Does fluid restriction improve outcomes of surgical patients?

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INTRODUCTION
Perioperative fluid management has been a topic of much debate over the years and has intensified especially over the past several years. The controversies include the type of fluid, the timing of administration and the volume administered. Following much discussions and ongoing controversy on colloids versus crystalloids (1-4) and the ideal composition of the various intravenous solutions (5-7), the main focus more recently has been on the volume of fluids. Over a decade of clinical studies demonstrating the benefits of goal directed fluid therapy (GDT), more recent studies have shown improved postoperative outcomes with a restricted fluid administration in the perioperative period.

FLUID COMPARTMENT PHYSIOLOGY
Total body water for a 75 kg individual is around 45 liters. Two thirds of this (30 liters) is intracellular water. The remaining third (15 liters) in the extracellular compartment is divided between the intravascular (3 liters) and extravascular (12 liters) compartments. The total intravascular volume (or blood volume) is around 5 liters and has intracellular (red and white cells, platelets make up 40% or 2 liters) and extracellular (plasma makes up 60% or 3 liters) components. Plasma is a solution in water of inorganic ions (predominantly sodium chloride), simple molecules such as urea and larger organic molecules such as albumin and the globulins (Figure 1).

It is important to note that the extracellular deficit after usual fasting is low.(9) The basal fluid loss via insensible perspiration is approximately 0.5 to 1 mL/kg/h during major abdominal surgery.(10) It has been demonstrated that a primarily fluid-consuming third space does not exist. (11) Plasma losses out of the circulation have to be replaced with iso-oncotic colloids, assuming the vascular barrier to be primarily intact and acknowledging that colloidal volume effects are context sensitive. There also should be a timely replacement of visible blood losses, and supplemented by additional fluid guided by hemodynamic variables.

“RESTRICTED” VERSUS “LIBERAL” FLUID ADMINISTRATION STRATEGY
More recently, clinical trials in the surgical literature have advocated a “restricted” fluid administration strategy in the perioperative period and demonstrated its advantages in improvement in postoperative outcomes over a more “liberal” strategy.

Nisenavich et al. (12) prospectively evaluated in 152 patients undergoing elective intraabdominal surgery. Patients were randomized to receive intraoperatively either with a bolus of 10 mL/kg followed by 12 mL/kg/h of lactated Ringer's solution (liberal protocol group) or a continuous 4 mL/kg/h of the same solution with no bolus (restrictive protocol group). The primary endpoint was the number of patients who died or experienced complications. The secondary endpoints included time to initial passage of flatus and feces, duration of hospital stay, and changes in body weight, hematocrit, and albumin serum concentration in the first 3 postoperative days. The amount of fluid the patients received were 3,670 mL (1,880–8,800) and 1,230 mL (490–7,810) (mean [range]) in the liberal and restrictive groups, respectively.

The authors found a lower complication rate in patients in the restrictive protocol group (RGP). The liberal group (LPG) passed flatus and feces significantly later (flatus, median [range]: 4 [3–7] days in the LPG vs. 3 [2–7] days in the RPG; P < 0.001; feces: 6 [4 –9] days in the LPG vs. 4 [3–9] days in the RPG; P < 0.001), and their postoperative hospital stay was significantly longer (9 [7–24] days in the LPG vs. 8 [6–21] days in the RPG; P < 0.01). Significantly larger increases in body weight were observed in the LPG compared with the RPG (P < 0.01). They concluded that patients undergoing elective intraabdominal surgery, intraoperative use of restrictive fluid management was associated with a reduction in postoperative morbidity and shortens hospital stay.

Bandstrup et al (13) investigated restricted fluid regimen versus standard regimen in patients undergoing colorectal surgery. All patients received an epidural for postoperative analgesia in addition to a general anesthetic. As for fluid management regimen, the restricted group did not receive fluid preloading prior to epidural placement or replacement of “third space” loss. Blood loss was replaced with equal volume of 6% hydroxyethyl starch with replacement of red blood cell based on hematocrit. In the standard regimen, fluid administration was similar to the restricted group. In addition, 500 mL of 6% hetastarch was administered before placement of the epidural and normal saline in a range of 3-7 mL/kg/h was delivered during the intraoperative period.

The restricted group had a significantly reduced postoperative complications (33% versus 51%, P<0.05). The numbers of both cardiopulmonary (7% versus 24%, P < 0.007) and tissue-healing...
complications (16% versus 31%, P < 0.04) were also significantly reduced. No patients died in the restricted group compared with 4 deaths in the standard group (0% versus 4.7%, P < 0.12).

Interestingly, there was significant weight gain in patients in the standard fluid regimen group. Patients in this group received more than 3 L of normal saline on the day of surgery compared to the restricted regimen group. It is unclear if the increased in complication rate was attributed to the larger volume of crystalloid (predominantly saline) or due to the unbalanced nature of the fluid.

In contrast, other studies have shown better outcomes when a liberal fluid administration regimen were adopted. In a double-blind study, Holte et al (14) investigated 48 relatively healthy patients undergoing laparoscopic cholecystectomy. They were randomized to 15 mL/kg (restricted group) or 40 mL/kg (liberal group) intraoperative administration of lactated Ringer’s solution.

Intraoperative administration of 40 mL/kg compared with 15 mL/kg LR led to significant improvements in postoperative pulmonary function and exercise capacity and a reduced stress response as measure by a lower aldosterone, anti-diuretic hormone, and angiotensin II.

Nausea, general well-being, thirst, dizziness, drowsiness, fatigue, and balance function were also significantly improved, as well as significantly more patients fulfilled discharge criteria and were discharged on the day of surgery with the high-volume fluid substitution. The volume administered in the 15 mL/kg group vs. 40 mL/kg group were 997.5 (721.5–1455.0) and 12928 (1950–3920) (mean±range), respectively. The authors concluded that a more liberal intraoperative fluid administration compared with a restricted one improves postoperative organ functions and recovery and shortens hospital stay after laparoscopic cholecystectomy.

In a follow up study, the same group of investigators randomized 32 patients undergoing elective colonic surgery to restrictive or liberal perioperative fluid administration. (15) Fluid algorithms were based on fixed rates of crystalloid infusions and a standardized volume of colloid. Pulmonary function measured by spirometry was the primary outcome measure, with secondary outcomes of exercise capacity (submaximal exercise test), orthostatic tolerance, cardiovascular hormonal responses, postoperative ileus (transit of radio-opaque markers), postoperative nocturnal hypoxemia, and overall recovery within a well-defined multimodal, fast-track recovery program. Hospital stay and complications were also noted.

The volumes of fluid administered were (median 1640 mL, range 935–2250 mL) and (median 5050 mL, range 3563–8050 mL) in the restrictive and liberal groups, respectively. The liberal group was associated with a significant improvement in pulmonary function and postoperative hypoxemia, with lower concentrations of cardiovasculary active hormones such as renin, aldosterone, and angiotensin II. Although the average length of hospital stay was not significantly different between the groups, total hospital stay including readmission was significantly longer in the restrictive group compared with the liberal group [4 (2–39) vs. 2.5 (2–9) days], median (range); P<0.03. Six patients developed a total of 18 complications in restrictive group compared with one patient in the liberal group. The authors advocated that goal-directed fluid therapy strategies should be individualized rather than a fixed fluid amounts.

MECHANISMS UNDERLYING OPTIMAL FLUID ADMINISTRATION

Both ‘dry’ and ‘wet’ strategies can both lead to postoperative complications and morbidity. A fluid replacement regimen that is conservative has the potential for a decrease in cardiac output and in perfusion to the splanchnic bed. This can lead to intestinal acidosis, postoperative ileus, and the translocation of bacteria and endotoxin into the vascular system, potentially causing sepsis or multiple system organ failure.

Conversely, the use of a liberal or ‘wet’ approach to fluid replacement especially when crystalloid is used can increase bowel edema, weight gain, decrease the tolerance for enteral feeding and increase the incidence of postoperative ileus. The liberal administration of fluid is also known to increase the venous pressure in the intestines (secondary to the edema) and therefore cause a decrease in splanchnic oxygenation by reducing the perfusion pressure. This can also lead to the transmigration of bacteria and endotoxin into the circulation.

It appears that more mechanistic studies in animal models are warranted to explain the observed discrepancies in the fluid administration strategies and clinical outcomes. Kimberger et al (16), in a recent study compares the effects of goal-directed colloid fluid therapy with goal-directed crystalloid and restricted crystalloid fluid therapy on healthy perianastomotic colon tissue in a pig model of colon anastomosis surgery. The animals were randomized to one of the following treatments: GDT-collod group, GDT-crystalloid group and a restrictive group. Boluses consisting of 250 mL of hydroxyethyl starch were administered to target a mixed venous oxygen saturation at or above 60%. Intestinal tissue oxygen tension and microcirculatory blood flow were measured continuously. The tissue oxygen tension in healthy colon increased to 150 ± 31% from baseline in the GDT-Colloid group versus 123 ± 40% in the GDT-crystalloid group versus 94 ± 23% in Restrictive group, mean ± SD; P < 0.01). Similarly perianastomatic tissue oxygen tension and microcirculatory blood flow increased in a similar manner.
There are many perioperative goal directed fluid therapy trials that demonstrated an improvement in outcomes from recovery of gastrointestinal functions to a reduction in hospital length of stay. (17-25) Giglio et al(26) recently performed a systematic analysis of 16 randomized controlled trials (>3000 subjects) with a focus on gastrointestinal outcome. They noted a significant reduction in major GI complications in the GDT group when compared with a control group (OR, 0.42; 95% CI, 0.27–0.65). Minor GI complications were also significantly decreased in the GDT group (OR, 0.29; 95% CI, 0.17–0.50).

CONCLUSIONS
Replacing fluid loss in the operating room should not follow a cookbook approach, but rather should be targeted to specific endpoints. Using heart rate, blood pressure and urine output might not be adequate monitor of end organ perfusion. Continuous monitoring of flow-based hemodynamics e.g. stroke volume and cardiac output may help in more optimal perioperative fluid management. The use of the terms liberal/wet or restrictive/dry fluid administration strategies do not precisely define the optimal volume of fluid needed, and it can add to confusion. The use of individualized goal directed therapy in surgical patients allows the clinician to target specific hemodynamic and tissue perfusion endpoints that will more likely improve patient outcome.

REFERENCES