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Sepsis

Persistent organ dysfunction after severe sepsis: A systematic review ☆

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ABSTRACT

Objective: Sepsis is a prevalent disease with high mortality. Survivors of sepsis often suffer significant resultant morbidity, including organ dysfunction. However, little is known about persistent or long-term organ dysfunction in this patient population. Our objective was to systematically review original research studies evaluating organ-specific outcomes at 28 days or greater in patients surviving severe sepsis.
Methods: We performed a systematic review of studies reporting organ-specific outcomes at 28 days or greater in survivors of severe sepsis.
Results: We identified 1,173 articles and five met our inclusion criteria. No study reported on organ dysfunction at greater than 30 days. Two studies contributed the majority of patients and had consistent rates of 1 month organ dysfunction for adult respiratory distress syndrome (ARDS) (8%-9%), renal (7%-8%), hepatic (3%-7%), and central nervous system (2%-5%). Another study reported higher rates of dysfunction for pulmonary (non-ARDS and ARDS), hepatic and renal but similar rates for central nervous system and disseminated intravascular coagulation when compared to the first two studies. The most recent study had the highest rates of dysfunction (>47%) across all organ systems. For organ failure resolution the rates were highly variable.
Conclusions: Our review found variable rates of organ dysfunction at 1 month after severe sepsis. Future studies should attempt to characterize organ dysfunction at greater than 1 month after an acute severe sepsis episode to determine the true prevalence long-term organ dysfunction and treatments for prevention. Additionally, standardized objective measures of organ dysfunction are needed so that future studies can be directly compared.

1. Introduction and background

Sepsis accounts for at least 300,000 annual emergency department visits and 2 to 11% of all hospital or intensive care unit admissions [1,2]. The incidence of severe sepsis in the United States is rising [3,4] and mortality is substantial with approximately 215,000 deaths annually. Costs of care associated with severe sepsis are estimated at 16.7 billion dollars a year in the United States alone [5].

Recent treatments for sepsis have focused on decreasing mortality through aggressive resuscitation. Interventions such as early quantitative resuscitation have been adopted and have reportedly resulted in significant mortality reduction [6–8]. One of the most significant efforts to date is the Surviving Sepsis Campaign, an international guideline effort aimed at improving sepsis survival [9]. Studies have suggested that implementation of these guidelines might result in lower mortality, up to 12% from 2000 to 2007 and/or a 2% yearly hospital mortality reduction [4,10].

Many survivors of sepsis have long-term complications. These include critical illness weakness, delirium, and acute lung injury [11]. A recent systematic review evaluating long-term survival and health-related quality of life in sepsis survivors demonstrated that long-term survival and health-related quality of life is infrequently and inconsistently reported [11]. Furthermore, sepsis survivors have been shown to have a decline in physical functioning, vitality, ability to care for themselves, general health, depression, social functioning, and experience increased pain [12–17].

Most longitudinal studies of sepsis survivors to date have focused on quality of life. While it is known that patients who survive sepsis admission live to have long-term physical, cognitive, and emotional sequelae, we are aware of no studies that have evaluated persistent organ dysfunction in sepsis survivors.

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Our aim was to review the available literature to determine the type and prevalence of organ dysfunction at 28 days and beyond resulting from severe sepsis. We defined persistent organ dysfunction as continued dysfunction between 28 and 90 days from the initial septic insult. Long-term organ dysfunction was defined as dysfunction present at 90 days or greater. Further delineation, of which organs are most likely to be affected by persistent or long-term dysfunction, could direct the development of organ-specific therapies for use during the initial resuscitation of patients with severe sepsis.

2. Methods

2.1. Search strategy

We followed a written protocol developed a priori that conformed to the recommendations from the Preferred Reporting Items for Systematic Reviews and Meta-Analyses statement [18]. To identify studies reporting on persistent or long-term, organ dysfunction in survivors of severe sepsis or septic shock, Scopus, PubMed, the Cochrane Library, and Web of Science databases were searched up to November 28, 2012. The following search strategy was used with the appropriate MeSH subject headings: ("sepsis" OR "severe sepsis" OR "septic shock") AND ("organ failure" OR "organ dysfunction" OR "multiple organ failure" OR "multi-organ failure" OR "multi-organ dysfunction syndrome"). Studies were limited to human subjects, English language, and adult population (>18 years) with no date restrictions. Two investigators then reviewed all titles and abstracts to identify potentially relevant studies. In addition, the authors searched bibliographies and review articles for additional references. Agreement between the two reviewers was calculated by percentage agreement and the kappa statistic.

2.2. Study selection

Studies were considered for inclusion if the title or abstract referred to "prognosis", "outcome", or "long-term outcome" in patients with sepsis, severe sepsis, or septic shock or that mentioned "organ dysfunction", "organ failure", "multi-organ dysfunction syndrome", or "multi-organ failure" with follow up of at least 28 days. The inclusion criteria were intended to be broad to give the greatest likelihood of identifying relevant studies. For organ-specific outcomes, the following organ systems were specifically identified: pulmonary (non-ARDS), pulmonary (ARDS), renal, hepatic, disseminated intravascular coagulation, and central nervous system (CNS). Studies were selected if they included an objective assessment of organ function at least 28 days from the index sepsis admission. Baseline organ function and organ recovery at 28 days or longer was preferred and included if available.

2.3. Data extraction and quality assessment

Two authors independently reviewed citations, abstracts and full text articles for eligible studies. Any disagreement regarding study inclusion was resolved by a third author. Agreement was calculated using percent agreement and the κ statistic. Studies of other populations were included only if they separately reported on organ-specific outcome or organ dysfunction in the septic population. The results (organ dysfunction at 28 days or longer) of the final included studies were tabulated by two authors independently and were compared for discrepancies. The data was carefully assessed to prevent error in interpretation of individual study findings and any disagreement between the two authors was resolved by a third author.

Quality assessment for included studies was based on the US Agency for Healthcare Research and Quality's 'Systems to Rate the

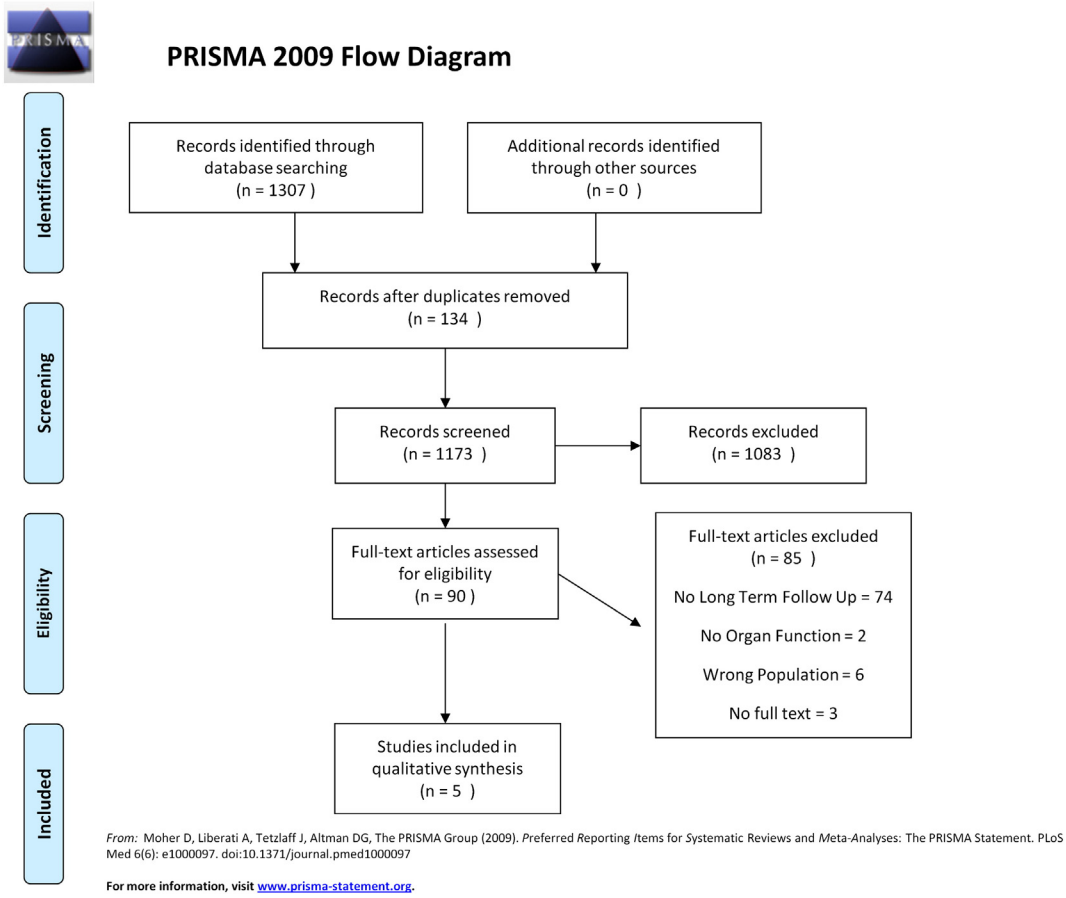

Fig. 1. Flow diagram of literature search and results.