Review Article

Intraoperative fluid management: Past and future, where is the evidence?

ABSTRACT

Currently, there is no consensus about the optimum intraoperative fluid therapy strategy. There is growing body of evidence supports the beneficial effects of adopting "Goal-directed therapy" over either the "liberal" or "restrictive" fluid therapy strategies. In this narrative review, we have presented the evidence to support the optimum strategy for intraoperative therapy. In conclusion, whatever the intravenous fluid replacement strategy used, the anesthesiologist must be prepared to adjust the composition and rate of the fluids administered to provide sufficient intravascular fluid volume for adequate perfusion of vital organs without overwhelming the glycocalyx function with fluid overloads.

Key words: Anesthesia; fluid therapy; goal-directed; intraoperative; liberal; monitoring; restrictive

Introduction

Intraoperative administration of fluids aims to maintain or restore effective circulating blood and hence assuring adequate organ perfusion. There is continuous debate about the optimum intraoperative fluid therapy. There is wide variability of practice, both among individuals and institutions in terms of the type of fluid used, the timing of administration and the volume administered. Over the last decade, this debate gave rise to three strategies of fluid management: the "liberal", "restricted", and "goal-directed" fluid therapy strategy.[1]

Although administering large volume of fluids may expand intravascular space and improve organ perfusion,[2] it may also increase the incidence of perioperative cardiopulmonary and tissue-healing complications.[3,4] On the other hand, fluid restriction may reduce the length of hospital stay; however, it might increase the risks for postoperative acute kidney injury (AKI).[5] Goal-directed therapy (GDT), in which individualized fluid administration based on reproducible end-points, have been associated with improved perioperative outcomes.[6]

The present review aims to summarize the existing evidence supporting the different approaches of intraoperative fluid therapy.

Liberal versus Restrictive Fluid Management

Liberal strategy

Conventionally, infusion of large volumes of crystalloid was used for long decades to achieve a good blood volume.[7] This concept assumed that surgical patients are hypovolemic due to prolonged fasting over the midnight, bowel preparation, and ongoing losses from perspiration and urinary output.

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There was also a widespread misconception that surgical exposure required aggressive replacement of nebulous insensible fluid loss, often termed "third space" losses. In addition, the 4-2-1 rule for perioperative fluid therapy was adopted for a long time without any supporting evidence base proofs. The latter can potentially lead for overzealous fluid administration and postoperative fluid-based weight gain which in turn might result in increased major morbidity.

The preoperative dehydration has been almost eliminated by reduced fasting times and use of oral fluids up to 2 h before operation. Studies have shown that in patients without significant cardiopulmonary diseases, blood volume is normal even after prolonged fasting.[8] In addition, a transthoracic echocardiography study demonstrated that the preoperative fasting did not alter the dynamic and static preload indices in adult patients with the American Society of Anesthesiologists (ASA) I to III.[9] Moreover, the mechanical bowel preparations can be overlooked because there is growing evidence showing the minimal difference in the surgical conditions where this is used.[10]

The concept of "third space" fluid loss has been emphatically refuted. Previous studies have expanded our understanding of fluid movement across the endothelial vascular barrier. The endothelium barrier is a one-cell thickness and is coated on its luminal side with a fragile layer, the glycocalyx, which provides a first-line barrier to regulating cellular and macromolecule transport across the endothelium.[11] The endothelial glycocalyx can be destroyed not only by ischemia and surgery but also by acute hypervolemia from large volume fluid loading.[12] There several systematic reviews, emphasizing the measurement of the extracellular volume changes, have concluded that a classic third space does not exist. They have considered the fluid shift to occur from the vascular to the interstitial space because of glycocalyx destruction.[13-15] Hence, no need to flood the patient with unnecessary extra fluids which proportionately increased risk of morbidity and mortality.[16-18]

In outpatient surgery, 1–2 L of balanced crystalloids reduces postoperative nausea and vomiting and improves well-being.[19]

Restrictive fluid management

Fluid restrictive strategies are often used as a standard practice for special types of surgery like as lung surgery because of the inherent risk of postpneumonectomy pulmonary edema which is directly related to the amount of positive fluid balance.[20] In addition, maintenance of low intraoperative central venous pressure (CVP) using restrictive fluid strategy was found to be associated with less intraoperative blood loss and need for blood transfusion in patients undergoing hepatic resection.[21]

A "restrictive" intraoperative fluid regimen, avoiding hypovolemia but limiting infusion to the minimum necessary, initially reduced major complications after complex surgery, but inconsistencies in the type of fluid infused and in definitions of adverse outcomes have produced conflicting results in clinical trials.[22]

Several protocols for restrictive fluid regimens have been described including (1) replacement of blood loss with colloids on a "1 mL per 1 mL" basis, (2) nonreplacement of intraoperative interstitial/third space loss or urine output, (3) nonfluid loading, and (4) administration of vasopressor for correcting intraoperative hypotension.[1,13,22-24]

Where does evidence stand?

It has been noted that routine fluid prescription among anesthesiologists varies largely according to the individual habit[25,26] as well as other independent factors such as differences in surgical types, trauma, preoperative hydration, anesthetic technique, comorbidity, gender, and age. Currently, there is no a clear consensus on the definition of liberal versus restrictive fluid therapy (i.e., how less is too less?).[27]

In 2009, Bundgaard-Nielsen *et al*.[28] performed a narrative synthesis including 705 patients from 7 retrieved randomized controlled trials (RCTs) comparing liberal versus restrictive fixed-volume regimens during the period from 1986 to 2008. Three RCTs only reported improved outcomes with a restrictive fluid regimen after major abdominal surgery in terms of improved gastrointestinal recovery and reduced length of stay (by −2 to −3 days). Contradictory, two RCTs found no difference between both fluid regimens in terms of wound infection (one RCT) or gastrointestinal recovery and length of stay (one RCT). This might be explained with the heterogeneity between the included RCTs in terms of the definition of liberal versus restricted fluid regimens and measured outcomes.

A retrospective cohort study,[29] randomized 89 patients undergoing orthotopic liver transplantation into liberal fluid strategy and restrictive therapy. The restrictive strategy was associated with less need for intraoperative transfusion of packed red blood cells (5.02 ± 4.5 IU vs. 8.5 ± 7.02 IU, $P < 0.001$), fresh frozen plasma (8.7 ± 6.04 IU vs. 15.02 ± 8.2 IU, $P < 0.001$), and platelet concentrates transfusion (2.0 ± 1.08 IU vs. 2.05 ± 1.1 IU, $P = 0.014$), and less demonstration of colloids.

Similarly, an RCT focusing on the use of restrictive intraoperative fluid therapy combined with a concomitant administration of norepinephrine during radical cystectomy demonstrated reduced intraoperative blood loss, the need for blood transfusion, and morbidity.[30]

In contrast, a small RCT including 16 patients undergoing esophageal cancer surgery found that the restrictive volume of intraoperative fluid (≤8 ml/kg/h) does not significantly affect pulmonary exchange function or tissue perfusion.[31] That study included few patients. Patients in the restrictive group received 480 ml/h in 60 kg patient.

A recent retrospective study,[32] including 553 patients who underwent pancreaticoduodenectomy at a tertiary hospital over 12-year-period, found that patients who received >6000 ml intraoperative fluid had more wound infections ($P = 0.049$), intra-abdominal abscesses ($P = 0.020$), and postoperative interventions ($P = 0.007$). In addition, patients who received >14,000 ml fluid until the 5th postoperative experienced all types of postoperative complications (infectious, fistula, delayed gastric emptying, and bleeding).

Straub *et al*.[33] have randomly allocated 100 women undergoing gynecological laparoscopy to receive either 10 ml/kg or 30 ml/kg of intravenous compound sodium lactate during the intraoperative period. Pulmonary function (forced expiratory volume in 1 s, forced vital capacity, and peak expiratory flow rate) and oxygen saturation were similar between the two study groups. However, liberal administration of crystalloid was associated with a clinical modest reduction in pain scores. That study included only patients with ASA physical Class I and Class II who would not be affected with liberal fluid therapy. In addition, that study was powered to study the changes in pain scores, and the use of 10 ml/kg might be not considered as a restrictive regimen.

In a small pediatric study, Mandee *et al*.[34] randomized 25 children (mean age <3 years) undergoing major abdominal surgery to receive maintenance plus deficit with or without interstitial space replacement. They reported higher heart rates ($P = 0.012$) and more negative base excess ($P = 0.049$) in the restrictive group, despite there were no differences between the groups in terms of the total volume requirement, postoperative kidney function, chest X-ray, variation of body weight, and the postoperative outcomes. That study included few patients to study the more important postoperative clinical outcomes.

In another small RCT, Niescery *et al*.,[35] including 45 patients undergoing posterior scoliosis surgery, who received crystalloids at a rate of 5.5 ml/kg/h or 11 ml/kg/h. Patients received 5.5 ml/kg/h of crystalloids had a less frequent reintubation rate ($P = 0.015$) and better postoperative oxygen saturations ($P = 0.043$). That study included few patients, and 5.5 ml/kg/h cannot be considered as a restrictive regimen.

A multicenter prospective study[36] in the intensive care settings included 479 patients (mean age 61.2 ± 17.0 years) who needed postoperative admission to the Intensive Care Unit (ICU) after major surgery in three tertiary hospitals. Fluid balance was calculated as sum of (the preoperative fasting, insensible losses from surgeries, and urine output) minus fluid replacement intraoperatively. They found that an intraoperative fluid balance of + 550 ml might distinguish between from nonsurvivors and survivors ($P < 0.001$). Patients with fluid balance above 2000 ml intraoperatively had a longer ICU stay (4.0 vs. 3.0 days, $P < 0.001$) and higher incidence of infectious (41.9% vs. 25.9%, $P = 0.001$), neurological (46.2% vs. 13.2%, $P < 0.001$), cardiovascular (63.2% vs. 39.6%, $P < 0.001$), and respiratory complications (34.3% vs. 11.6%, $P < 0.001$). Interestingly, the multivariate analysis showed that the fluid balance was an independent factor for death (odds ratio [odds ratio] per 100 ml = 1.024; $P = 0.006$; 95% confidence interval [CI] 1.007−1.041). Of note, in that study, patients who underwent palliative surgery and whose fluid balance could change in outcome were excluded from the study. We think that study could help our understanding for the difference between the liberal and restrictive fluid therapy regimen as being a positive balance of 550 ml (550 ml in 70 kg patient equals approximately 7.9 ml/kg). This can potentially reduce the heterogeneity in the methodology of the future RCTs.

A recent systematic review and meta-analysis[37] included patients with reported ASA physical classes from 1 to 3 in three RCTs. The primary outcome was the total number of patients with a complication and the complication rate. They analyzed data of 1397 patients (693 restrictive protocol and 704 liberal protocol). Compared with the liberal group, they found that fewer patients in the restrictive group experienced a complication (−35%) (relative risk [RR], 0.65; 95% CI, 0.55−0.78) and the total complication rate (RR, 0.57; 95% CI, 0.52−0.64), risk of infection (RR, 0.62; 95% CI, 0.48-0.79), and transfusion rate (RR, 0.81; 95% CI, 0.66−0.99) were also lower.

There is an alerting question: Does the evidence support the concept of the associated increased incidence of the acute kidney injury with the use of restrictive fluid therapy?

A systematic review and meta-analysis included 15 RCTs (1966 to present) with a total of 1594 adult patients undergoing surgery comparing restrictive fluid management with a conventional fluid management protocol and reporting the occurrence of postoperative AKI.[38] Interestingly, there was insufficient evidence to associate restrictive fluid management with an increase in oliguria or more frequent occurrence of the AKI. There was no statistically significant difference in acute renal failure occurrence between studies targeting oliguria reversal and not targeting oliguria reversal (OR 0.31; 95% CI, 0.08−1.22; $P = 0.088$).

Goal-Directed Fluid Therapy

The concept of individualized goal-directed cardiovascular optimization and finally assessed on a procedure-specific basis. GDT utilizes monitoring techniques to help guide clinicians with administering fluids, vasopressors, inotropes, or other treatments to patients in various clinical settings. It depends on individual intravascular volume optimization to get a maximum cardiac stroke volume.[39-41]

Kimberger *et al*.[42] investigated the underlying tissue mechanisms during GDT management with crystalloids or colloids for abdominal surgery with a colonic anastomosis in 27 pigs. Three types of fluid management were instituted at the end of surgery: restricted Ringer lactate (RL) versus GDT RL or GDT colloid to achieve a mixed venous oxygen saturation greater than 60%. The results show no significant differences between the groups in conventional cardiovascular functional parameters or urinary output, but an increased oxygen tension in healthy colonic tissue compared with RL and a further increase with GDT colloid compared with GDT RL. Interestingly, compared with lactated ringers (LR), oxygen tension in perianastomotic tissue (245% with GDT colloid vs. 147% in the GDT RL group vs. 116% in the restricted RL group) and microcirculatory flow were significantly higher with the administration of colloids.

It has been shown in several RCTs that the GDT strategy improved outcome compared with the fixed volume regimens as it can offer a state of normovolemia.[43-45]

The advent of individualized goal-directed fluid therapy, facilitated by minimally invasive, flow-based cardiovascular monitoring, for example, esophageal Doppler monitoring, has improved outcomes in colorectal surgery, and this monitor has been approved by clinical guidance authorities.

In elective major abdominal surgery, a "zero-balance approach" intraoperative fluid strategy aiming at avoiding fluid overload and comparable to the so-called restrictive approach, has shown to reduce postoperative complications and is easily applied for most patients. It is less expensive and simpler than the zero-balance GDT approach and therefore recommended in this review.[46]

Goals used to guide fluid administration in goal-directed therapy

Table 1 shows the parameters used to monitor fluid administration in the perioperative period. Classic static preload measurement, by whatever technique, is still commonly used to guide fluid therapy but can fail to estimate the response to fluids in one-half of the patients, thus rendering them exposed to the hazards of unnecessary fluid therapy. A systematic review of the role of CVP measurement in fluid therapy concluded that neither CVP nor the rate of change of CVP have been shown to be accurate markers of right ventricular and left ventricular end-diastolic volumes or in predicting the response to a fluid challenge. Therefore, caution should be exercised in interpreting CVP data to guide fluid administration.[47] Dynamic parameters of fluid responsiveness relying on cardiopulmonary interactions in patients under general anesthesia and mechanical ventilation.[48] Studies have demonstrated the higher value of dynamic parameters (analyzing cardiopulmonary interactions) compared with classic static preload indicators in predicting fluid responsiveness.[49]

Table 1: Parameters used to guide fluid administration in the perioperative period

Static parameters
HR, BP, urine output
Lack specificity in identifying volume deficit
Do not correlate with cardiac output
Lead to over or under-transfusion
CVP, RAP, PAOP
Lack specificity in identifying volume deficit
Do not correlate with cardiac output
Lead to over or undertransfusion
Dynamic parameters (fluid responsiveness)
Fluid challenge tests
Heterogeneous: Volume and type of fluid, duration of the trial, definition of fluid response
Not able to predict the effects of volume expansion before performing volume expansion
Not suitable in the OR
Ventilatory variability
SVV
SPV
PPV
Aortic blood flow variation by esophageal laser Doppler
Change in PWV amplitude
PVI

SVV: Stroke volume variation; SPV: Systolic pressure variation; PPV: Pulse pressure variation; PWV: Plethysmographic waveform variation; PVI: Plethysmographic variability index; CVP: Central venous pressure; RAP: Right atrial pressure; PAOP: Pulmonary artery occlusive pressure; BP: Blood pressure; HR: Heart rate; OR: Odds ratio

In patients under general anesthesia, positive pressure ventilation induces cyclic changes in vena cava blood flow, pulmonary artery flow, and aortic blood flow [Figure 1]. During inspiration, vena cava blood flow (venous return) decreases and according to the Frank-Starling relationship, pulmonary artery flow decreases. Depending on the position of the patient on the Frank-Starling relationship mechanical ventilation is going to induce either high respiratory variations in the left ventricular stroke volume (when the patient is on the steep portion and more likely to be a responder to volume expansion) or low respiratory variations in the left ventricular stroke volume (when the patient is on the plateau and more likely to be a nonresponder to volume expansion) [Figure 2].

Currently used dynamic indices include systolic pressure variation, pulse pressure variation (PPV), stroke volume variation (SVV), and plethysmographic waveform variation. The clinical utility of dynamic parameters is limited by many confounding factors that must be clearly understood by the clinician utilizing them.[44]

The role of echocardiography, both transthoracic and transesophageal, can be critical when evaluating both fluid responsiveness and cardiac function. In addition, echocardiography is of particular use when assessing volume responsiveness in patients undergoing open-chest surgery where the predictive ability of dynamic indices is also reduced.[45]

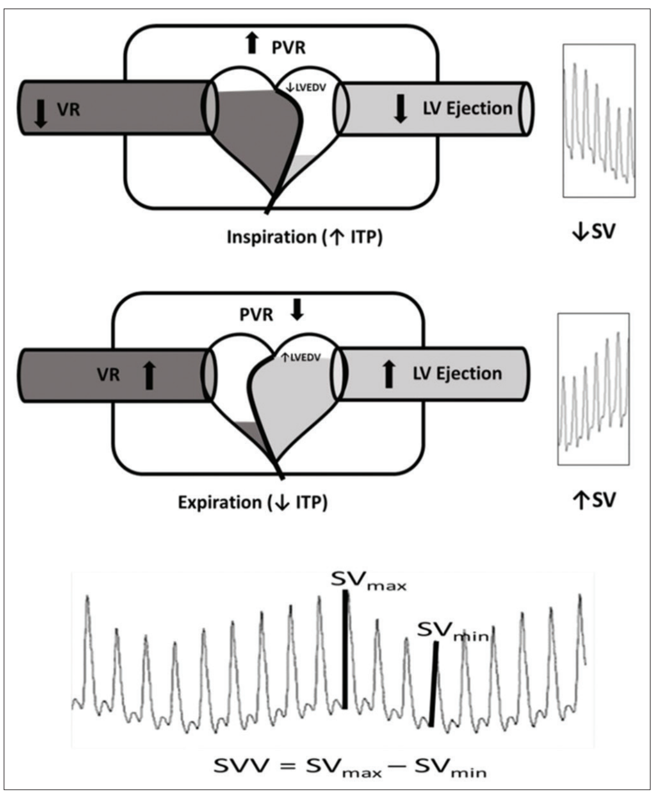

Figure 1: Cardiopulmonary interactions during general anesthesia and mechanical ventilation

Where does evidence stand?

A recent multicenter RCT[50] in four high volume hepatobiliary-pancreatic surgery centers randomly assigned 52 consecutive adult patients with or without a cardiac output GDT algorithm. Compared with the non-GDT group, patients in the GDT group received less volume of fluid administered intraoperatively (2050 ml vs. 4088, $P < 0.0001$) and more frequent administration of vasoactive medications and shorter median length of hospital stay (9.5 days vs. 12.5 days, $P = 0.002$).

A recent RCT,[51] including 80 adult patients undergoing elective supratentorial brain tumor resection randomly divided into a low SVV and a high SVV group, found that the former had a shorter ICU stay (1.4 vs. 2.6 days, $P = 0.03$), fewer postoperative neurological events (17.5% vs. 40%, $P = 0.05$), and lower intraoperative serum lactate ($P < 0.05$).

Similarly, the use of the fluid protocol based on PPV assessed using continuous noninvasive arterial pressure measurement during total knee, and hip replacement was associated with a reduction in postoperative complications and transfusion needs as compared to standard no protocol treatment.[52]

A retrospective comparative study,[53] including 145 consecutive patients undergoing pancreaticoduodenectomy in a high-volume center, found that the GDT was associated with fewer cardiorespiratory complications, shorter median hospital stays (10 days vs. 13 days, $P \leq 0.01$), and median total volume of administered fluid intraoperatively.

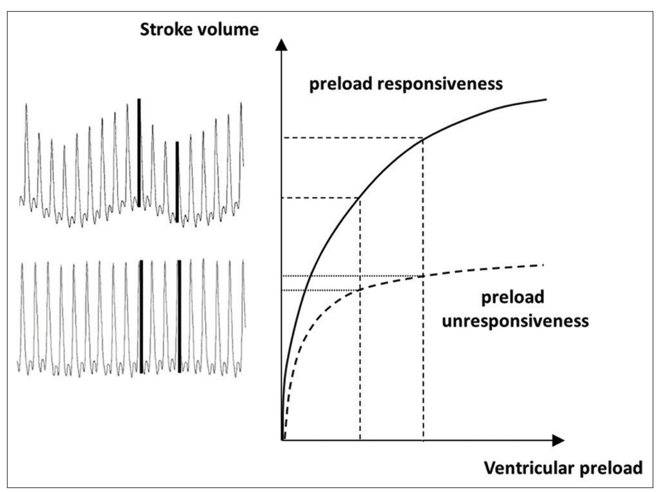

Figure 2: Relation between stroke volume variability and position of the patient on Frank–Starling law predicts fluid responsiveness

Conclusion

Whatever the intravenous fluid replacement strategy used, the anesthesiologist must be prepared to adjust the composition and rate of the fluids administered to provide sufficient intravascular fluid volume for adequate perfusion of vital organs without overwhelming the glycocalyx function with fluid overloads. The GDT or zero-balance strategies can potentially improve the patients' outcomes.

Further larger longitudinal studies are needed to test the reliability of different perioperative dynamic fluid therapy monitors.

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Conflicts of interest
There are no conflicts of interest.

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