Sepsis Resuscitation
Fluid Choice and Dose

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KEYWORDS

• Fluid resuscitation • Sepsis • Crystalloids • Colloids • Albumin • Early goal-directed therapy

KEY POINTS

- Fluid resuscitation to correct hypovolemia and support organ perfusion is central to current management of severe sepsis and septic shock.
- Recent randomized trials have not confirmed a benefit for targeting invasive physiologic parameters; the ideal fluid volume and end points in sepsis resuscitation remain unknown.
- Increased fluid balance is associated with increased mortality in early and late sepsis; whether conservative fluid management can improve sepsis outcomes requires further study.
- Hydroxyethyl starch increases risk of acute kidney injury and may increase mortality in patients with sepsis.
- Whether albumin or physiologically balanced crystalloids improve clinical outcomes in sepsis remains the focus of ongoing study.

INTRODUCTION

Sepsis is an inflammatory response to severe infection characterized by hypovolemia and vasodilation and treated with early antibiotics and fluid resuscitation.[1] In the United States, sepsis with organ dysfunction (severe sepsis) or fluid-resistant hypotension (septic shock) accounts for 2% of hospital admissions and 10% of intensive care unit (ICU) admissions.[1] In-hospital mortality rates have decreased from 80% in the early years of intensive care to 20% to 30% in the modern era[2–4] through improved surveillance, early treatment of underlying infection, and advances in support for failing organs. Despite the central role intravenous (IV) fluid administration has played in sepsis management for the last 15 years,[5,6] fundamental questions regarding "which fluid" and "in what amount" remain unanswered. This article addresses the physiologic principles and scientific evidence available to help clinicians address those questions in practice.

PHYSIOLOGY OF FLUID RESUSCITATION IN SEPSIS

Patients with early sepsis are frequently hypovolemic from decreased intake and increased insensible losses. In addition, inflammation alters vascular resistance, venous capacitance, and vascular leak generating a "relative hypovolemia." Resultant decreases in stroke volume and cardiac output imbalance oxygen delivery and demand, precipitating tissue hypoxia, anaerobic metabolism, and lactic acidosis.

The classic physiologic rationale for fluid resuscitation in sepsis is to restore intravascular volume, cardiac output, and oxygen delivery. Volume and choice of resuscitation fluids have largely been predicated on this model. Resuscitation end points, such as central venous pressure (CVP), inferior vena cava filling, mixed venous oxygen saturation, and lactate, are used to restore preload independence and match oxygen demand and supply. Selection of colloids over crystalloids is

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intended to optimize volume expansion through colloid retention in the intravascular space.

It is increasingly clear, however, that the hemodynamic response to fluid administration is determined by an intricate interaction of mean systemic filling pressure, right atrial pressure, venous resistance, and ventricular compliance, which makes predicting a critically ill patient's response to fluid challenging.[7] Impaired oxygen use and nonhypoxemic causes of lactic acidosis may elevate lactate levels despite adequate perfusion. Perhaps most importantly, the century-old Starling model conceptualizing maintenance of vascular volume as the balance of hydrostatic and oncotic pressure gradients between the vessel lumen and interstitial space has been challenged by the recent recognition of the importance of the endothelial glycocalyx (Fig. 1).[8] Because it is a primary determinant of membrane permeability, damage to the glycocalyx during sepsis may alter patients' response to fluid resuscitation. Although the clinical implications of these findings are not yet fully understood, they argue against an overly simplified approach to fluid dose ("fill the tank") and fluid choice ("colloids stay in the vasculature").

FLUID DOSE

Fluid Administration in Sepsis Resuscitation

Fluid resuscitation is currently considered an essential component of early sepsis management.[1] Prompt IV fluid administration for patients with sepsis was advanced by a 2001 study of early goal-directed therapy (EGDT).[5] In that landmark trial, 263 patients with sepsis and hypoperfusion were randomized to either standard therapy or EGDT. Standard therapy involved arterial and central venous catheterization and a protocol targeting CVP of 8 to 12 mm Hg, mean arterial pressure (MAP) at least 65 mm Hg, and urine output at

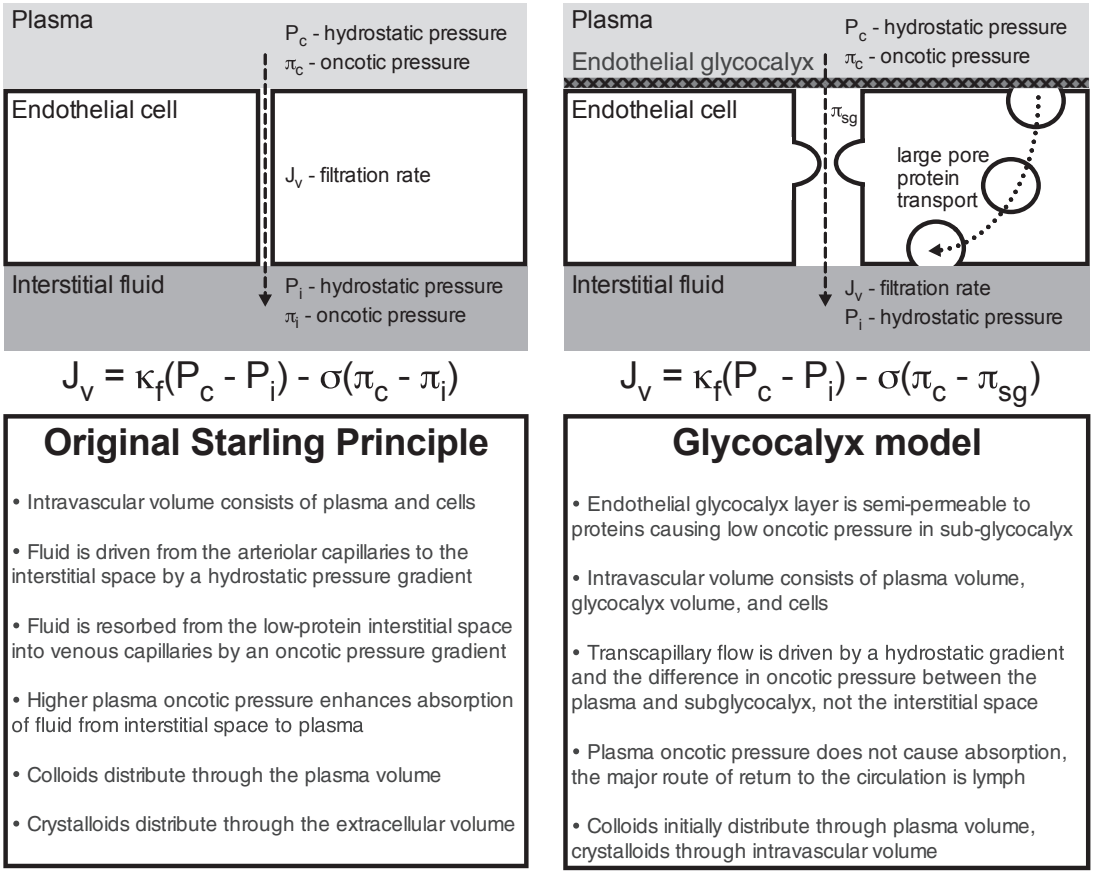

Fig. 1. Models of transvascular fluid exchange. In the original Starling model, the gradient of hydrostatic pressure from the capillary (P_c) to the interstitium (P_i) is opposed by the gradient of oncotic pressure from the capillary (π_c) to the interstitium (π_i), with filtration (K_f) and reflection (σ) coefficients. Understanding the web of membrane-bound glycoproteins and proteoglycans on the luminal side of endothelial cells (endothelial glycocalyx layer) suggests the low oncotic pressure under this semipermeable membrane (π_{sg}) is a more important regulator of transcapillary flow than the interstitial oncotic pressure.