

Perioperative Fluid Management

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Perioperative fluid management is currently undergoing such rapid changes that it is difficult to predict likely perioperative fluid protocols even a few years hence. Important preclinical and clinical information is accumulating in three major areas: 1) Perioperative fluid restriction; 2) Influence of types of infused fluids on clinical outcomes; and 3) Selecting endpoints for fluid administration.

Perioperative Fluid Restriction

Clinical trials suggest that perioperative fluid management may strongly influence both minor and major morbidity in ways that are specific to the type of surgery and to the types of fluids used. Conventionally, replacement of intraoperative fluid losses has included consideration of fluid that accumulates extravascularly in surgically manipulated tissue. Therefore, simple conventional guidelines for replacement of fluid losses during surgical procedures provide, in addition to maintenance fluids and replacement of estimated blood loss, $4 \text{ mL} \cdot \text{kg}^{-1} \cdot \text{h}^{-1}$ for procedures involving minimal trauma, $6 \text{ mL} \cdot \text{kg}^{-1} \cdot \text{h}^{-1}$ for those involving moderate trauma, and $8 \text{ mL} \cdot \text{kg}^{-1} \cdot \text{h}^{-1}$ for those involving extreme trauma. Over the past few years, clinical investigations have strongly suggested that conventional perioperative fluid therapy is often excessive, results in adverse consequences, and should be reduced (1,2).

However, in relatively uncomplicated ambulatory surgery, strict fluid restriction has been associated with less favorable outcomes than more liberal fluid administration. Yogendran et al. (3) randomized 200 ASA I–III ambulatory surgical patients to receive either 2 mL/kg or 20 mL/kg of Plasmalyte as a bolus over 30 min before surgery; patients receiving the higher dose had less postoperative thirst, drowsiness, dizziness, and nausea. Maharaj et al. (4) randomized 80 ASA I–II patients' schedules for outpatient gynecological laparoscopy to receive a small volume of balanced salt solution (3.0 mL/kg over 20 min preoperatively) or a large volume ($20 \text{ mL} \cdot \text{kg}^{-1} \cdot \text{h}^{-1}$ of fasting) over 20 min preoperatively. For a 60-kg patient who had been nil per os for 12 h the small volume

regimen would deliver 180 mL; the large volume regimen would deliver 1440 mL. The patients receiving the restricted volume suffered more frequent postoperative nausea and vomiting, experienced more pain, and required more anti-emetic and analgesic treatment. Holte et al. (5) randomized 48 ASA I–II patients undergoing laparoscopic cholecystectomy to receive either 15 mL/kg or 40 mL/kg of lactated Ringer's solution intraoperatively; the higher dose of fluid was associated with improved postoperative pulmonary function and exercise capacity, reduced neurohumoral stress response, and improvements in nausea, general sense of well-being, thirst, dizziness, drowsiness, fatigue, and balance function (Fig. 1).

In marked contrast, patients undergoing major intra-abdominal surgery appear to be harmed by more liberal fluid administration. Brandstrup et al. (6) randomized 172 elective colon surgery patients to either restrictive perioperative fluid management or standard perioperative fluid management with the primary goal of maintaining preoperative body weight in the fluid-restricted group. By design, the fluid-restricted group received less perioperative fluid and acutely gained $<1 \text{ kg}$ in contrast to $>3 \text{ kg}$ in the standard therapy group. More importantly, cardiopulmonary complications, tissue-healing complications, and total postoperative complications were significantly fewer in the fluid-restricted group (Table 1). Nisanevich et al. (7) randomized 152 ASA I–III patients undergoing elective intraabdominal surgery to a liberal protocol group, which received a bolus of lactated Ringer's solution of 10 mL/kg followed by $12 \text{ mL} \cdot \text{kg}^{-1} \cdot \text{h}^{-1}$, or a restricted protocol group, which received no bolus followed by lactated Ringer's solution at a rate of $4 \text{ mL} \cdot \text{kg}^{-1} \cdot \text{h}^{-1}$. The liberal protocol group had a lower postoperative hematocrit and serum albumin concentration, gained more fluid weight, suffered more total complications, required more time before postoperative flatus (4 versus 3 days) and bowel movements (6 versus 4 days), and had longer hospital stays (9 versus 8 days). The authors concluded that restrictive fluid may be advantageous.

How much fluid should be given perioperatively? The above trials, both in ambulatory patients and patients undergoing major abdominal surgery, compared quite severe fluid restriction with relatively

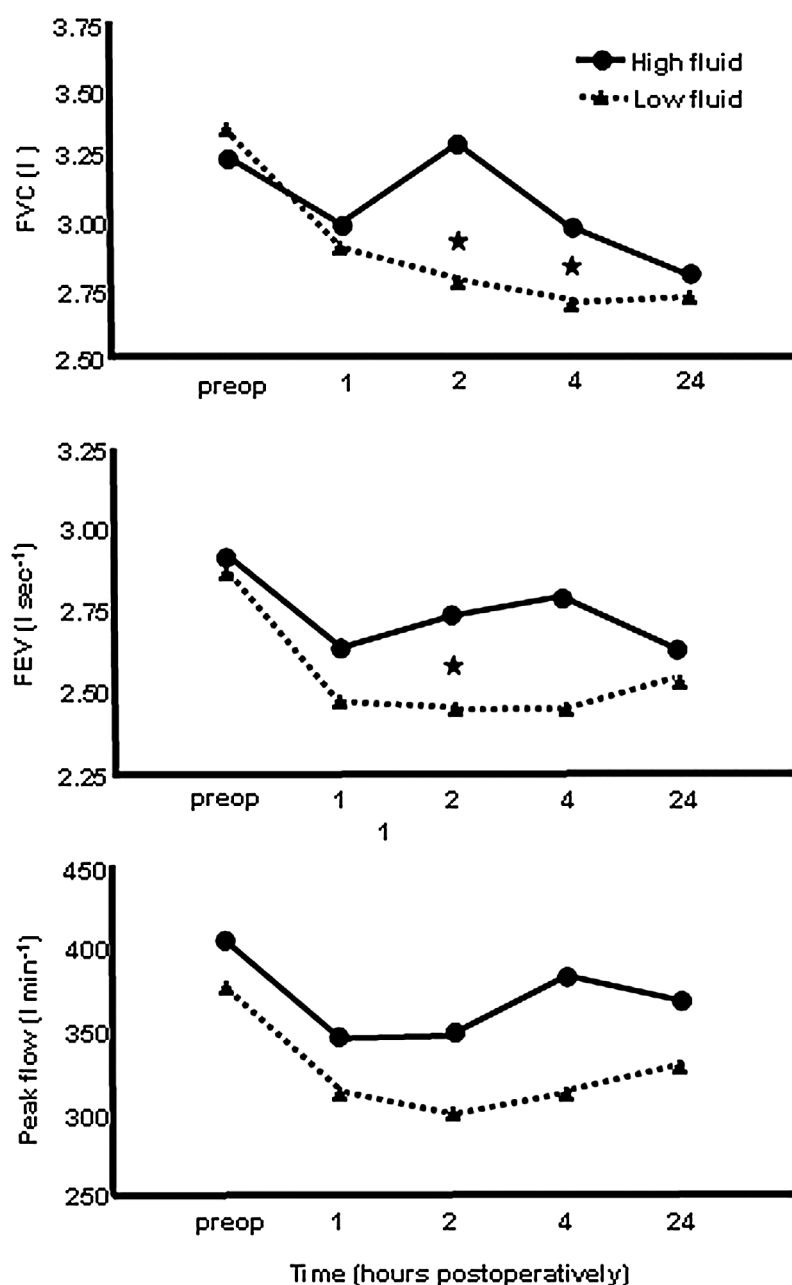


Figure 1. Postoperative changes in pulmonary function after laparoscopic cholecystectomy in patients receiving 15 mL/kg or 40 mL/kg of lactated Ringer's solution intraoperatively. Forced vital capacity (FVC), forced expiratory volume in one second (FEV_{1.0}) and peak flow recovered more rapidly in patients receiving the higher dose of fluid. *Statistically significant differences. Reprinted with permission from (5).

large fluid volumes. The results of the above trials suggest that additional information must be generated by other randomized clinical trials. Specifically, it is necessary to study more patients undergoing specific surgical procedures and to compare not only rigorous fluid restriction with permissive fluid infusion but to examine intermediate fluid regimens.

Influence of Types of Infused Fluids on Clinical Outcome

The three areas of fluid administration in which knowledge has advanced most in recent years have

been 1) acid-base and electrolyte effects of various fluids; 2) influence of hyperglycemia on outcome in critically ill and surgical patients; and 3) the kinetics of commonly used crystalloid and colloid fluids.

Acid-Base and Electrolyte Effects of IV Fluids

Perhaps one of the more surprising sets of observations regarding fluid therapy in the last decade has been the recognition that perioperative infusion of 0.9% saline produces dose-dependent hyperchloremic metabolic acidosis (Fig. 2). Taken as a group, several recent articles (8–10) illustrate that metabolic acidosis

Table 1. Number of Patients with Complications in Fluid-Restricted and Standard Therapy Groups (Per-Protocol Analysis)

	Blinded assessment			Unblinded assessment		
	Restricted group	Standard group	<i>P</i> value	Restricted group	Standard group	<i>P</i> value
Overall complications	21	40	0.003	21	43	0.000
Major complications†	8	18	0.040	8	19	0.026
Minor complications†	15	36	0.000	15	37	0.000
Tissue-healing complications†	11	22	0.040	10	24	0.009
Cardiopulmonary complications†	5	17	0.007	4	18	0.002

n = 69 in restricted group and *n* = 72 in standard group.

† Number of patients in subgroups does not add up to number of overall complications because some patients had more than 1 complication.

Reproduced with permission from Brandstrup et al. (6).

is a direct consequence of rapid replacement or expansion of extracellular volume with fluid containing no bicarbonate or bicarbonate substrate (e.g., lactate) (11,12) (Table 2).

One of the more interesting aspects of saline-induced hyperchloremic metabolic acidosis is that the influence of acidemia may produce hyperkalemia, despite the fact that 0.9% saline contains no potassium. O'Malley et al. (13) randomized 51 patients undergoing renal transplants (48 living donor, 3 cadaveric) to receive either lactated Ringer's solution (which contains a $[K^+]$ of 3.0 mEq/L) or 0.9% saline. No patient in the lactated Ringer's group developed serum potassium exceeding 6.0 mEq/L in comparison with 5 patients in the saline group; no patient in the lactated Ringer's group required treatment for metabolic acidosis in comparison with 8 in the saline group.

An additional important effect of the infusion of crystalloid fluids in large quantities is the generation of hypoalbuminemia, which in turn reduces the normal anion gap, requiring adjustment of the calculated anion gap for the reduction in serum albumin. The simplest correction is to multiply the difference between a normal serum albumin (4.0 g/dL) and the measured serum albumin by 2.5, then add the result to the calculated anion gap (calculated as $[Na^+] - ([Cl^-] + [HCO_3^-])$; normally 6–12 mEq/L (14).

Influence of Hyperglycemia on Outcome in Critically Ill and Surgical Patients

Traditionally, glucose-containing IV fluids have been given in an effort to prevent hypoglycemia and limit protein catabolism. However, because of the hyperglycemic response associated with surgical stress, only infants and patients receiving insulin or drugs that interfere with glucose synthesis are at risk for hypoglycemia. Iatrogenic hyperglycemia can limit the effectiveness of fluid resuscitation by inducing an osmotic diuresis and, in animals, may aggravate ischemic neurologic injury (15). Although associated with worse outcome after subarachnoid hemorrhage (16)

and traumatic brain injury (17) in humans, hyperglycemia may also constitute a hormonally mediated response to more severe injury. In critically ill patients, evidence strongly suggests that tight control of plasma glucose (maintenance of plasma glucose between 80 and 110 mg/dL) is associated with reduced mortality and morbidity (18–21). Evidence also suggests that glucose control improves outcome in surgical patients (22).

Kinetics of IV Fluids

The expected effects of IV fluids depend in part on their distribution volumes and in part on the speed with which they are excreted. The distribution volume of sodium-free water is total body water (TBW), which constitutes 60% of total body weight. The distribution volume of infused sodium is extracellular volume (ECV), which includes both plasma volume (PV) and interstitial fluid volume (IFV) and constitutes 20% of body weight. Sodium concentration ($[Na^+]$) is approximately 140 mEq/L in PV and IFV. Intracellular volume (ICV) constitutes 40% of total body weight. The predominant intracellular cation, potassium, has an intracellular concentration ($[K^+]$) approximating 150 mEq/L. Albumin, the most important oncologically active constituent of ECV, is unequally distributed in PV (~4 g/dL) and IFV (~1 g/dL). The ECV is the distribution volume for colloid solutions although IFV concentrations of albumin vary greatly among tissues.

Conventional clinical prediction of PV expansion (PVE) after fluid infusion assumes that body fluid spaces are static. As an example of the static approach, assume that a 70-kg patient has suffered an acute blood loss of 2000 mL, approximately 40% of the predicted 5 liters blood volume. The formula describing the effects of attempts to replace shed blood volume with an infused fluid (e.g., lactated Ringer's solution) is as follows:

$$\text{Expected PV increment} = \text{volume infused} \times \frac{\text{normal PV}}{\text{distribution volume}} \quad (1)$$

Figure 2. Changes in pH and serum sodium, chloride and albumin concentrations in gynecologic surgical patients receiving approximately 60 mL/kg of 0.9% saline (open circles) or lactated Ringer's solution (closed circles) over 120 min. Saline was associated with acidemia accompanied by a moderate increase in serum sodium concentration and a marked increased in serum chloride concentration. Both fluids at this rate of infusion generate hypoalbuminemia. Reprinted with permission from (39).

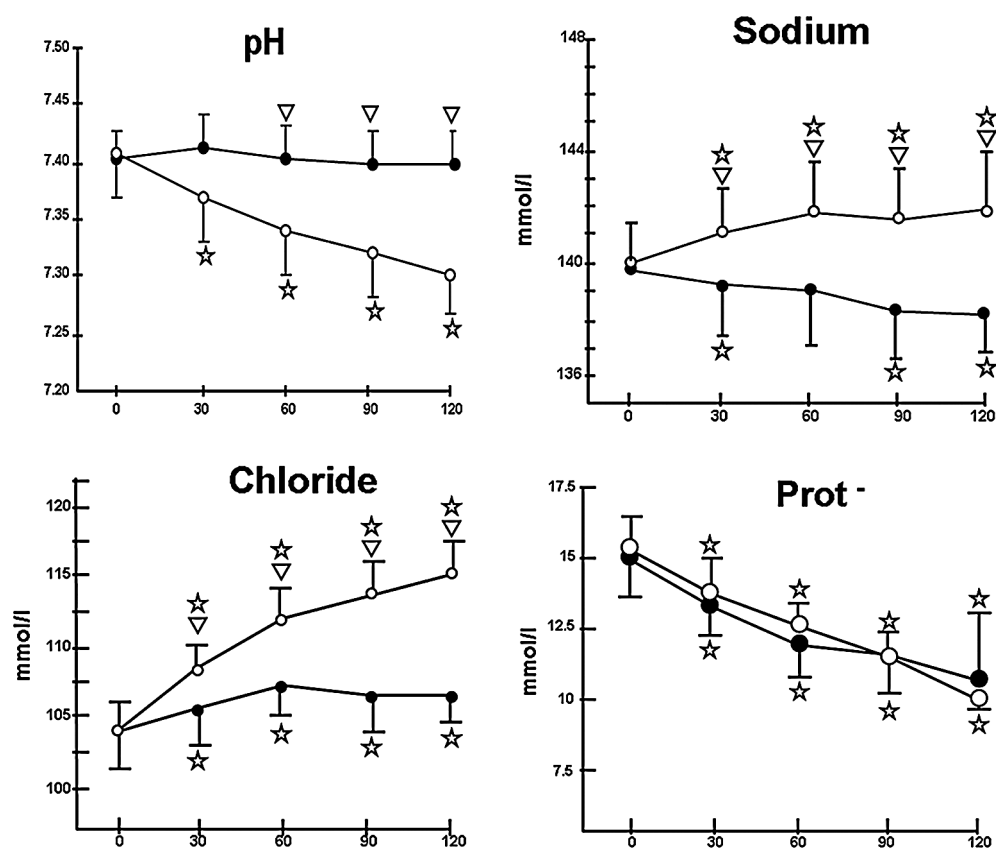


Table 2. Recent Literature on Perioperative Saline-Induced Hyperchloremic Metabolic Acidosis

First author	Infusion		Estimated ECV (L)	Postinfusion	
	Volume (mL/kg)	[HCO ₃ ⁻] (mEq/L)		Predicted [HCO ₃ ⁻] (mEq/L)	Actual [HCO ₃ ⁻] (mEq/L)
Waters (10)	14.9	0	15.8	25.1	25.0
Rehm (9)	23.7	0	13.1	21.0	21.6
Liskaser (8)	19.7	0	16.7	22.9	20.4
McFarlane (40)	53.4	0	14.2	20.4	21.0
Scheingraber (39)	71	0	17.1	18.6	18.4

Rearranging this equation yields the following:

$$\text{Volume infused} = \text{expected PV increment} \times \frac{\text{distribution volume}}{\text{normal PV}} \quad (2)$$

To restore blood volume using lactated Ringer's solution requires 9.1 liters:

$$9.1 \text{ liters} = 2 \text{ liters} \times 14 \text{ liters} / 3 \text{ liters} \quad (3)$$

where 2 liters is the desired PV increment, 14 liters = ECV in a 70-kg person, and 3 liters is the normal estimated PV.

If 5% albumin, which exerts colloid osmotic pressure similar to plasma, were infused, much of the infused volume initially would remain in the PV.

However, in kinetic terms, these analyses are simplistic. Infused fluid does not simply equilibrate throughout an assumed distribution volume but is added to a highly regulated system that controls intravascular, interstitial, and intracellular volume. Volume kinetic analysis permits estimation of peak volume expansion and rates of clearance of infused fluid and complements analysis of "pharmacodynamic" effects, such as changes in cardiac output or cardiac filling pressures.

Figure 3 illustrates the conceptual kinetic model proposed by Svensen and Hahn, (23) who used hemoglobin concentration ([Hb]) as an endogenous tracer that reflects changes in PV. Svensen and Hahn (23) infused acetated Ringer's solution, 6% dextran 70, or

7.5% saline in volunteers and fitted the changes in [Hb] to one- and two-volume-of-fluid-space (VOFS) models.

Using this approach, the effects of common physiologic and pharmacologic influences can be examined in experimental animals or humans. For example, in chronically instrumented sheep, isoflurane-anesthetized and conscious sheep had similar kinetics of PV expansion after fluid infusion, but anesthetized sheep had reduced urinary output, suggesting that anesthesia promoted expansion of extravascular volume (24). Subsequent experiments demonstrated that this effect was attributable to isoflurane and not to mechanical ventilation during anesthesia in sheep (25). These observations must be confirmed in anesthetized humans and other anesthetics must be examined.

Selecting Endpoints for Fluid Administration

Assessment of perioperative fluid requirements is notoriously difficult as is assessment of mild hypovolemia or mild hypervolemia. Laboratory evidence that suggests hypovolemia or ECV depletion includes low urinary $[\text{Na}^+]$ (≤ 20 mEq/L), metabolic alkalosis (if hypovolemia is mild), metabolic acidosis (if hypovolemia is severe) and azotemia. Blood urea nitrogen (BUN), normally 8.0–20 mg/dL, is increased by hypovolemia, high protein intake, gastrointestinal bleeding, or accelerated catabolism and is decreased by severe hepatic dysfunction. Serum creatinine (SCr), a product of muscle catabolism, may be misleadingly low in elderly adults, females, and debilitated or malnourished patients. In contrast, in muscular or acutely catabolic patients, SCr may exceed the normal range (0.5–1.5 mg/dL) because of more rapid muscle breakdown. A ratio of BUN:SCr exceeding the normal range (10–20) suggests dehydration. In prerenal oliguria, enhanced sodium reabsorption should reduce and enhanced water reabsorption should increase urinary concentration (i.e., urinary osmolality >400 ; urine/plasma creatinine ratio $>40:1$). However, the sensitivity and specificity of measurements of urinary electrolytes and osmolality may be misleading.

Intraoperative Clinical Assessment

Visual estimation, the simplest technique for quantifying intraoperative blood loss, assesses the amount of blood absorbed by gauze squares and laparotomy pads and adds an estimate of blood accumulation on the floor and surgical drapes and in suction containers. Both surgeons and anesthesia providers tend to underestimate losses.

Assessment of the adequacy of intraoperative fluid resuscitation integrates multiple clinical variables, including heart rate, blood pressure, urinary output,

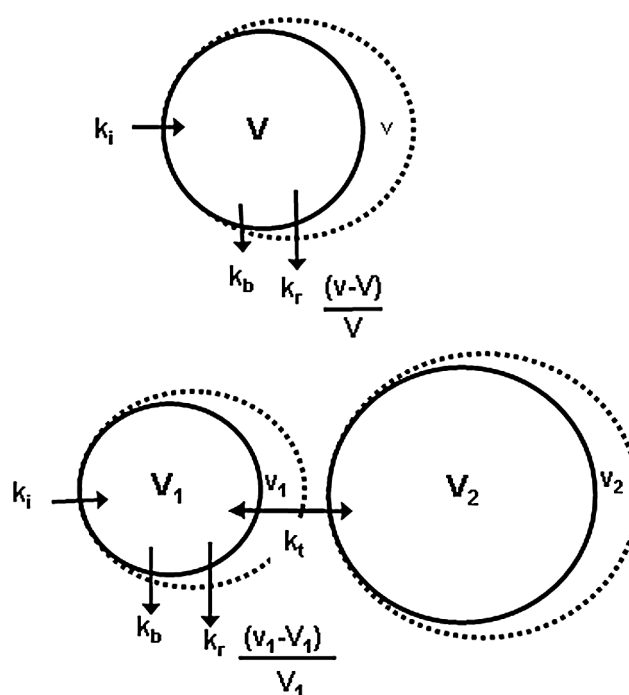


Figure 3. Schematic drawing of the kinetic model used to calculate the size of the body fluid spaces expanded by IV infusions of fluid in humans. Data are fitted to a one-volume or two-volume-of-fluid-space (VOFS) model. The assumptions underlying the one-compartment VOFS model (top) are as follows: 1) during fluid infusion, fluid enters an expandable space of volume v at a constant rate k_i ; 2) the expandable fluid space has a target volume V , which the body strives to maintain; 3) volume v changes by fluid being eliminated from the fluid space at a basal rate, k_b (perspiration and basal diuresis), and at a controlled rate. The controlled rate is proportional to a constant k_r to the relative deviation of v from the target volume V . The assumptions behind the two-compartment VOFS model (bottom) are similar: 1) during fluid infusion, fluid enters an expandable space of volume v_1 at a constant rate k_i ; 2) there is a secondary expandable fluid space of volume v_2 exchanging fluid with the primary fluid space; 3) volume v_1 changes through exchange with the secondary fluid space and as a result of fluid being eliminated from the primary fluid space at a basal rate, k_b (perspiration and basal diuresis), and at a controlled rate (4). The primary and secondary fluid spaces have target volumes V_1 and V_2 which the system strives to maintain by acting on the controlled elimination mechanism k_r , which is proportional to the relative deviation from the target volume of the primary fluid space, and by acting on the fluid exchange mechanism; (5) the net rate of fluid exchange between the two spaces is proportional to the difference in relative deviations from the target volumes by a constant k_t . Reprinted with permission from (23).

arterial oxygenation, and pH. Tachycardia is an insensitive, nonspecific indicator of hypovolemia. In patients receiving anesthetic doses of potent inhalational agents, maintenance of a satisfactory blood pressure implies adequate intravascular volume. During profound hypovolemia, indirect measurements of blood pressure may significantly underestimate true blood pressure. In patients undergoing extensive procedures, direct arterial pressure measurements are more accurate than indirect techniques and provide convenient access for obtaining arterial blood samples. An

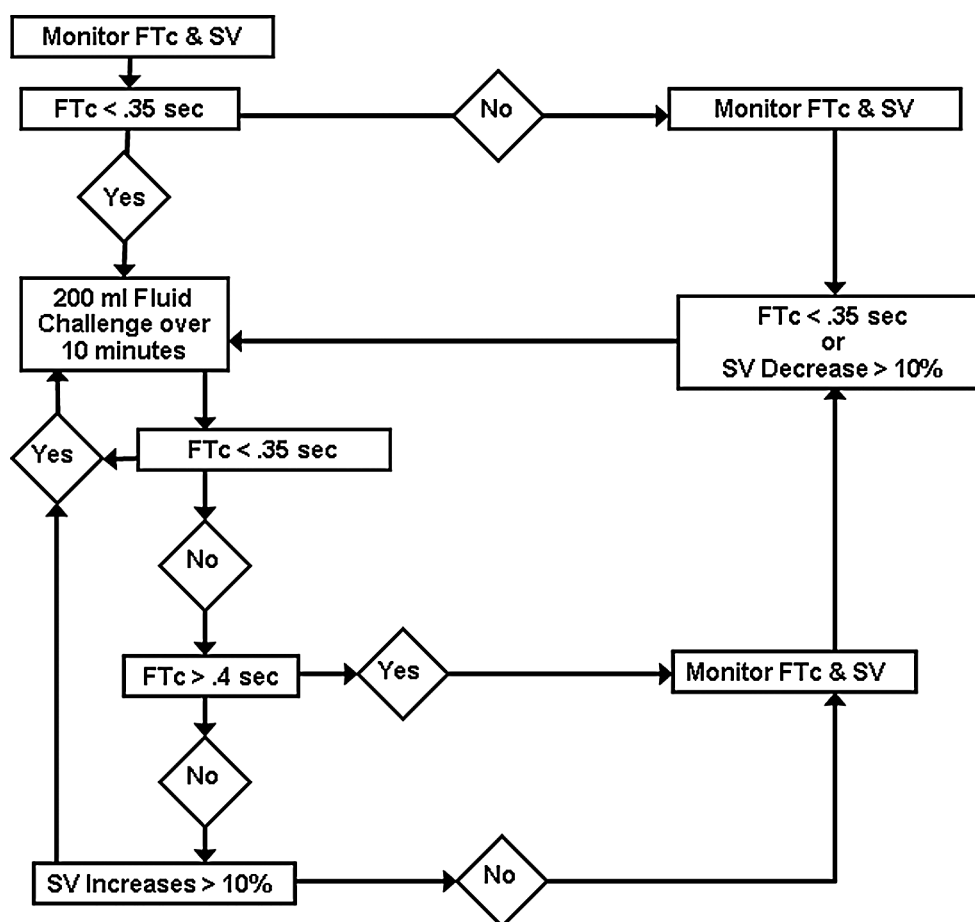


Figure 4. Protocol used by Gan et al. (37) who used esophageal Doppler monitoring to manage perioperative fluid management during surgery with expected blood loss exceeding 500 mL. SV, stroke volume; FTc, corrected flow time obtained from the esophageal Doppler monitor. Reprinted with permission.

additional advantage of direct arterial pressure monitoring may be recognition of increased systolic blood pressure variation accompanying positive pressure ventilation in the presence of hypovolemia (26,27).

Urinary output usually declines precipitously during moderate to severe hypovolemia. Therefore, in the absence of glycosuria or diuretic administration, a urinary output of $0.5\text{--}1.0\text{ mL} \cdot \text{kg}^{-1} \cdot \text{h}^{-1}$ during anesthesia suggests adequate renal perfusion. Arterial pH may decrease only when tissue hypoperfusion becomes severe. Cardiac output can be normal despite severely reduced regional blood flow. Mixed venous hemoglobin desaturation, a specific indicator of poor systemic perfusion, reflects average perfusion in multiple organs and cannot supplant regional monitors such as urinary output.

Oxygen Delivery as a Goal of Management

Because no intraoperative monitor is sufficiently sensitive or specific to diagnose hypoperfusion in all

patients, clinicians have proposed a variety of endpoints for hemodynamic resuscitation in high-risk surgical patients. One key variable that has been associated with improved outcome in high-risk surgical patients and critically ill patients is a systemic oxygen delivery ($\dot{V}O_2$) $\geq 600\text{ mL O}_2 \cdot \text{m}^2/\text{min}^{-1}$ (equivalent to a CI of $3.0\text{ L} \cdot \text{m}^2 \cdot \text{min}^{-1}$, a [Hgb] of 14 g/dL , and 98% oxyhemoglobin saturation). Boyd et al. (28) randomized 107 patients to conventional treatment or fluid plus dopexamine to maintain oxygen delivery $\geq 600\text{ mL O}_2/\text{m}^2 \cdot \text{min}^{-1}$ and demonstrated a decrease in mortality and in the number of complications in the patients managed at the higher level of oxygen delivery. Based on these results, the authors calculated that the cost of obtaining a survivor was 31% lower in the protocol group (29). Wilson et al. (30) randomized 138 patients undergoing major elective surgery into three groups. One group received routine perioperative care; one received fluid and dopexamine preoperatively, intraoperatively, and postoperatively to maintain oxygen delivery

$\geq 600 \text{ mL O}_2/\text{m}^2 \cdot \text{min}^{-1}$; and the third group received fluid plus epinephrine preoperatively, intraoperatively, and postoperatively to achieve the same endpoints. In the two groups in which oxygen delivery was supported, only 3 of 92 patients died, compared with 8 of 46 control patients. However, the complication rate was significantly lower in the dopexamine group than in the epinephrine group. At present, available data are consistent with several inferences. First, there is no apparent benefit of targeting oxygen delivery for patients other than surgical patients (31) and patients undergoing initial resuscitation from septic shock in the emergency room (32). In surgical patients, early initiation of goal-directed resuscitation is associated with better outcome than delayed initiation (33). Second, outcome may be strongly influenced by the choice of inotropic agents. Third, increased fluid given as part of goal-oriented resuscitation has been associated with an increased incidence of abdominal compartment syndrome in trauma patients (34) and burned patients (35).

Recently, several studies have reported improved outcome based on adjustment of perioperative fluids through the use of an esophageal Doppler monitor that estimates descending aortic blood flow and quantifies the duration of systole (36). Using the esophageal Doppler to guide administration of colloid boluses, Gan et al. (37) have reported shortened length of hospital stay after major surgery, using a relatively straightforward protocol (Fig. 4) to determine when to administer colloid boluses (consisting of hydroxyethyl starch up to a total dose of 20 mL/kg). Interestingly, Horowitz and Kumar (38) have speculated that the infusion of colloid rather than the monitor-driven algorithm was responsible for the improved results. From a kinetic perspective, the longer persistence of plasma volume expansion after colloid as opposed to crystalloid boluses could explain more stable perfusion.

Summary

The basic and clinical science underlying perioperative fluid administration is rapidly progressing. Within the next decade, surgical patients will receive more appropriate, individually customized fluid management.

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