

Intraoperative Fluid Restriction Improves Outcome After Major Elective Gastrointestinal Surgery

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Fluid therapy is one of the most controversial topics in perioperative management. There is continuing debate with regard to the quantity and the type of fluid resuscitation during elective major surgery. However, there are increasing reports of perioperative excessive intravascular volume leading to increased postoperative morbidity and mortality. Recent evidence suggests that judicious perioperative fluid therapy improves outcome after major elective gastrointestinal surgery. The observed benefits may not be solely attributable to crystalloid restriction but also to the use of colloids instead. Some clinically useful guidelines based on the studies discussed in this review include avoidance of deep general anesthesia and elimination of preload for patients who receive epidural analgesia. A balanced approach to fluid

management is recommended, with colloids administered to provide hemodynamic stability and maintain urine output of $0.5 \text{ mL} \cdot \text{kg}^{-1} \cdot \text{h}^{-1}$ and crystalloids administered only for maintenance. In addition, blood loss may be replaced with colloid on a volume-to-volume basis. Furthermore, predetermined algorithms that suggest replacement of third space losses and losses through diuresis are unnecessary. Significant reduction in crystalloid volume can be achieved without encountering intraoperative hemodynamic instability or reduced (i.e., $< 0.5 \text{ mL} \cdot \text{kg}^{-1} \cdot \text{h}^{-1}$) urinary output just by avoiding replacement of third space losses and preloading. Finally, there is a need for well-controlled studies in a well-defined patient population using clear criteria or endpoints for perioperative fluid therapy.

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Fluid therapy is one of the most controversial topics in perioperative management (1,2). Current perioperative fluid therapy is largely based on concepts developed in the late 1950s and early 1960s (3,4). Moore (3) postulated that metabolic response to surgical stress caused sodium and water retention and proposed fluid restriction in the perioperative period. In contrast, Shires et al. (4) postulated that extracellular fluid volume is decreased during major surgery as a result of redistribution of fluid to a hypothetical space (i.e., the "third space") and therefore proposed replacement of the third space losses with crystalloid administration to maintain adequate plasma volume. This led to excessive use of crystalloids and prompted an editorial by both Moore and Shires urging moderation (5).

However, the doctrine of Shires still dictates current perioperative fluid therapy (6,7). Current intraoperative

fluid therapy is guided by algorithms based on the assumption that preoperative deficits, maintenance requirements, third space losses, and blood loss are to be replaced by crystalloids using an $\text{mL} \cdot \text{kg}^{-1} \cdot \text{h}^{-1}$ formula (8). However, the bases of such formulae are being questioned (1). For example, the studies suggesting the replacement of third space losses (1) and amount of crystalloid required to replace blood loss (i.e., replacement of blood loss by thrice the amount of crystalloid) may be flawed (9). Furthermore, several reports of significant deleterious effects of overhydration with crystalloids (10-13) question this practice. This article will briefly review several studies reporting improved outcome with judicious intraoperative fluid administration during major elective gastrointestinal surgery (14-18).

Excessive Perioperative Fluid Therapy

Determination of adequate volume resuscitation is a major clinical challenge. It is not uncommon for patients undergoing major surgical procedures to gain 5-10 kg from their preoperative weight (6,18). Postoperative weight gain is generally the result of positive fluid balance from perioperatively administered fluids. Lowell et al. (7) prospectively monitored 48 consecutive postoperative patients admitted to a surgical

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intensive care unit (ICU). They found that 40% of patients had excessive intravascular volume (defined as weight gain of more than 10% from preoperative or pre-morbid weight). The patients with excessive intravascular volume had statistically significantly more frequent morbidity and longer length of ICU stay. Mortality in the patients who gained more than 10% body weight was 31.6% (versus 10.3% in the group that gained <10% body weight). Mortality increased with increases in weight gain (patients who gained more than 20% body weight had 100% mortality). Of note, there were no differences in admission Acute Physiology and Chronic Health Evaluation (APACHE) II scores in the different groups, suggesting that all patients had similar degree of illness.

The consequences of excessive intravascular volume are well recognized (6). It increases demands on cardiac function and may result in myocardial dysfunction and associated morbidity (6). In a provocative article, Arieff (10) analyzed 13 generally healthy patients (average age, 38 yr; no comorbidities) with fatal postoperative pulmonary edema. He concluded that routinely used end-points (e.g., heart rate, mean arterial blood pressure, central venous pressure, and urine output) neither detect nor predict impending pulmonary edema. In addition, he also suggested that pulmonary edema can occur when the net fluid retention exceeds $67 \text{ mL} \cdot \text{kg}^{-1} \cdot \text{day}^{-1}$. Arieff (10) then reviewed the records of patients undergoing major surgery at two university medical centers over a period of 1 yr. He found that the overall incidence of postoperative pulmonary edema was 7.6% ($n = 612$) with mortality of 11.9%. Of these, 2.6% ($n = 204$) had no comorbidities, suggesting that the most likely cause of postoperative pulmonary edema in these patients was perioperative excessive intravascular volume (the net fluid retention in these patients was $90 \pm 36 \text{ mL} \cdot \text{kg}^{-1} \cdot \text{day}^{-1}$).

Increased extravascular lung water from excessive intravascular volume may predispose patients to pneumonia and respiratory failure (6). Holte et al. (11) found that administration of 40 mL/kg lactated Ringer's solution (which is an average amount of fluids used in moderate surgical procedures) significantly reduced pulmonary function in healthy volunteers (with average age 63 yr). Moller et al. (12) reported that a positive fluid balance exceeding 4000 mL was associated with an increased risk of postoperative pulmonary complications and in-hospital mortality after pneumonectomy. In addition, excessive intravascular volume increases the excretory work of the kidneys (6). It can lead to edema of the gut, which may inhibit gastrointestinal motility and prolong postoperative ileus and intolerance for enteric alimentation (6). The potential for bacterial translocation and development of sepsis and multiorgan failure is also increased. An even more severe complication is the occurrence of

abdominal compartment syndrome (i.e., increase of intraabdominal pressure) leading to physiological effects such as respiratory and renal dysfunction (13). Excessive crystalloids can also cause coagulation abnormalities (6). Increased cutaneous edema may decrease tissue oxygenation, which can lead to delayed wound healing (6). Of note, most complications of excessive intravascular volume occur during the period from the third to the fifth postoperative day, when fluid is mobilized into the vascular space and the kidneys cannot diurese this extra fluid (6).

Liberal Versus Restricted Perioperative Fluid Administration

With increased reports of excessive intravascular volume (1,7,10), there is a suggestion that a "restricted" perioperative IV fluid regimen, rather than the current "standard" fluid regimen, may improve outcome after major elective gastrointestinal surgery (14–18). A retrospective study compared postoperative pulmonary complications in patients ($n = 112$) undergoing trans-thoracic esophagectomy for carcinoma before and after introduction of restricted fluid administration regimen (14). The anesthetic technique included a combined general anesthesia with thoracic epidural analgesia. During the restricted period, crystalloid solution was $4\text{--}5 \text{ mL} \cdot \text{kg}^{-1} \cdot \text{h}^{-1}$, which was administered to maintain a fluid balance (i.e., [fluid infusion + blood transfusion] – [urinary volume + blood loss]) between 1 mL and $2 \text{ mL} \cdot \text{kg}^{-1} \cdot \text{h}^{-1}$ and a central venous pressure of $<5 \text{ mm Hg}$. Initial blood loss was replaced with crystalloid and/or colloid solutions until the hematocrit was 25% or less. Blood was transfused if the hematocrit values were less than 25%. Patient characteristics, surgical technique, and the duration of surgery were similar in the standard and the restricted periods of the trial; however, the blood loss was statistically significantly less in the restricted period. The intraoperative volume balance in the restricted period was statistically significantly less ($749 \pm 697 \text{ mL}$ versus $2386 \pm 1307 \text{ mL}$). The investigators found that restricted intraoperative fluid administration reduced postoperative pulmonary complications and shortened the recovery period in the hospital (14). The limitations of this study include its retrospective, non-randomized case series design with a relatively small sample size.

An observational case series of 56 consecutive patients undergoing near-total esophagectomy evaluated the benefits of a standardized multimodal anesthetic management, which included intraoperative fluid restriction, smaller ($<1 \text{ MAC}$) concentrations of inhaled anesthetics, minimal opioids (fentanyl $\leq 250 \mu\text{g}$), and intraoperative epidural lidocaine 1.5%–2% (15). The mean surgical duration was 6.5 h and the

mean blood loss was 175 mL (maximum, 400 mL). No predetermined algorithm for fluid administration was used. All patients received 500 mL of 5% albumin. Intraoperative fluids were administered to maintain adequate hemodynamics (systolic blood pressure within 20% of baseline) and urinary output of 0.3 to 0.5 mL · kg⁻¹ · h⁻¹. Although no preload was used before epidural analgesia, 20%–25% of total intraoperative crystalloid volume was administered in the first 30–45 min. The median crystalloid (lactated Ringer's solution) administration was 650 mL/h (mean, 661 ± 194 mL/h). Interestingly, hemodynamic stability was not difficult to maintain despite intraoperative fluid restriction. In addition, the authors were able to maintain a mean intraoperative urinary output of 0.57 mL · kg⁻¹ · h⁻¹. There was no case of renal failure. All patients were tracheally extubated in the operating room. Postoperatively patients received 1–1.5 mL · kg⁻¹ · h⁻¹ of lactated Ringer's solution. The median length of ICU stay was 1 day and patients ambulated early (median, 1.6 days; range, 0–3 days). The authors concluded that the improved outcome may have been associated with use of the multimodal approach, which included use of smaller concentrations of inhaled anesthetics, judicious use of crystalloids, use of colloids, and acceptance of a lower urinary output (<0.5 mL · kg⁻¹ · h⁻¹), and use of patient-controlled epidural analgesia (14). The authors report similar outcomes in 250 near-total esophagectomies. The limitations of this study include its observational, non-randomized case series design and small sample size. A randomized, double-blind, controlled trial of intraoperative fluid restriction is warranted to further validate the findings of this study.

Lobo et al. (16) performed a prospective trial in which otherwise normal patients (*n* = 20) undergoing colon surgery were randomized to receive either standard fluid therapy (≥3 L crystalloids, 1L 0.9% saline, and 2 L 5% dextrose) or restricted fluid therapy (≤2 L crystalloid, 0.5 L 0.9% saline, and 1.5 L 5% dextrose or 2 L 0.9% saline/0.18% dextrose) in the postoperative period. Although intraoperative fluid administration was not controlled, both groups received similar amount of crystalloids (mean, 2800 mL). The duration of surgery was short (<2 h) and the mean blood loss was 275 mL (no intraoperative blood transfusion was required). Urine output did not differ between the groups. Patients in the restricted group had statistically significantly shorter gastric emptying times for both liquids and solids and drank significantly more fluids. Compared with the restricted group, the median passage of flatus was 1 day later, median passage of stools was 2.5 days later, and median postoperative hospital stay 3 days longer in the standard group; these were statistically significant differences (15). The patients in the standard practice group had a

more frequent incidence of complications (e.g., peripheral edema, hyponatremia, vomiting, confusion, and readmission within 30 days).

A recent randomized, observer-blinded, controlled trial evaluated the effects of standard and restricted fluid therapy on complications after colorectal surgery (17). Anesthetic technique included epidural analgesia combined with general anesthesia. Patients (*n* = 72) in the standard fluid therapy group received 500 mL saline 0.9% for the fasting period and 500 mL hydroxyethyl starch 6% in normal saline as preload before epidural analgesia and saline 0.9% (7 mL · kg⁻¹ · h⁻¹ for first hour, 5 mL · kg⁻¹ · h⁻¹ second and third hours, and 3 mL · kg⁻¹ · h⁻¹ thereafter) to replace third space losses. Blood loss was replaced with 1000–1500 crystalloid mL for the first 500 mL and hydroxyethyl starch 6% for any additional loss (17).

Patients (*n* = 69) in the restricted fluid therapy group received 500 mL glucose 5% in water for the fasting period, no preload before epidural analgesia, and no replacement for third space loss (17). Blood loss was replaced with hydroxyethyl starch 6% on a volume-to-volume basis after 500 mL blood lost. Diuresis was not replaced. In both groups a hematocrit was maintained between 25% and 35% (higher limits in patients with cardiovascular disease). If the maximum dose of hydroxyethyl starch 6% (i.e., 33 mL · kg⁻¹ · day⁻¹) was achieved, albumin 5% was administered. Patients in both the groups received vasoactive drugs (ephedrine and/or dopamine) to achieve a mean arterial blood pressure of more than 60 mm Hg (17).

The postoperative fluid regimen in the standard group was 1000–2000 mL crystalloid. On the other hand, the restricted group received 1000 mL of glucose 5% (with potassium if needed) and hydroxyethyl starch 6% for volume-to-volume loss through drains. A weight increase exceeding 1 kg was treated with furosemide. Postoperative hypotension or small urinary output (<0.5 mL · kg⁻¹ · h⁻¹) was treated according to standard practice (e.g., change epidural analgesic dose, vasoactive therapy when appropriate, and fluid therapy). Feeding (through nasogastric tube) commenced 4 h postoperatively and all patients were encouraged to eat and drink from 4 h after surgery (17).

IV fluid administration was significantly less in the fluid restricted group on the day of surgery (mean, 2740 mL versus 5388 mL) and on day 1 postoperatively (mean, 500 mL versus 1500 mL). Both groups received similar volumes of hydroxyethyl starch 6%; thus the differences were attributable to differences in crystalloid administration (17). A 3–4 kg increase in body weight occurred over the first 2 days. The number of patients with postoperative complications was significantly reduced in the fluid restricted group

(33% versus 51% in the standard therapy group, $P = 0.013$). Patients with complications had an average of 1.2 complications in the restricted group and 2.1 complications in the standard group. A dose-response relation was observed between complications and increasing IV fluid volumes as well as increasing body weight. There were no deaths in the fluid restricted group whereas 4 patients (4.7%) died in the standard group (causes of death included pulmonary edema in 2 patients, pneumonia with septicemia, and pulmonary embolism). The urinary output was larger and the serum creatinine was lower in the standard group on the day of surgery, but there was no difference thereafter. Only one patient (in the standard group) had renal failure after sepsis. The authors concluded that restricted fluid administration by eliminating preloading and replacement for "third spacing" and maintenance of body weight reduced postoperative complications after colorectal surgery (17). Although this was a well-designed study, the limitations include more proximal anastomoses and more smokers in the restricted group, which may have favored this group with respect to anastomotic leaks. There may have been some "learning bias," as there was a tendency towards fluid restriction even in the standard group, which was likely an effect of the lack of blinding of the anesthesiologists and surgeons. Additional studies evaluating different surgical procedures and fluid therapies are necessary to validate these findings (18).

Conclusion

There is a continuing debate with regard to the quantity and the type of fluid administration during elective major surgery. There are increasing reports of postoperative excessive intravascular volume leading to increased morbidity and mortality. Recent evidence suggests that crystalloid restriction may improve outcome after major elective gastrointestinal surgery. However, there are only a few studies with small sample sizes evaluating the effects of perioperative fluid restriction (or avoidance of excessive intravascular volume) on postoperative outcome. In addition, the quality of these studies varies from observational trials to randomized controlled trials. Furthermore, the major reason for the observed benefits may not be solely attributable to crystalloid restriction but also to the use of colloids instead. Nevertheless, the findings of these studies suggest that perioperative fluid restriction deserves further investigation. There is a need for well-controlled studies in well-defined patient populations using clear criteria or end-points for perioperative fluid therapy.

Although no convincing guidelines regarding perioperative fluid therapy, including the amount and the choice of fluid, can be derived from these studies

because the definitions of standard fluid therapy and restricted fluid therapy varied, certain observations can be implemented in our current practice while we wait for further evidence for optimal fluid regimens. Some clinically useful guidelines based on the studies discussed in this review include avoidance of deep general anesthesia, which requires larger fluid administration to maintain adequate hemodynamics, and elimination of preload for patients who receive epidural analgesia. In addition, it is unnecessary to use algorithms that suggest replacement of third space losses and losses through diuresis. Blood loss may be replaced with colloid on a volume-to-volume basis. Although neither crystalloid nor colloid solutions can be expected to be ideal for every individual or in all circumstances, most authors recommend a balanced approach to fluid management with colloids administered to provide hemodynamic stability and maintain urine output of $0.5 \text{ mL} \cdot \text{kg}^{-1} \cdot \text{h}^{-1}$ and crystalloids administered as maintenance fluids. Significant reduction in crystalloid load can be achieved without encountering intraoperative hemodynamic instability or reduced (i.e., $< 0.5 \text{ mL} \cdot \text{kg}^{-1} \cdot \text{h}^{-1}$) urinary output, just by avoiding replacement of third space losses and preloading. Postoperatively, patients who gain more than 1 kg may receive furosemide. Finally, a multidisciplinary approach to the development of clinical pathways that would include appropriate intraoperative and postoperative fluid therapy to improve postoperative outcome is needed.

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