## Early Administration of Intravenous Fluids in Sepsis Pros and Cons

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### **KEYWORDS**

- Sepsis Septic shock Intravenous fluid administration Fluid resuscitation
- Early goal-directed resuscitation
  Fluid management

### **KEY POINTS**

- Sepsis is one of the leading causes of morbidity.
- Early administration of intravenous fluid is commonly used to decrease signs and symptoms of sepsis.
- The timing, volume, and type of fluid administered to patients diagnosed with sepsis impacts patient outcomes.
- Recent studies have challenged the notion that aggressive fluid resuscitation is beneficial in the management of sepsis.

### INTRODUCTION

Sepsis is a potentially life-threatening response of the immune system to a severe infection.<sup>1-4</sup> It is a dynamic process requiring constant reassessment by nurses and other health care professionals.<sup>5</sup> Multiple definitions and terminologies are currently used for sepsis and septic shock, and this can lead to discrepancies in accurate reporting.<sup>6</sup> A taskforce that included experts in sepsis pathobiology, clinical trials, and epidemiology was convened by the Society of Critical Care Medicine and the European Society of Intensive Care Medicine to evaluate and update the current definitions for sepsis and septic shock. The revised definitions by Singer and colleagues<sup>6</sup> are commonly referred to as Sepsis-3:

Sepsis: "a life-threatening organ dysfunction caused by a dysregulated host response to infection."  $^{\rm no(p804)}$ 

Organ dysfunction "represented by an increase in the Sequential Organ Failure Assessment (SOFA) score of 2 points or higher that is associated with a mortality

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greater than 10%."<sup>6(p805)</sup> The baseline SOFA score is assumed to be zero absent of any preexisting organ dysfunction. The quick SOFA (q SOFA) provides simple bedside criteria to identify adult patients and these criteria include<sup>6(p805)</sup>:

- Respiratory rate ≥22
- Altered mentation
- Systolic blood pressure  $\leq$ 100 mm Hg

Septic Shock "a subset of sepsis in which particularly profound circulatory, cellular, and metabolic abnormalities are associated with a greater risk of mortality than with sepsis alone."<sup>6(p805)</sup> Associated with mortality rate greater than 40%.

- Vasopressor requirement to maintain mean arterial pressure (MAP) of 65 mm Hg or greater
- Serum lactate level >2 mmol/L (>18 mg/dL) in the absence of hypovolemia

The physiologic response, signs, and symptoms of sepsis can vary depending on the source and severity of the infection.<sup>3</sup> Common signs and symptoms include low blood pressure, fever, tachycardia, and tachypnea. Prompt detection and diagnosis of sepsis is critical because of the necessity to begin interventions early, which includes the administration of intravenous (IV) fluids, antibiotics, and vasoactive agents followed by source control.<sup>4,7</sup> A delay in beginning therapy correlates with an increased incidence of organ failure and higher mortality rate.<sup>6</sup>

The early management of sepsis is focused on the administration of antibiotics, IV fluids, and vasoactive agents, followed by controlling the source of the sepsis.<sup>7</sup> However, how to approach to the resuscitation of patients with septic shock is controversial. Although fluid resuscitation may be a necessity to manage life-threatening conditions in the early stages of shock, continuing resuscitation beyond that period may have detrimental effects.

In 2001, Rivers and colleagues<sup>8</sup> conducted a single-center randomized control trial (RCT) on the use of early goal-directed therapy (EGDT) to achieve certain hemodynamic optimization for the management of patients in the emergency room with septic shock. In this study, an EGDT 6-hour protocol for resuscitation was guided by specific hemodynamic goals targeting arterial pressure (MAP), central venous pressure (CVP), and central venous oxygen saturation (SVO2) of 70% or greater.<sup>9</sup> It is unclear whether the mortality benefits observed in the study by Rivers and colleagues<sup>8</sup> were the result of invasive hemodynamic monitoring and rigid protocol usage, or perhaps in early recognition and intervention afforded by the protocol.<sup>4</sup>

Since this 2001 study, there have been subsequent single and multicenter RCTs that suggest fluid administration is beneficial in septic shock. However, most of these studies show the benefits of a multimodal approach to the initial management of sepsis of which EGDT was central.<sup>10</sup> Fluid resuscitation is necessary at the early stages of septic shock to maintain hemodynamic stability. However, whether fluid resuscitation should continue beyond that period is questionable.<sup>11</sup> More recent studies suggest that aggressive fluid resuscitation results in volume overload and organ dysfunction, which has been associated with increased patient mortality.<sup>7,10,11</sup> Recently, 3 large, multicenter RCTs conducted in the United States, Australia, and the United Kingdom failed to find that EGDT decreased mortality.<sup>9</sup> In these RCTs designed to compare EGDT to usual care, the use of CVP level has been implicated in volume overload.<sup>9</sup>

"Empiric fluid loading is the administration of a predetermined volume of fluid with the intent to ensure adequate organ perfusion."<sup>12(p68)</sup> In the study by Rivers and

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