



Importance of intravenous fluid dose and composition in surgical ICU patients

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Purpose of review

This review discusses the importance of intravenous fluid dose and composition in surgical ICU patients. On the basis of updated physiologic postulates, we suggest guidelines for the use of crystalloids and colloids. Goal-directed fluid therapy is advocated as a means for avoiding both hypovolemia and hypervolemia.

Recent findings

Integrity of the endothelial surface layer (ESL) and 'volume context' are key determinants of fluid disposition. During critical illness the ESL is compromised. Optimal resuscitation may be guided by functional measures of fluid responsiveness with some caveats. The best approach may be to use physiologically balanced crystalloids for hypovolemic resuscitation and colloids for euvoletic hemodynamic augmentation.

Summary

The routine replacement of unmeasured presumed fluid deficits is not appropriate. In critically ill patients, resuscitation with intravenous fluids should produce a demonstrable enhancement of perfusion. Individualized goal-directed therapy using functional hemodynamic parameters can optimize resuscitation and 'deresuscitation'.

Keywords

fluid composition, fluid dosing, functional hemodynamics, goal-directed therapy, revised Starling model

INTRODUCTION

Patients frequently require admission to the surgical ICU (SICU) following major elective surgery, trauma, certain emergency procedures, or after experiencing perioperative complications. The journey to optimal outcomes (i.e., decreasing mortality, reducing complications and length of stay) may begin in the preoperative period (through clinical and biomarker-based risk stratification) [1], continue through intraoperative hemodynamic optimization [2^{***}] ending with balanced dosing and 'choice of fluid' in the SICU. The ideal amount and type of intravenous fluids would avoid both hypovolemia (impaired perfusion), and hypervolemia. Volume overload is increasingly recognized as contributing to both morbidity and mortality [3,4^{***}]. Goal-directed fluid therapy integrating revised physiologic principles [5^{***}] can be applied to high-risk surgical patients and deliver precise fluid prescriptions treading the fine balance between 'too little' and 'not enough' [3].

PURPOSE OF REVIEW

Fluids are widely used and although the literature is replete with studies, there is no defined 'universal strategy' appropriate for all situations. Strategies vary and in broad terms may be liberal, restrictive, or goal-directed. A look at current textbooks [6,7], or recent practice surveys [8], suggests that conventional recommendations may be based on persisting dogma. Despite compelling evidence to the

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KEY POINTS

- Avoid routine replacement of presumed unmeasured fluid deficits.
- During critical illness, endothelial integrity is compromised with loss of proteins from circulation.
- Goal-directed therapy is a means for avoiding both hypovolemia and hypervolemia.
- Volume therapy should be guided by functional parameters with some caveats.
- Crystalloids are effective for resuscitation from low capillary pressure shock states, whereas colloids are useful in euvolemic patients.

contrary, threshold central venous pressure (CVP) values are used as targets by clinicians [3,8–10]. Recent reports suggest that such CVP-guided fluid therapy may be harmful [11]. Recipes abound for formulaic fluid administration, for example, replacement of ‘third space losses’ following major abdominal surgery with crystalloid infusions at 4–6 ml/kg per h [7]. This review will emphasize the importance of a goal-directed approach recognizing that goals need to be objectively defined for individual patients. Functional parameters reflecting fluid responsiveness such as pulse pressure variation (PPV) [2^{••},3,12[•],13] or flow-based/cardiac output-related variables [3] need to be adopted. As proposed in recent reviews [2^{••},4^{••},13], clinicians might consider the paradigm shift summarized in this manuscript rather than merely exercising caution in the interpretation of routinely used clinical signs [changes in CVP, heart rate or mean arterial pressure (MAP)].

Choice of fluids is addressed by reviewing current physiologic principles and contrasting conventional with newer postulates to reframe the colloid versus crystalloid debate [13–15]. The distinction between physiologically balanced [strong ion difference (SID) close to plasma] and unbalanced fluids (SID=0) may be important. We caution against the routine use of isotonic saline (SID=0) for resuscitation [16,17] and suggest that saline be restricted to coadministration with blood products. Finally, some clinical scenarios in the SICU are addressed.

THE CONVENTIONAL STARLING MODEL AND CRYSTALLOIDS VERSUS COLLOIDS

The traditional view of fluid compartments has been that total body water (TBW) accounts for 60% of the lean body weight in adults. TBW is proportioned

into intracellular (approximately 40%) and extracellular spaces (approximately 20%). Extracellular volume is further divided into intravascular (approximately 5% of TBW) and interstitial fluid (ISF) areas (approximately 15% of TBW), see Fig. 1. This traditional model conceptualizes transvascular exchange based on opposing hydrostatic and oncotic forces acting across semipermeable barriers [cellular membranes (extracellular to intracellular) or capillary endothelium (plasma to ISF)]. Net filtration, that is, transvascular movement of fluid may be calculated based on pressure differentials per the classic Starling–Landis equation:

Net fluid movement = filtration coefficient times [(capillary hydrostatic pressure – ISF hydrostatic pressure) – reflection coefficient (capillary oncotic pressure – ISF oncotic pressure)] [7].

Predictions about fluid distribution after infusion (‘volume kinetics’) consider mainly tonicity, oncotic, and hydrostatic pressure gradients. Accordingly, isotonic crystalloids are expected to distribute quickly into the extracellular space and, later slowly, into TBW space. Hypotonic fluids (dextrose solutions) are expected to equilibrate across TBW, whereas hypertonic solutions (3% saline) shrink the intracellular space ‘pulling fluids into circulation’. This classic model would expect colloids to distribute into the intravascular space and, by raising oncotic pressures, recruit fluids into the circulation from the ISF [5^{••}]. Colloids might also be expected to be better at resuscitating (usually) hypoalbuminemic critically ill patients. However, this model is not consistent with the observed effects, especially after high-risk surgery or during critical illness [5^{••},18[•]]. Fundamental questions about how fluid resuscitation works were raised most recently by the premature termination of a large randomized ‘fluid expansion’ trial in hypovolemic pediatric patients where authors [18[•]] could not identify a single subgroup in which bolus resuscitation was beneficial and evidence for a beneficial effect of albumin over saline was absent.

THE MODIFIED STARLING MODEL AND FLUID DISPOSITION

To address the inconsistencies between observations [18[•]] and prior theoretical predictions, a revised model has been developed. The modified Starling model is based on an increased appreciation for the central role of the endothelial surface layer (ESL) [5^{••}]. This surface interface between blood and the capillary wall resists fluid and solute filtration to varying degrees depending on ESL continuity and on fenestrations in the endothelium. Different types of tissue capillary arrangements exist with

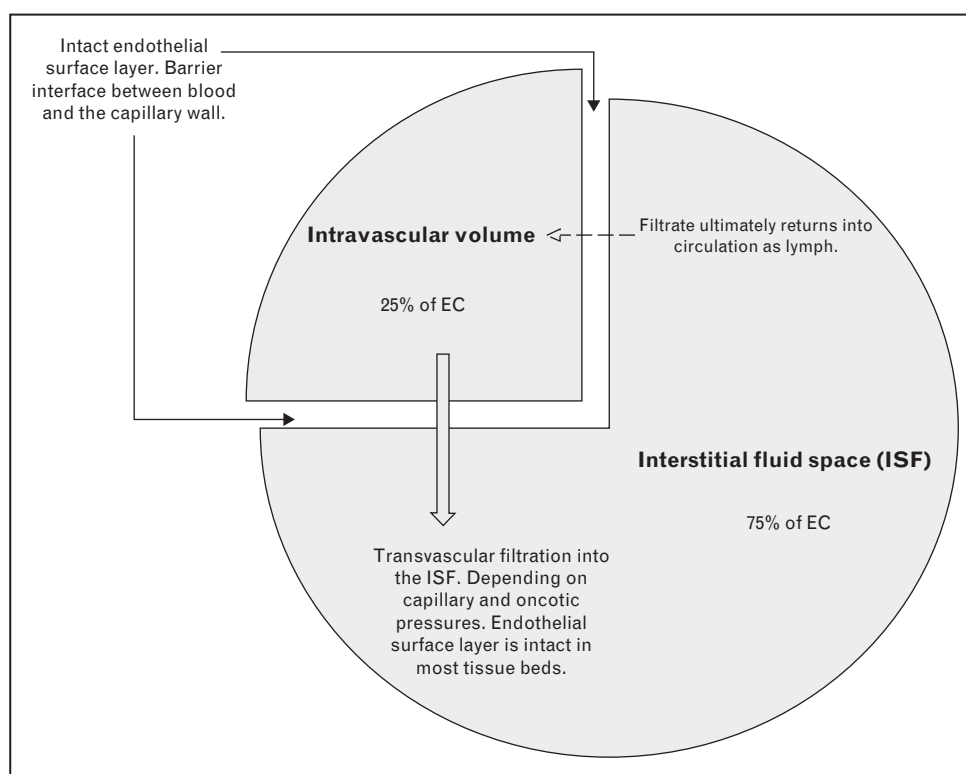


FIGURE 1. Extracellular volume (ECF) distribution with an intact endothelial surface layer (ESL). In health the ESL interfaces between blood and the capillary wall resist fluid and solute filtration to varying degrees depending on ESL continuity and depending on fenestrations in the endothelium. Different types of tissue capillary arrangements exist. The ESL is composed of the endothelial glycocalyx layer (EGL) (membrane-bound glycoproteins/proteoglycans on the luminal side of endothelial cells), an endothelial basement membrane, and extracellular matrix. There is no net fluid absorption across the capillary wall and filtered fluid is returned into circulation as lymph.

sinusoidal tissues being basically continuous with plasma (marrow, spleen, and liver); glomerular filtration occurring via open fenestrated capillaries; and continuous nonfenestrated capillaries being intact barriers (muscle, lung, connective tissue, etc.). The endothelial glycocalyx layer (EGL) is semipermeable and an oncotic gradient exists across it rather than across the vessel wall. Plasma proteins, including albumin, leak into the ISF via a relatively small number of large pores. There is no net fluid absorption across the capillary wall and filtered fluid is returned into circulation as lymph, see Fig. 1.

The revised model explains observed volume kinetics better and reframes the ‘crystalloid versus colloid’ debate. During critical illness and in systemic inflammatory states, the EGL is compromised (i.e., diabetes, hyperglycemia, surgery, trauma, and sepsis [19,20]), see Fig. 2. Endothelial dysfunction and loss of ESL increases vascular permeability, leading to dramatic transcapillary escape of albumin to tissues [5[■]]. Filtration will occur at lower capillary pressures, as proteins are lost from circulation. Colloids (albumin or starches) used for plasma volume expansion have limited

hemodynamic effects due to increased filtration. Further, colloids will not actually recruit any ISF into circulation and, therefore, will not affect pulmonary or peripheral edema any differently than crystalloids [5[■],18[■]]. Substantial amounts of fluids accumulate in compliant loose connective tissues such as lungs [extravascular lung water (EVLW)], muscles, and gastrointestinal mesentery and mucosa, but not in other noncompliant tissues (marrow, liver, spleen, and kidney). In acute lung injury (ALI) [21], therapy with albumin with or without diuretics does not ‘pull’ fluids out of EVLW to improve outcomes. Crystalloids may be more efficient than expected because the actual extracellular space available for equilibration is limited by rigid structures (bone marrow) or fibrous capsules (liver, spleen, and kidney). Resuscitation with albumin, therefore, offers no benefit over crystalloids [18[■]].

VOLUME CONTEXT SENSITIVITY

Fluids distribute based on the underlying volume status of the patient and the kinetics observed

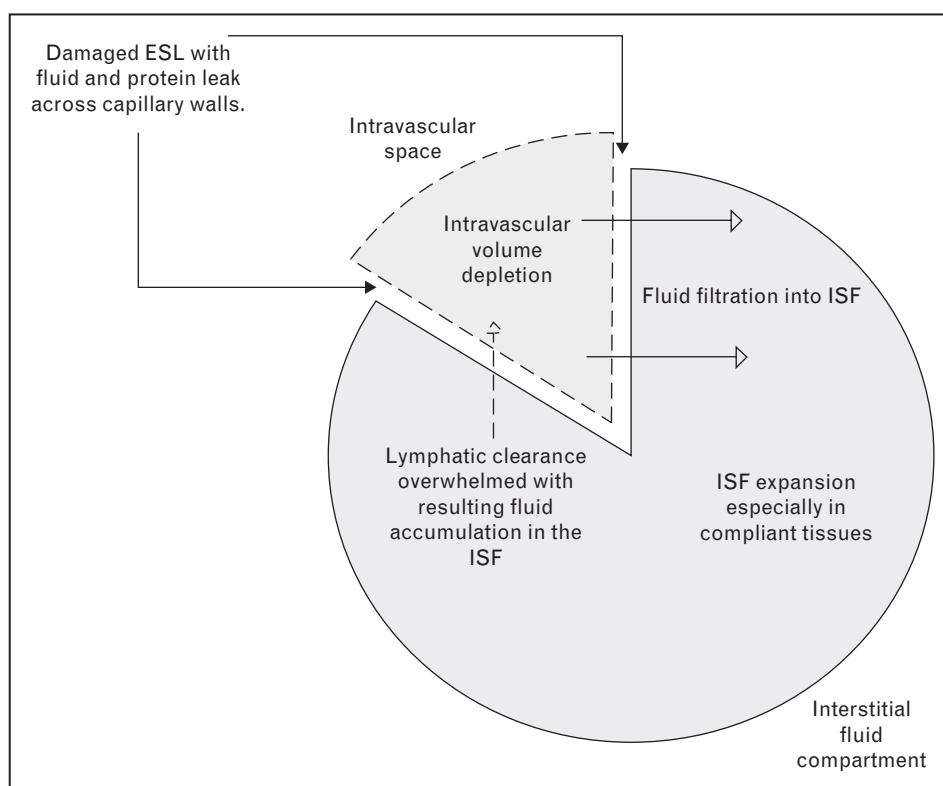


FIGURE 2. Endothelial surface layer (ESL) injury with critical illness. ESL is damaged with inflammation after surgery and with endothelial injury in critical illness. Crystalloids and colloids have equivalent volume effects during hypovolemia and with ESL damage as plasma proteins are lost to the interstitial compartment. Fluid accumulates in compliant tissues once capillary pressures rise to near normal. Less accumulation occurs in noncompliant tissues (such as encapsulated organs and/or rigid compartments).

in healthy volunteers do not extrapolate to the critically ill. Capillary pressures determine transvascular filtration effects. With supranormal capillary pressures, crystalloid infusions lower oncotic pressures, secondary to a dilutional effect, leading to greater filtration into compliant ISF. Therefore, in the presence of an intact EGL, euvolemic colloid infusions may sustain plasma expansion for a longer duration (e.g., during intraoperative goal-directed hemodynamic optimization) [2²²].

At lower capillary pressures such as during shock states, colloids and crystalloids will be similarly effective, as protein filtration is greatly increased with ESL damage. Volume expansion with either fluid is effective during subnormal capillary pressures [5²²]. Low MAP slows clearance of crystalloids from circulation as does anesthesia (probably as a result of lower pressures from internal redistribution of fluid and apparent beneficial effects on EGL integrity) [22]. Current evidence, therefore, supports crystalloid resuscitation during low capillary pressures (hypovolemia). This physiology suggests that colloids be used only at higher capillary pressures, for instance, when augmenting stroke

volume (SV) in the euvolemic patient (preemptive goal-directed fluid therapy in high-risk surgical patients) [2²²], but not with a damaged EGL and hypovolemia.

ABNORMAL SALINE

The plasma SID closely reflects the sodium to chloride difference and is about 40 in the healthy adult. With metabolic acidosis, as in shock states, this SID is decreased. Isotonic saline has a chloride concentration 1.5 times higher than plasma and a SID of 0. Resuscitation with fluids that have an SID lower than plasma will result in further acidosis. Clinical studies have also shown that when saline is given as the primary perioperative fluid, the result is a predictable hyperchloremic metabolic acidosis [23–25]. Hyperchloremia has been shown to have unfavorable effects on survival in an animal model of sepsis and resuscitation [26]. Effects include immune dysfunction [27], gastrointestinal dysfunction [28], and renal dysfunction [16,28]. Worsening acidosis, due to a saline-based resuscitation strategy, may be mistaken for inadequate

tissue perfusion in the setting of septic shock [29]. Unwarranted corrective measures may involve further aggressive volume loading to remedy the presumed perfusion deficit. Such misguided attempts to reverse or correct acidosis may result in increased morbidity and mortality. Studies in surgical populations have suggested that balanced crystalloid solutions with a higher SID (closer to plasma) and a lower chloride load compared with saline may predispose to favorable outcomes in terms of postoperative morbidity and costs [16,17].

CLINICAL PRACTICE: ART AND SCIENCE

With adequate physiologic reserve, management can be straightforward. Such patients will be able to maintain adequate hemodynamics (adjusting cardiac output, vascular tone, minute ventilation, or glomerular filtration rate) despite wide variations in fluid dosing or composition. SICU patients often have limited physiologic reserve with considerable derangement of homeostasis and organ dysfunction. In this setting a fine balance of the right fluid [15], in the right amount and at the right time, is needed. Dosing of maintenance fluids should be adjusted only for ongoing defined measurable losses. Unmeasured deficits, based on assumed loss of fluids into injured tissue or into

the peritoneal cavity ('third space'), should not be generically calculated or replaced with arbitrary hourly rates.

Intravenous fluid therapy in the SICU is best guided by changes in functional measures of volume responsiveness, such as PPV, SV variation (SVV), systolic pressure variation, or similar parameters, see Fig. 3 [9]. These parameters are reliable in patients with normal sinus rhythm receiving controlled positive pressure ventilation with adequate tidal volumes (above 8ml/kg ideal body weight). There are important caveats in the presence of arrhythmias, during spontaneous breathing, with reduced lung compliance or low tidal volumes [30–32]. In such patients typical PPV thresholds might not apply [12[•]]. Volume challenges or minichallenges of as little as 200ml given over 5 min [33] allow clinicians to predict the effects of subsequent fluid administration based on changes in functional measures. A reversible volume challenge maneuver [31] such as passive leg raising avoids even the administration of small quantities of 'test fluid' and distinguishes fluid responders from nonresponders [31,34]. On the other end of the spectrum, volume overloaded patients may benefit from volume removal during the recovery stages of illness guided by both functional measures and measures of SV [35[•]].

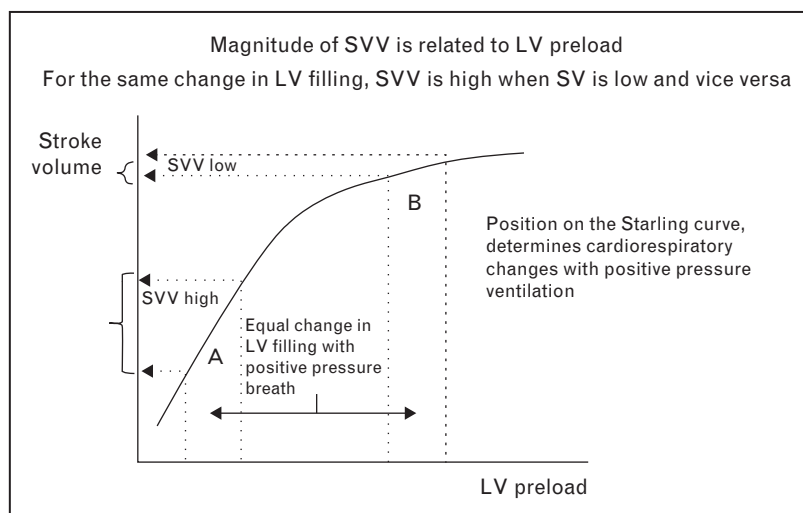


FIGURE 3. Stroke volume variation (SVV) related to left ventricular (LV) preload. Panels A and B represent different locations on the Frank–Starling curve. The change in preload induced by positive pressure ventilation is identical, but the impact on SV is not. The change in SV induced by one positive pressure breath is proportional to SVV. SVV is determined by the magnitude of preload dependency. Patients with higher SVV are more volume responsive (point A on the graph: preload dependent) functioning on the steeper proportion of the Frank–Starling curve. SVV decreases as preload dependent LV function is optimized (point B on the graph: preload independent). In these patients (B) volume can be safely removed as cardiac performance is not significantly influenced by changes in preload. SVV/SV pairs allow individual discrimination of a patient's Starling curve that can determine when volume is required to improve cardiac performance and conversely when volume can be removed safely.

GOAL-DIRECTED THERAPY

Goal-directed approaches prescribe fluids based on an individualized demonstration of flow augmentation (e.g. fluids only given to patients showing at least a 10% increase in SV; or fluid therapy targeted at patients with PPV greater than 12% in appropriate patients), see Fig. 3 [2[■],3,4[■],12[■]]. Patients will be 'Starling-ized', that is, receive fluids based on an assessment of left ventricular preload responsiveness, see Fig. 3. Thereby, flow is recruited earlier and continually to meet demand and organ hypoperfusion is avoided. In addition, fluids are restricted in nonresponders and, hence, hypervolemia is avoided. With decreasing use of the pulmonary artery catheter, minimally invasive technologies have become popular to assess flow and fluid responsiveness [7]. The noninvasive method used to measure flow may be important as well as the specific parameter being optimized [2[■],14]. Greater support exists for the esophageal Doppler (especially around bowel surgery) [36,37]; echocardiographic assessment of inferior vena cava respiratory variability [9]; and PPV [12[■]] than for the arterial pulse contour-based methods [38] or venous oximetry [13].

SEPSIS

Septic shock is often an initial clinical presentation with acute surgical disease or is a postoperative complication. Protocol-guided management of these patients, with targeted fluid administration as part of a bundle, is reported to improve outcomes [39]. Surgical septic shock often results in massive volume resuscitation [40] that may negatively impact outcome as shown by the observation that a positive fluid balance may increase risk of mortality [11] and morbidity [41]. An individualized approach that targets flow-based measures as a physiologic endpoint [42] and uses functional hemodynamic data rather than the CVP [3] should be used in septic patients. This strategy provides assurance that desired goals are achieved while minimizing detrimental over-resuscitation [18[■],43]. Functional parameters could be targeted from both hypovolemic and hypervolemic patient profiles depending on the phase of management. Mortality is significantly impacted by both ALI and acute kidney injury (AKI) and the severity of these may be modified by volume therapy. An appropriately timed strategy, early resuscitation and later 'de-resuscitation' significantly impacts length of mechanical ventilation and length of ICU stay for patients with ALI/acute respiratory distress syndrome (ARDS) [44]. EVLW measurement and its manipulation have great potential to

further refine volume therapy in this population [45].

ACUTE LUNG INJURY AND ACUTE KIDNEY INJURY

AKI identified after adjustment for fluid balance influences the duration of renal replacement therapy (RRT), diagnosis, and prognosis [45–47]. As fluid management itself influences the measured serum creatinine, changes in renal function require interpretation in light of volume therapy to appreciate the true extent of renal dysfunction [46]. Roughly 5–7% of high-risk surgical patients require RRT (dialysis) and this population presents specific challenges as homeostatic ability is truly lost. Data based on our published experience (evaluating physiologic endpoints as a guide to volume management in ICU patients requiring renal replacement) suggest that a SV index (SVI) greater than 35 ml/beat per m² and SVV less than 13% provide assurance that volume may be safely removed. This enables more aggressive 'deresuscitation' in certain patients over traditional approaches [35[■]], see Fig. 4. Highlighting this important concept – of using goals when fluid 'loading' and 'unloading' – is the observation that septic ARDS patients initially receiving aggressive resuscitation followed by a negative fluid balance beyond 48 h had the best outcomes when compared with other volume management strategies [47].

SPECIFIC PROCEDURES

Systemic inflammatory response can be expected with cardiopulmonary bypass (CPB), but ESL damage is minimized by avoiding CPB (off-pump cardiac surgery) and minimizing ischemia reperfusion [48]. Fluid management is challenging but as cardiac surgical patients are intensively monitored, a flow-directed algorithm applied postoperatively may reduce complications and length of hospital stay [49]. Goal-directed resuscitation in off-pump cardiac surgery [50] also improves outcomes and appropriate fluid use reduces vasopressor and catecholamine use [51].

After thoracic surgery, patients are at risk for ALI. Fluids may accumulate as EVLW [52]. A conservative strategy using a functional parameter may minimize volume overload to the extent possible without risking AKI, rather than merely following urine output as a guide to keeping the patient 'dry', see Fig. 4. In colorectal patients, in whom restrictive approaches guided by flow measures (particularly using the esophageal Doppler) improve outcomes, hypervolemia-related problems such as wound

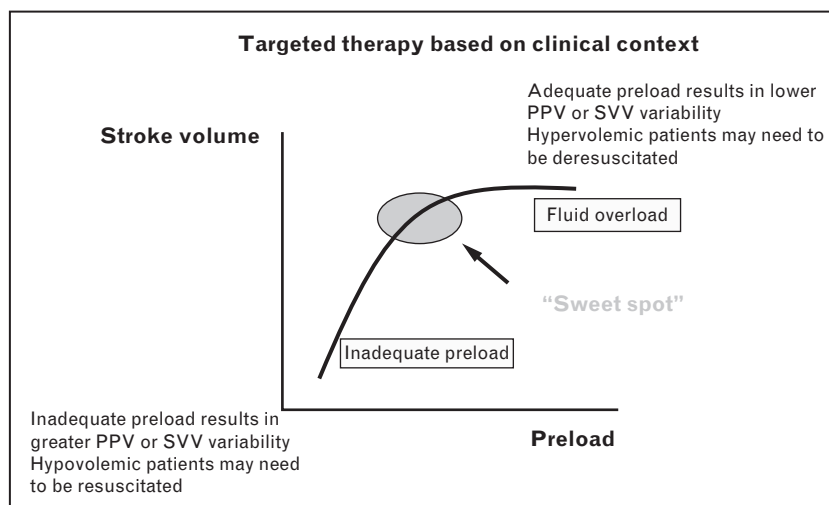


FIGURE 4. Targeted resuscitation and deresuscitation. The 'sweet spot' marks that part of the Frank–Starling curve where left ventricular function is optimal or 'ideal' for the clinical context. Below this left ventricle (LV) is under-filled and cardiac performance is significantly preload dependent, whereas above this LV is overfilled and cardiac performance is mostly preload independent. The 'sweet spot' could be approached from either direction depending on the clinical context. In the presence of excessive volume, necessary fluid removal is often required and can be guided by dynamic indices (see Fig. 3). An example is diuresis to remove extravascular lung water in patients with worsening lung injury. Conversely, in the presence of inadequate volume, necessary fluid loading is required to improve circulation by augmenting left ventricular filling. An example is the hypovolemic septic patient in whom resuscitation may be guided by pulse pressure variation (PPV) or stroke volume variation (SVV).

infection and ileus [38,39] are reduced by goal-directed therapy.

CONCLUSION

The dosing of intravenous fluids and choice of composition should be based on underlying pathophysiology. In critically ill surgical patients, fluids should produce a demonstrable enhancement of perfusion. The key is an individualized approach using volume loading only in responders and otherwise avoiding fluids. Management may include mini-boluses or reversible physiologic maneuvers to distinguish responders from non-responders. Functional measures allow goal-directed management while adapting to the clinical context with some limitations. Targeted 'deresuscitation' may be important to improve outcomes. Crystalloids may be used for resuscitation from subnormal capillary pressures and colloids when preemptively augmenting hemodynamics in euvolemic patients.

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Conflicts of interest

W.M. is on a speakers bureau for Edwards LifeSciences. T.H. has been a consultant and on the speaker bureau for Edwards LifeSciences, who manufacture both the arterial waveform monitors and pulmonary artery catheters. K.R. has nothing to declare.

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