

Fluid Overload



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KEYWORDS

• Fluid overload • Edema • Critical illness • Diuretics • Ultrafiltration

KEY POINTS

- Fluid overload is an almost universal finding in the critically ill, despite little evidence to justify fluid therapy within the intensive care unit after initial resuscitation.
- Hemodynamic responses to fluid administration are unpredictable and short lived, which may contribute to recurrent fluid administration.
- Positive fluid balances have been consistently associated with adverse outcomes and organ dysfunction in critical illness.
- Structural and functional changes in the endothelium and extracellular matrix during systemic inflammation leads to sequestration of administered fluid outside the circulation, promoting fluid accumulation and impeding its removal.
- Strategies to manage fluid balances in the critically ill require close attention to true need for fluid administration and active prevention or management of fluid overload.

INTRODUCTION: ASSOCIATION BETWEEN FLUID OVERLOAD AND ADVERSE OUTCOMES IN CRITICAL ILLNESS

When delivered correctly for the right reasons and at the appropriate time, intravenous fluid can be lifesaving. However, in established critical illness, a combination of increased fluid intake and relatively reduced urine output frequently results in accumulation of excess fluid within the body (**Table 1**). In particular, critically ill patients with sepsis frequently receive very large volumes of fluid resulting in significantly positive fluid balances; for example, in a retrospective analysis of data from the Vasopressin in Septic Shock Trial (VASST), the mean fluid balance was on average +4.2 L at 12 hours after

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	Early in Admission to Intensive Care	Later in Admission to Intensive Care
Excessive intake of fluid	Need for blood products Intravenous fluid resuscitation	Obligate daily fluid needs in terms of drug therapies and nutrition Intercurrent clinical events requiring fluid resuscitation
Inadequate fluid elimination	Acute or chronic kidney disease Acute hemodynamic instability Fluid losses from circulation to interstitial space	Ongoing renal impairment Cardiac and liver dysfunction Sequestration of fluid in the interstitium and body cavities

presentation with severe sepsis and +11.0 L by day 4 after enrollment.¹ Crucially, in this analysis, the upper 2 quartiles of fluid balance were associated with progressively worse survival than patients with less positive fluid balance, even after adjustment for baseline illness severity and demographics. It is pertinent to consider the magnitude of fluid excess we are dealing with here. The fluid balance in the mid upper quartile of the VASST analysis at 4 days was +20.5 L; that is about 50% of the normal total body water, clearly far in excess of any plausible volume deficit at baseline. Despite clinicians' apparent willingness to administer very large volumes of fluid over several days to the sickest critically ill patients, when the relationship between fluid balance and outcome has been examined a consistent association has been demonstrated between positive fluid balance and prolonged intensive care unit (ICU) stay, development or worsening of organ dysfunction and excess mortality.^{2–11} A recent systematic review considered 17 observational studies reporting fluid balances in relation to clinical outcomes including data from more than 5000 ICU patients; in these results, nonsurvivors (48% mortality) had a more positive cumulative fluid balance by day 7 of their ICU stay than survivors by, on average, 4.35 L.¹² In parallel to the adverse effects of fluid overload, patients instead achieving a negative fluid balance in the ICU have an increased survival from septic shock¹³ and in acute kidney injury (AKI) treated with continuous renal replacement therapy⁸ and have a shorter duration of mechanical ventilation and ICU stay.^{6,14} Of course, demonstration of an association between positive fluid balance and adverse outcomes does not prove a causative role of fluid overload in mediating adverse outcomes; undoubtedly, positive fluid balances are a marker of severity critical illness both as a reflection of the degree of physiologic instability and physician response to it.¹⁵ However, the authors think there are strong biological arguments, supported by a wealth of observational evidence, that fluid overload does worsen organ function; therefore, excessive fluid accumulation is an avoidable source of iatrogenic morbidity and mortality in at least a proportion of patients. Many causative mechanisms could mediate a direct association between the development of interstitial edema and the development of progressive organ dysfunction; these include impaired oxygen and metabolite diffusion, distorted tissue architecture, obstruction of organ perfusion, venous outflow and lymphatic drainage, and disturbed cell-cell interaction.

Evidence of the adverse effects of fluid overload can be found in almost all organ systems (Fig. 1), including the gastrointestinal tract,¹⁶ the liver,^{17,18} the cardiovascular system,^{19–22} the central nervous system,^{23,24} and skin and soft tissues.^{25–28} In particular, fluid overload and the resultant visceral edema is a risk factor for intra-abdominal hypertension (IAH). In an ICU population, positive fluid balances have been associated with an increased risk of IAH,^{29–31} which in turn is strongly associated with the development of other organ dysfunction, particularly the development of AKI.^{12,29,31–34} The

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