focused on Sepsis-3, SOFA, qSOFA, and their clinical applications.
- Written in English or Indonesian.

Exclusion criteria were:

- Studies that did not directly address sepsis definitions or diagnostic tools.
- Articles not related to clinical utility, prognostic value, or critiques of Sepsis-3, SOFA, or qSOFA.

2.3 Data Extraction and Analysis

Data from the included articles were extracted to identify key themes related to the definition of sepsis, the development of SOFA and qSOFA, their advantages, and their limitations. A thematic analysis approach was used to categorize the findings into broader themes, including:

- The historical evolution of sepsis definitions (from Sepsis-1 to Sepsis-3).
- The clinical utility of SOFA and qSOFA in different settings (ICU vs. non-ICU).
- Criticisms and challenges regarding Sepsis-3 and its diagnostic criteria.

The review aims to provide a balanced view of the current state of sepsis definitions and tools, highlighting both their clinical relevance and the debates surrounding their implementation.

RESULTS AND DISCUSSION

Sepsis continues to be a major challenge in global health, contributing significantly to morbidity, mortality, and healthcare costs. Despite decades of research, its diagnosis remains

complex due to the heterogeneous clinical presentation and overlapping features with other critical illnesses. A clear and standardized definition has therefore been essential, both to improve patient management and to facilitate comparability across clinical studies. Over the years, international expert groups have convened multiple consensus conferences to refine the definition of sepsis, aiming to strike a balance between sensitivity for early recognition and specificity for prognostic accuracy. These efforts have led to three major iterations of sepsis definitions—Sepsis-1, Sepsis-2, and Sepsis-3—which collectively reflect the evolving understanding of the syndrome and the search for reliable assessment tools.

3.1 Development and Refinement of Sepsis Definitions (Sepsis-1 to Sepsis-3)

The effort to establish a standardized definition of sepsis arose from the increasing recognition of its global burden and the difficulty of comparing clinical studies due to the lack of uniform diagnostic criteria. By the late 20th century, clinicians faced challenges in distinguishing sepsis from other systemic inflammatory conditions, resulting in inconsistent diagnoses and treatment approaches across institutions. To address this issue, the first international consensus conference on sepsis (Sepsis-1, 1992) was convened by the Society of Critical Care Medicine (SCCM) and the American College of Chest Physicians (ACCP). This consensus defined sepsis as the presence of infection associated with two or more criteria of the systemic inflammatory response syndrome (SIRS). These included abnormalities in body temperature (>38°C or <36°C), heart rate (>90 beats/min), respiratory rate (>20 breaths/min or $PaCO_2$ <32 mmHg), and white blood cell count (>12,000/μL, <4,000/μL, or >10% immature forms). The terms “severe sepsis” and “septic shock” were also introduced, where severe sepsis referred to sepsis with organ dysfunction, hypoperfusion, or hypotension, while septic shock was defined as sepsis-induced hypotension persisting despite adequate fluid resuscitation (Balk et al., 1992; Gary et al., 2016).

The limitations of Sepsis-1 soon became apparent, particularly the overdiagnosis caused by the low specificity of SIRS criteria. Many non-infectious conditions such as trauma, burns, and pancreatitis could fulfill the criteria, leading to diagnostic ambiguity. In response, the second international consensus (Sepsis-2, 2001) was organized, involving SCCM, the European Society of Intensive Care Medicine (ESICM), ACCP, the American Thoracic Society (ATS), and the Surgical Infection Society (SIS). This consensus retained the Sepsis-1 framework but expanded the diagnostic list to 21 clinical and laboratory indicators, covering markers of inflammation, tissue perfusion abnormalities, and organ dysfunction. Additionally, the PIRO model (Predisposition, Infection, Response, Organ dysfunction) was

introduced to provide a more structured staging of sepsis. Despite these refinements, Sepsis-2 still faced criticism for its complexity and lack of specificity, limiting its widespread application (Gary et al., 2016; Levy et al., 2003)

To overcome these challenges, the third international consensus (Sepsis-3, 2016) was convened by SCCM and ESICM with 19 experts in critical care, infectious diseases, surgery, and pulmonology. Using large datasets of over one million patient records, the task force concluded that SIRS was neither necessary nor sufficient for diagnosing sepsis. Sepsis was redefined as "life-threatening organ dysfunction caused by a dysregulated host response to infection." Organ dysfunction was operationalized as an acute increase of ≥2 points in the Sequential Organ Failure Assessment (SOFA) score. To support rapid bedside identification outside intensive care settings, the quick SOFA (qSOFA) score was introduced, based on altered mentation, respiratory rate ≥22/min, and systolic blood pressure ≤100 mmHg. The category "severe sepsis" was eliminated as redundant, while septic shock was redefined as a subset of sepsis associated with profound circulatory, cellular, and metabolic abnormalities that carry a higher risk of mortality (Gary et al., 2016; Singer et al., 2016).

Table 1. Comparison between Sepsis-1, Sepsis-2, and Sepsis-3

Aspect	**Sepsis-1 (1992)**	**Sepsis-2 (2001)**	**Sepsis-3 (2016)**
Organizers	SCCM & ACCP	SCCM, ESICM, ACCP, ATS, SIS	SCCM & ESICM
Core Definition	Sepsis = infection + ≥2 SIRS criteria	Retained Sepsis-1 definition; expanded diagnostic indicators	Sepsis = life-threatening organ dysfunction caused by a dysregulated host response to infection
Diagnostic Criteria	SIRS: • Temp >38°C or <36°C • HR >90 bpm • RR >20/min or $PaCO_2$ <32 mmHg • WBC >12,000/μL, <4,000/μL, or >10% immature	21 clinical and laboratory criteria: inflammation, hemodynamics, tissue perfusion, organ dysfunction	Organ dysfunction = acute ↑ ≥2 SOFA points qSOFA: altered mentation, RR ≥22/min, SBP ≤100 mmHg
Additional Terms	Severe sepsis = sepsis + organ dysfunction Septic shock = sepsis with refractory hypotension	Same as Sepsis-1, plus PIRO model (Predisposition, Infection, Response, Organ dysfunction)	Severe sepsis removed Septic shock = sepsis with profound circulatory, cellular, metabolic abnormalities

Introduced Tools	SIRS framework	PIRO model	SOFA, quick SOFA (qSOFA)

3.2 SOFA and qSOFA in Sepsis-3: Tools for Organ Dysfunction Assessment

The Sequential Organ Failure Assessment (SOFA) score was originally developed to describe organ dysfunction in critically ill patients and was later adopted as part of the Sepsis-3 consensus. It evaluates six organ systems—respiratory, cardiovascular, hepatic, coagulation, renal, and neurological—each scored from 0 to 4 according to the degree of dysfunction. A cumulative score ≥2 points above baseline is considered indicative of significant organ dysfunction, representing an increased risk of mortality in patients with suspected infection. The SOFA score thereby provides an objective and standardized means to quantify sepsis-associated organ failure (Singer et al., 2016).

Table 2. Sequential Organ Failure Assessment (SOFA) Score

Variable	**SOFA Score**				
	0	**1**	**2**	**3**	**4**
Respiratory	PaO_2/FIO_2 >400 Sp$O_{2/}$FIO_2>302	PaO_2/FIO_2<400 Sp$O_{2/}$FIO_2<302	PaO_2/FIO_2<300 Sp$O_{2/}$FIO_2<221	PaO_2/FIO_2<200 Sp$O_{2/}$FIO_2<142	PaO_2/FIO_2<100 Sp$O_{2/}$FIO_2<67
Cardiovascular (mcg/kg/min)	MAP≥70mm Hg	MAP≥70mm Hg	Dopamine ≤5 *or any* *D*obutamine	Dopamine ≤5 Norepinephrine ≤ 0.1 Dopamine ≤ 0.8	Dopamine >15 or Norepinephrine> 0.1 Phenylephrine >0.8
Liver (bilirubin, mg/dL)	<1.2	1.2-1.9	2.0-5.9	6.0-11.9	>12
Renal (Creatinine, mg/dL)	<1.2	1.2-1.9	2.0-3.4	3.5-4.9	>5.0
Coagulation (platelet x $10^3/mm^3$	≥150	<150	<100	<50	<20
Central Nervous System (GCS score)	15	13-14	16-12	6-9	<6

While SOFA is widely accepted for use in intensive care units (ICUs), its reliance on laboratory data limits its utility for rapid assessment outside of critical care settings. To address this limitation, the Sepsis-3 task force introduced the quick SOFA (qSOFA) score as a simplified bedside tool. qSOFA is based on three readily obtainable clinical parameters: altered mental status (Glasgow Coma Scale <15), respiratory rate ≥22 breaths/min, and systolic blood pressure ≤100 mmHg. The presence of at least two of these criteria is associated with poor outcomes, including increased mortality and prolonged ICU stay, among patients with suspected infection (Singer et al., 2016).

Table 3. qSOFA score

qSOFA Criteria	Point
Respiratory rate ≥22x/menit	1
Change in mental status	1
Systolic BP ≤100 mmHg	1

The introduction of qSOFA was aimed at improving early recognition of patients at risk of sepsis in non-ICU settings such as emergency departments and general wards. Unlike SIRS criteria, which focused on systemic inflammation, qSOFA emphasizes markers of organ dysfunction, thereby aligning with the updated Sepsis-3 definition. Although qSOFA does not replace SOFA in diagnostic or prognostic accuracy within ICUs, it serves as a practical triage tool that guides clinicians toward further evaluation and timely intervention in high-risk patients (Singer et al., 2016).

3.3 Advantages of SOFA and qSOFA over SIRS in Sepsis Prognostication

Several comparative studies have evaluated the prognostic accuracy of SOFA, qSOFA, and SIRS in patients with suspected sepsis. In a large multinational cohort study conducted across hospitals in North America, Europe, and Africa, the predictive validity of sepsis criteria was analyzed in both ICU and non-ICU populations. The study found that outside the ICU, qSOFA provided better predictive validity for mortality and prolonged ICU stay compared to SIRS. qSOFA, consisting of altered mental status, respiratory rate ≥22 breaths/min, and systolic blood pressure ≤100 mmHg, was more strongly associated with adverse outcomes in non-ICU patients, while SOFA demonstrated the highest accuracy forpredicting mortality among ICU patients (Seymour et al., 2016).

A retrospective analysis of 184,875 ICU patients across multiple centers further supported the prognostic superiority of SOFA over SIRS. An increase in SOFA score within the first 24 hours of ICU admission was strongly associated with in-hospital mortality. SOFA

outperformed both qSOFA and SIRS in ICU settings, while SIRS frequently identified patients as septic despite the absence of organ dysfunction. This reduced the prognostic reliability of SIRS compared to organ dysfunction–based scoring systems such as SOFA (Raith et al., 2017).

In a prospective observational study conducted at a tertiary care hospital in India, SOFA, qSOFA, and SIRS were compared in predicting sepsis-related outcomes. Both SOFA and qSOFA were significantly associated with in-hospital mortality, with AUROC values of 0.74 and 0.678 respectively, whereas SIRS did not show statistical significance. These findings confirmed that SOFA and qSOFA had greater prognostic utility than SIRS for identifying patients at risk of poor outcomes (Khwannimit et al., 2018).

Taken together, these studies demonstrate that SOFA consistently showed the strongest prognostic performance in ICU populations, while qSOFA performed better than SIRS in non-ICU or resource-limited settings. In contrast, SIRS was shown to have low specificity and limited association with adverse outcomes when compared to SOFA and qSOFA (Khwannimit et al., 2018; Raith et al., 2017; Seymour et al., 2016).

3.4 Criticisms of SOFA and qSOFA as Assessment Tools in Sepsis-3

Several criticisms have emerged following the introduction of Sepsis-3 definitions, especially concerning the replacement of SIRS with SOFA and qSOFA. It has been argued that abandoning SIRS criteria could be harmful, as SIRS—despite its poor specificity—was highly sensitive in detecting patients with early infection and risk of organ dysfunction. Removing SIRS may delay recognition and timely intervention, thereby endangering patients who could have been identified earlier under the previous criteria (Simpson, 2016).

Additional challenges regarding the clinical implementation of SOFA have also been reported. SOFA scoring was not routinely applied in many non-academic hospitals, limiting its practical use. Furthermore, Sepsis-3 criteria were considered to place greater emphasis on mortality prediction than on early detection, which may reduce opportunities for immediate treatment at an early stage (Shankar-Hari et al., 2016).

More recently, the effectiveness of qSOFA as a screening tool has been questioned due to its relatively low sensitivity. Although qSOFA was designed as a rapid bedside assessment, it failed to identify a considerable proportion of septic patients who later experienced adverse outcomes. This limitation raised concerns about relying solely on qSOFA in clinical practice. It has therefore been suggested that while Sepsis-3 criteria provide improvements in specificity, they should complement rather than replace older definitions such as SIRS to ensure a balanced approach to sepsis recognition (Rudd et al., 2020).

CONCLUSION AND RECOMENDATION

The evolution of sepsis definitions from Sepsis-1 to Sepsis-3 reflects continuous efforts to improve diagnostic accuracy and prognostic value in clinical practice. Sepsis-1, based on SIRS criteria, provided sensitivity for early recognition but lacked specificity, leading to frequent overdiagnosis. Sepsis-2 attempted to refine this framework by incorporating a broader range of clinical and laboratory indicators, yet its complexity limited its widespread application. Sepsis-3 introduced a paradigm shift by defining sepsis as life-threatening organ dysfunction due to a dysregulated host response to infection, operationalized through SOFA and supported by qSOFA for bedside screening.

Comparative studies have consistently shown that SOFA has superior prognostic accuracy in intensive care settings, while qSOFA performs better than SIRS in non-ICU or resource-limited environments. Both tools align with the emphasis of Sepsis-3 on organ dysfunction as the central criterion, providing greater specificity than SIRS. However, criticisms remain regarding their clinical utility: SOFA requires laboratory testing that may not be feasible in all settings, and qSOFA demonstrates lower sensitivity, raising concerns about delayed identification of at-risk patients. Moreover, some experts caution against abandoning SIRS altogether, as it remains useful for early detection in certain contexts.

Taken together, Sepsis-3 represents a significant advancement in unifying sepsis definitions and emphasizing organ dysfunction, but its limitations highlight the need for contextual application. Future research should aim to refine diagnostic tools that balance sensitivity and specificity, ensuring both timely recognition and accurate prognostication across diverse healthcare settings.

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