Perioperative Fluids: An Evidence-Based Review

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Many questions have arisen and much controversy has emerged regarding how much fluid should be given perioperatively, which fluids should be given, when they should be given, and whether outcomes can be influenced. It’s been called the “Great Fluid Debate.” In fact, one might ask whether the anesthesiologist can even make a difference in the long run. Several goals of fluid administration have been identified: Tissue perfusion should be optimized; and heart rate, stroke volume, hemoglobin, and oxygen saturation should be appropriately manipulated.

But just how to achieve these end points, and whether they can be done by fluid administration, remains unclear. Our current standard therapy—cannulate a vein, give fluids to maintain blood pressure, and make up for supposed losses—has been challenged for almost a century. Canon noted that fluids administered before operative control of an injury were ineffective, an observation emphasized by Bickell and others some 70 years later. Nevertheless, standard U.S. Army protocols called for massive crystalloid resuscitation in the arena of war—especially in Vietnam—to preserve the kidneys. Thus, the Da Nang lung, or adult respiratory distress syndrome, was born.

Background

Galen was among the first to appreciate the circulation of the blood in the second century A.D., recognizing a difference between venous (dark) and arterial (bright) blood. He posited 2 circulations, venous through the liver and arterial via the heart. It was not until 1628 when the role of the heart as a pump was described by Harvey in de Motu Cordis. Sir Christopher Wren along with Robert Boyle are credited with being the first to propose and demonstrate IV administration of medications (wine and opium) into dogs, using an animal bladder and quills. O’Shaughnessy, an Irish physician who trained in Edinburgh and then moved to London, examined the blood in a healthy state and in cases of cholera,
noting a deficiency in salt in the latter samples. He recommended the injection of aqueous fluid into the veins.

Building on these observations, Thomas Latta, during the cholera epidemic of Scotland in 1831-1832, decided to “throw the fluid immediately into the circulation.” He described inserting a tube into a basilica vein and injecting ounce after ounce of a solution containing “two to three drachms of muriate of soda and two scruples of the subcarbonate of soda in six pints of water.” He used a pump that had been patented in 1830 by Reid to remove stomach contents. Francis Rynd, another Irish physician, is credited with the introduction of the hypodermic syringe during the 1840s. Some 10 years later, Alexander Wood produced the first hypodermic syringe that had a hollow needle attached.

IV infusion of anesthetic agents, first chloral hydrate and later hedonal, became popular during the latter part of the 19th century. For a brief period, both ether and chloroform were administered in saline solutions. By the middle of the 20th century, short-acting agents, especially pentothal and amytal, were used for minor and major surgeries, administered as infusions, and often combined with local infiltration and nitrous oxide. A more routine use of continuous fluid infusion during surgery was introduced by Hirshfeld, Hyman, and Wang in 1931, but they also noted that too rapid administration could cause “speed shock.” Nevertheless, by the mid-1950s, various solutions were available and were administered using glass bottles and red rubber resterilizable infusion sets. In Europe, however, many centers continued the practice of securing a vein preoperatively with a metal needle, the end of which was then closed with a moveable external rubber stopper. Induction agents were given, but fluids only if deemed necessary.

The Third Space?

Traditionally, we have been taught that there are 3 spaces—intravascular, extravascular, and a space that appears during surgery or trauma. The origin of this third space came about some 60 years ago in Texas. Using 2 groups of patients, 5 undergoing minor surgery (group 1) and 13 having major procedures such as cholecystectomy, gastrectomy, or colectomy (group 2), Shires and colleagues measured plasma volume, red blood cell mass, and extracellular volumes on 2 occasions using tagged substances. No IV fluids were given. They found a decrease in functional extracellular fluid in group 2 and thus determined that fluid (up to 28% of the extracellular water) was redistributed due to the surgery and needed to be replaced. Two years previously, Moore, a Boston surgeon, had suggested that there was a metabolic response to surgical stress and the release of antidiuretic hormone (ADH) that caused the retention of sodium and water and that, therefore, perioperative fluids should be restricted. He also emphasized that the type of anesthesia (in the Texas studies, cyclopropane and ether were used), the complexity of the surgery, the time involved, and other comorbidities should all be taken into consideration. A debate developed in the literature, with both sides ultimately calling for moderation in fluid replacement.

However, the idea of a mysterious third space took hold; protocols were developed to compensate for it and for other supposed intraoperative requirements. The 4:2:1 or 100-50-20 rule was developed and has remained in general practice, despite its lack of relevance to anesthesia today. Basically, depending on weight, the rule calls for IV fluids: 4 mL/kg/h for the first 10 kg to be followed by 2 mL/kg/h for the next 10 kg and finally 1 mL/kg/h thereafter; or, in daily replacement, 100 mL/kg for the first 10 kg, 50 mL/kg for the next 10 kg, and 20 mL/kg for any weight over that. In other words, a 70-kg patient should receive 110 mL/h replacement, or around 2,500 mL fluid/d. What should be realized is that Holday’s article was intended for pediatric application and not specifically for intraoperative application. It was based on 3 theories from earlier work:

- Surface area can estimate water expenditure.
- Caloric needs depend on age, weight, activity, and food (a comparison was made between a steer and a rat).
- Urinary output and insensible losses correspond to age (but only up to age 20 and weight <60 kg, based on the theory that caloric need/kg = 100 – 3x age).

These papers were founded on even earlier studies, some from as few as 2 patients and using gasometer estimates of body surface area from the 1920s. The relevance of these rules must be considered in light of present-day practice. They were developed without scientific evidence, much of which was supposition based on unpublished data; the anesthetic and surgical techniques since have changed drastically; the application of the rules was intended for children on a daily basis; and, at the very least, they were meant only as a very rough guide. Nevertheless, we continue to fluid load.

The Case For and Against Fluid Loading

Clinicians have presented cases for and against perioperative fluid administration for decades.

For

Several assumptions are made to explain why fluids should and indeed must be given perioperatively:

- The patient is fasted preoperatively and is thus hypovolemic.
- Insensible losses continue during surgery and must be accounted for.
- Fluid shifts to the “third space” must be replaced.
- Blood must be replaced at 3 or 4:1 crystalloid.
- Hypotension following induction is due to vasodilation and the vascular space must be filled.
- Urine output must be taken into consideration and replaced.
- Even if the patient is overloaded, the kidneys will regulate.
- We have always done it that way.
Each of these arguments can be examined and found flawed, resulting in a case for at least a review of this line of thinking.

**AGAINST**

A patient’s preoperative hydration state is largely unknown and the target is unclear. Pulmonary artery wedge pressures and central venous pressures do not indicate volume responsiveness. Preoperative fasting for 8 to 10 hours results in a slight decrease in extravascular fluid. However, intravascular volume is maintained. Putting it in perspective, 1 L crystalloid is the approximate volume of 4 cups of coffee, an amount that rarely has to be consumed before 8 AM to avoid dehydration. Also, the recommendations for fasting guidelines from the American Society of Anesthesiologists now advocate water or clear fluid intake 2 hours preoperatively.21 Bowel preparation, also targeted as a cause of hypovolemia, is undertaken less frequently. The effecent drugs used today mean that the patient is awake and able to take fluids much sooner. Combinations of antiemetics and better pain control also have hastened the patient’s return to the preoperative state. Hypotension following induction is more likely related to administration of the anesthetic drug or to other comorbidities.

Much surgery today is performed using laparoscopic, robotic, or minimally invasive techniques. Even in the case of open approaches, irrigation is constant. Temperature control and humidification systems further reduce insensible losses. Urinary output is frequently low during periods of stress due to ADH release; giving fluid boluses is more likely to result in fluid overload than in diuresis. This begs the question: “If the kidneys are already under stress can they compensate, and if so during what time period?” Preexisting renal problems or administration of drugs that hamper kidney function may further delay diuresis, resulting in greater weight gain.

Regarding the argument concerning the third space, we might ask, if it exists, how do we measure it? There are ongoing fluid shifts that may peak around 5 hours, persisting for days.22 Infused fluids may take up to 3 weeks to be excreted. Indeed, the very existence of a third space has been emphatically rejected.23 The rationale of replacement of blood by 3 or 4 times as much crystalloid stems from the fast movement of the latter out of the vascular space, leaving less than one-third to actually replace the blood. This extravasated fluid moves rapidly to dependent and soft tissue areas such as the lungs and gut, with the end result of weight gain.

The argument that “we have always done it this way” may be the most difficult to refute. Generally, a minimum of 20 years is required for proven measures to become universally adopted, or as Boswell remarked in 1770, “That fellow seems to me to possess but one idea, and that is a wrong one.”

**Problems With Study Designs**

Although it might seem simple to arrive at a formula that could be applied universally, many difficulties have arisen. First, there has been little consensus as to what represents liberal (20 mL/kg/h), standard (5-10 mL/kg/h), or restrictive (2-5 mL/kg/h) replacement. Most studies have not been standardized for reasonable comparison. Study targets also are open to speculation (Table 1). Many clinicians are unwilling to change “established” protocols. Clear differentiation between major and minor surgery does not exist.

Perhaps the target that has been most closely associated with adverse outcome is that of weight gain. Lowell found that several parameters were improved with reduced crystalloid infusion (Table 2).22

### Table 1. Targets Used Without Standardization

<table>
<thead>
<tr>
<th>Study Targets</th>
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<tbody>
<tr>
<td>Weight gain</td>
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<tr>
<td>Postoperative nausea and vomiting</td>
</tr>
<tr>
<td>Pain</td>
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<tr>
<td>Tissue oxygenation</td>
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<tr>
<td>Postoperative ileus</td>
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<tr>
<td>Pneumonia</td>
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<td>Revision surgery</td>
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<td>Wound healing</td>
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<tr>
<td>Infection</td>
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<td>Cardiovascular diseases</td>
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<td>Hospital stay</td>
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<td>Coagulopathies</td>
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### Table 2. Outcomes With Low Versus Aggressive Crystalloid Infusion

<table>
<thead>
<tr>
<th>Crystalloid Infusion</th>
<th>Low: 4 L</th>
<th>Aggressive: 12 L</th>
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</thead>
<tbody>
<tr>
<td>Weight gain, %</td>
<td>4.7</td>
<td>32</td>
</tr>
<tr>
<td>Postoperative ventilation, d</td>
<td>1.7</td>
<td>6</td>
</tr>
<tr>
<td>Vasopressors, d</td>
<td>2.8</td>
<td>26</td>
</tr>
<tr>
<td>ARF, %</td>
<td>17</td>
<td>33</td>
</tr>
<tr>
<td>Mortality, %</td>
<td>10</td>
<td>100</td>
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ARF, acute renal failure

From reference 22.
Conflicting data surround the effect of fluid administration on postoperative nausea and vomiting. Liberal fluid administration especially appears to be beneficial for younger women undergoing short gynecologic procedures.23

Time to wound healing has been used as a study target. Oxidative killing by neutrophils is essential to tissue repair. Mild hypothermia reduces tissue oxygenation by a factor of 3. Although supplemental oxygen can increase availability, this effect is not seen in hypoperfused areas that may be edematous from extravasated fluid. In patients receiving liberal fluid replacement, the infection rate and time of hospitalization increased.24-26

Major surgery is not well defined, whether it be by length or complexity of the procedure. Also, the experience and level of training of the surgeon and the identification of the hospital center as a tertiary care center are unknown factors.

**Fluids and Body Systems**

Due to the rapid rate at which crystalloids leave the vascular compartment, effects are seen in most body systems, especially when the fluid balance is markedly positive. Swelling of the face and neck is often marked after hours in the prone position, delaying time to safe extubation.

**Gastrointestinal Function**

As fluid accumulates in the gut wall, intraabdominal pressure (IAP) increases, especially in obese individuals in whom resting IAP is elevated. This rise in IAP results in impaired pulmonary function and decreased renal perfusion, especially when mean arterial pressure also is decreased. Increased IAP also stimulates the production of ADH, also contributing to oliguria. As fluid overload increases, gut wall edema allows the translocation of endotoxins and/or bacteria, leading eventually to sepsis and multiple organ failure.

Postoperative ileus remains a major problem following abdominal surgery. Several studies have indicated that fluid reduction and limiting positive fluid balance to 1 to 2 L contributes significantly to decreased severity and duration of this debilitating complication and reduces hospital length of stay.27,28

**Pulmonary Effects**

Direct correlation had been shown between the development of postoperative acute lung injury (adult respiratory distress syndrome [ARDS]) and liberal fluid administration.29 Fluid balance is best kept at no more than +1.5 L. In a study of patients undergoing vascular surgery, respiratory failure occurred in 10% of those who received more than 6 L of fluid in 24 hours.30 Of 89 patients who had respiratory failure postoperatively, 25 developed ARDS. Intraoperative fluid administration of 20 mL/kg/h was associated with a 3.8 times higher adjusted odds ratio of developing ARDS. The ratio was 2.4 times at 10 to 20 mL compared with patients who received less than 10 mL/kg.31

**Cardiac Effects**

Fluid overload, especially in patients with underlying cardiac disease, may result in congestive heart failure. In 4,059 patients undergoing major noncardiac surgery, cardiac events occurred 3 times more often in those with a positive fluid balance exceeding 3.2 L compared with those with a balance less than 2 L.32 Vretzakis et al studied 192 patients undergoing cardiac surgery. In group 1 (100 patients), fluids were turned off after induction.33 Fluids were unrestricted in group 2 (92 patients). Sixty-two patients in group 1 required blood transfusions compared with 76 in group 2. Also, the total number of units given in group 1 was 113 and in group 2 was 176 (P<0.001). The researchers concluded that hemodilution increased transfusion needs.

**Renal System**

Renal demands increase with fluid overload. The secretion of ADH, aldosterone, and renin after injury or stress decrease water and sodium excretion, delaying excretion of an acute saline load by days or weeks. Historically, fluids have been given to prevent renal failure, although there is no evidence of an association between oliguria and later renal failure. Moreover, oliguria intraoperatively often does not respond to fluid loading, and preloading may not prevent later renal failure.34

Chronic kidney disease often is associated with cardiovascular problems. Fluid and electrolyte balance is deregulated in patients with chronic kidney disease and excess fluid therapy contributes to postoperative morbidity and mortality.35 Diuresis forced through fluid overload does not offer any renoprotection; rather, the opposite. A rationale for fluid replacement involving the endocrine system (renin-angiotensin-aldosterone-vasopressin) may be appropriate with the concept of a zero-fluid balance policy, according to some recent studies.35

Although an older concept advised anesthesiologists to administer large amounts of fluid after kidney transplant to force the new organ to function, recent studies indicate that graft survival was better in patients in whom the mean arterial pressure was greater than 93 mm Hg and less than 2.5 L fluid was infused.36 Extremity reimplantation and flap survival also are improved when less fluids are given.37

**Postoperative Visual Loss**

Postoperative visual loss after long back surgery and robotic procedures performed in a steep Trendelenburg position has been linked with a compartment syndrome caused by excessive intraoperative fluid administration. Guidelines advise combining crystalloids and colloids, giving both in reduced amounts.38

**What To Infuse:**
**Blood, Crystalloids, or Colloids?**

Blood transfusions are rarely indicated in elective procedures. The American Society of Anesthesiologists noted that blood should rarely be given if hemoglobin
is greater than 10 g and almost always when hemoglobin is less than 6 g.\textsuperscript{39} As such, it is clear that blood transfusion must be individualized. Rate of loss must be considered, as should hemodynamic status and comorbidities.

The most commonly administered crystalloid is normal saline. However, in a study of nearly 23,000 patients, hyperchloremic metabolic acidosis occurred in 22% of patients and was independently associated with increased morbidity and mortality.\textsuperscript{40} Mortality at 30 days was 3% versus 1.9% in patients who did not have metabolic acidosis. Hospital lengths of stay increased by almost 1 day.

Hydroxyethyl starch (HES) is available in several preparations (Hespan, B.Braun; Voluven, Hospira; Volulyte, Fresenius Kabi). It is subclassified according to molecular weight and presence of electrolytes. In 2013, the FDA issued a black box warning that HES was not to be used in ICUs.\textsuperscript{41} A Cochrane review of colloid solutions and crystalloid fluids in 78 trials concluded that resuscitation with colloids did not reduce the risk for death and that HES increased mortality if the liver or kidneys were injured.\textsuperscript{42} Another Cochrane review examined the effects on kidney function in more than 11,000 patients. HES increased the need for renal replacement therapy\textsuperscript{43}; however, a safe volume of HES was not defined.

The Surviving Sepsis Campaign issued several guidelines regarding management of patients in sepsis.\textsuperscript{44} Several trials were reviewed—including the VISEP (Efficacy of Volume Substitution and Insulin Therapy in Severe Sepsis), CRYSTMAS (Effects of Voluven on Hemodynamics and Tolerability of Enteral Nutrition in Patients With Severe Sepsis), SAFE (Saline versus Albumin Fluid Evaluation), and CHEST (Crystalloid versus Hydroxethyl Starch Trial) studies—which did not show any difference in survival between patients administered colloids and saline resuscitation.\textsuperscript{45}

However, the conclusions drawn were that although colloid might increase renal damage in patients with preexisting kidney failure, extra fluid increased mortality and conservative fluid replacement was indicated. Further recommendations included the use of vasopressors (norepinephrine, then epinephrine, then vasopressin) to restore blood pressure rather than fluids and the use of stroke volume to guide therapy.

Phenylephrine, low-dose dopamine, and steroids probably have a limited place in the care of these patients.\textsuperscript{44} Following these reviews, many hospital pharmacies decided that based on the increased cost of synthetic colloids, they should be banned.

However, a more rational view might be to use both colloids and crystalloids but in reduced amounts. Colloids maintain vascular volume and maintain hemodynamic status better than crystalloids. A study of damage-control resuscitation indicated that mortality increased when greater than 6 L of crystalloids were given and was reduced when 1 L of colloid was used.\textsuperscript{46}

During normovolemic anemia, a third-generation tetrastarch (Voluven) maintained tissue perfusion in an animal model, whereas lung water increased and oxygen saturation decreased with lactated Ringer’s solution.\textsuperscript{47}

**Glycocalyx**

The glycocalyx, a very fragile system, coats the vascular endothelium and acts like a filter. Glycocalyx is the main constituent of the vascular barrier with selective protein filtration.\textsuperscript{48} It can easily be destroyed by surgery, trauma (central cannulation), ischemia/reperfusion, sepsis, inflammatory mediators, hyperglycemia, and acute hypervolemia. As the filter breaks down, destruction causes leukocyte adherence, platelet aggregation, and edema. Maintaining a physiologic concentration of plasma protein, particularly albumin, can prevent glycocalyx damage.

**Monitoring Fluid Balance**

Historically, anesthesiologists have cannulated a vein, connected the cannula to a flow system, and infused fluids hoping that the amount given will compensate for unknown losses and maintain hemodynamic stability. A more accurate means of assessing need and volume responsiveness is based on pulse pressure variation.\textsuperscript{49}

By looking at arterial pressure waveforms and respiratory excursions, stroke volume and cardiac output can be established by algorithm. Several commercial monitors are available, including Vigileo and FloTrac (Edwards Lifesciences) and LiDCO (LiDICO), among others. Fluid monitoring has become less invasive with innovation, such that invasive technologies of the past are not always necessary.

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**Table 3. Comparisons Between Crystalloids and Colloids**

<table>
<thead>
<tr>
<th>Crystalloids</th>
<th>Colloids</th>
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<tbody>
<tr>
<td>Distributed in entire extracellular compartment</td>
<td>Expands plasma volume by amount infused</td>
</tr>
<tr>
<td>80% leaves vasculature</td>
<td>More expensive</td>
</tr>
<tr>
<td>Infused amount correlates to weight gain</td>
<td>Infection and allergenic responses very low</td>
</tr>
<tr>
<td>Causes dilutional coagulopathies in large amounts</td>
<td>? coagulopathies in larger amounts</td>
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have been replaced with less invasive and even noninvasive modalities.

Transesophageal echocardiography also is valuable in measuring cardiac output and guiding fluid therapy. Real-time direct visualization of cardiac motion is possible, and allows preemptive maintenance of fluid requirements. Other monitors incorporate sensors on endotracheal tubes, again measuring pulse pressure variation.

For a prompt bedside evaluation, lung ultrasound may assess pulmonary congestion through the evaluation of vertical reverberation artifacts, known as B-lines. These handheld devices can easily indicate accumulation of extravascular lung water. A study of 55 patients in septic shock indicated that extravascular lung water was significantly higher by day 3 in nonsurvivors, as capillary permeability increased with a higher positive fluid balance.

Although central venous pressure continues to be used as a monitor, it does not indicate circulating blood volume or vascular responsiveness to a fluid challenge. It should not be used to make clinical decisions regarding fluid administration.

What To Infuse

Crystalloids in moderate amounts should be used to replace urine and insensible losses, the latter usually not more than 0.5 mL/kg/h. Colloids can replace plasma deficits, acute blood loss, and protein-rich fluids. The amount of colloid given should be approximately 1 to 2 L but should not be administered to patients with kidney or liver disease. There is no rationale for substituting 1 L blood loss with 3 to 4 times crystalloid infusion. Blood should be used sparingly. Overnight fasting does not deplete the vascular space, and the third space does not exist. The aim is to preserve normovolemia in all body compartments with a fluid balance as close to zero as possible.

Conclusion

After decades of research it is clear that current practices of fluid infusion should be reevaluated. No IV infusion should be continued simply because it is a routine. Optimizing the volume infused is the key to ideal postoperative outcome with maximum fluid shifts of no more than 2 to 3 L. The question arises, “Are we ready for the change?”

References


