

Volume optimization in surgical patients Wet or Dry ?

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Summary : Perioperative fluid therapy remains the subject of active controversy. Indeed, clinical trials investigating the effects of fluid administration on outcome in surgical patients report controversial results. Critical review of these trials reveals that current standard fluid therapy is not at all evidence-based. Although it is evident that fluid overload should be avoided, replacement of fluid lost clearly improves outcome. The debate “Wet or Dry” is not a real one. Fluids should be administered in the perioperative period through a goal-directed approach taking into account patients characteristics and surgical-related events, and not through a “recipe book” approach. The type of fluid to be administered should depend on the specific space that needs to be restored (intracellular, extracellular or intravascular) and on the pharmacokinetic properties of the different solutions.

Key words : Fluid therapy ; fluid balance ; crystalloids ; colloids ; measurement techniques : cardiac output, stroke volume ; oesophageal Doppler ultrasonography ; surgery : postoperative complication ; hospital length of stay.

Perioperative fluid therapy : “to fill or not to fill” ? This question is not new and was already a subject of controversy some 50 years ago. As metabolic and hormonal responses after surgical operations are altered to limit the need for salt and water, Francis Moore recommended to limit the amounts of water and sodium administered in the operative and early postoperative period (1). In the early 1960s, SHIRES *et al.* (2) reported that, as previously showed in experimental hemorrhagic studies, operation caused a similar contraction of the extracellular volume (ECV) independent of the measured blood loss, but instead apparently depending on the degree of operative trauma in patients undergoing abdominal surgical procedures. It was hypothesized that operative trauma caused extracellular fluid to be sequestered in compartments not available for the regeneration of lost plasma : the traumatized tissue, the intracellular compartment or the interstitial lumen. The missing extracellular fluid became known as the “loss to third space”. Although debated, this concept has led to the liberal use of intra-

venous fluids preoperatively, with administration of fluid volumes far exceeding the measured fluid and blood losses. From the beginning of the years 2000, several randomized controlled trials reported that the adoption of a “restrictive” fluid strategy in the perioperative period could be associated with an improved outcome in patients undergoing major abdominal surgery (3-5). These observations have re-fueled the debate on the “optimal” perioperative fluid therapy. The aim of this article is to review the evidence behind current standard fluid therapy and to analyze the different trials examining the effects of fluid therapy on postoperative outcome.

RATIONALE FOR A “LIBERAL” FLUID ADMINISTRATION

Absolute or relative volume deficits often occur during surgery. They may result from preoperative dehydration, bleeding, and/or vasodilation mediated by the use of vasoactive drugs or rewarming (6). Fluid deficit can also develop in the absence of fluid loss secondary to increased capillary permeability resulting in the development of a “third” space. Inadequate fluid administration can lead to a reduced effective circulating volume, redistribution of blood flow towards vital organ (brain and heart), resulting in under perfusion of other organs such as the gut, the kidneys, the muscles and the skin. Activation of the sympathetic nervous and the renine-aldosterone-angiotensin systems are compensatory mechanisms to maintain peripheral perfusion. Various circulating vasoactive substances and inflammatory mediators are also increased. Studies support the hypothesis that improving tissue perfusion may also result in reduced inflammatory activation and, hence, organ dysfunction (7). HOLTE *et al.* (8) recently demonstrated that intraoperative administration of approximately 3 liters of Ringers’s lactate significantly reduced the cardiovascular stress response and improved perioperative organ functions (pulmonary function, exercise capacity and balance function), recovery, and hospital stay after laparoscopic chole-

cystectomy. In a double-blind prospective randomized controlled trial, NOBLETT *et al.* showed that optimization of fluid administration using oesophageal Doppler is associated with a reduction in peak systemic cytokine IL6, suggesting that the maintenance of a high cardiac output may have reduced the systemic inflammatory response to surgical trauma. Inadequate tissue perfusion measured with gastric tonometry has been shown to be associated with adverse perioperative outcome (9). Interestingly, a very recent experimental study in anesthetized pigs showed that the amount of fluid administered significantly influences cardiac output and subcutaneous tissue oxygenation, without any deleterious effect on jejunum and colon tissue oxygen pressure (10).

RATIONALE FOR A "RESTRICTIVE" FLUID ADMINISTRATION

However, excessive administration of fluid may also result in adverse outcome. Excess fluid in the intravascular compartment leads to increased venous pressure and results in interstitial fluid accumulation. This leads to peripheral and pulmonary edema, and consequent compromise of tissue oxygenation. Pulmonary edema is a major adverse outcome that results in an increased alveolar-arterial oxygen gradient and systemic hypoxia. There is evidence that intestinal edema can be associated with impaired gastrointestinal function tolerance for enteral nutrition (11), an increased potential for the development of bacterial translocation and the development of multiple organ failure (12).

Current conventional fluid therapy is to a large extent based on the reported necessity of replacement of the fluid deficit caused by the contraction of the extracellular space. BRANDSTRUP *et al.* (13) recently performed a systematic review of original trials measuring ECV changes during hemorrhage or operations. Overall the evidence supporting the concept that hemorrhage or operations cause a sequestration of the ECV is weak, and probably is a result of flawed methodology. TATARA and TASHIRO (14) developed a mathematical model describing the dynamic distribution and transport of fluid and proteins with the goal of quantifying the balance of fluid between intra- and extra-vascular compartments. Fluid volume changes in the different compartments were calculated for a simulated 4h abdominal surgery in a 70 kg male. Although the model has not been validated to be used as a tool for predicting fluid balance for the individual patient, it demonstrates that when fluid infusion is gradually

increased with time during surgery (reaching 20 ml/kg.h at 4 h) in an attempt to maintain a normal plasma volume, there is a massive fluid sequestration in the interstitium of injured tissues. The model also shows that increasing the fluid replacement above 10 ml/kg.h does not have the desired impact on plasma volume but instead increases the volume of interstitial compartment. In another pharmacokinetic study, HOLTE *et al.* (15) evaluated the influence of a liberal (40 ml/kg) versus a restrictive (15 ml/kg) intraoperative fluid administration on elimination of a postoperative fluid load in patients undergoing laparoscopic cholecystectomy. They demonstrated that elimination of an intravenous volume load was increased after the surgical procedure per se, but not influenced by the volume of fluid administered intraoperatively.

WHERE IS THE TRUTH ?

The balance between inadequate fluid administration with decreased tissue perfusion and excess fluid with edema formation will vary for specific types of surgery. Perioperative fluid requirements will depend on preoperative patient's volume status, and the length and the complexity of the surgery.

Goals of perioperative fluid administration are to avoid dehydration, maintain an effective circulating blood volume and to prevent inadequate tissue perfusion (6, 16). In this setting, two important factors need to be considered: the type of fluid to be administered and the criteria for guiding volume therapy. The choice between the different available solutions should be based on the physiological compartment that needs to be restored (i.e. intravascular, interstitial, intracellular). It will take into account not only the pharmacokinetic and the pharmacodynamic properties of the different solutions, but also their possible side effects and their costs. Patients' pathophysiology is also important to consider. Available clinical outcome data (mortality and major morbidity) provide no evidence for the relative benefit between crystalloid and colloid fluid therapy, or between the different types of colloids. However, crystalloids appear less appropriate for resuscitation of the intravascular compartment as they are mainly distributed to the interstitial space. Colloids are more appropriate for treating intravascular volume deficits. Their use has been associated with an improvement in tissue oxygenation (17, 18), which might be related to their beneficial effects on the microcirculation (19, 20). Moreover, intraoperative fluid resuscitation with

colloid in patients undergoing elective major non-cardiac surgery could be associated with a reduction in postoperative nausea and vomiting, and with a better overall postoperative recovery profile (21). The lower cost of synthetic colloid solutions is a powerful argument for using them rather than human albumin.

HOW TO GUIDE PERIOPERATIVE FLUID ADMINISTRATION

Different approaches have been proposed to guide perioperative volume therapy. The traditional "recipe book" approach relies on the use of formulas based on a continuous predetermined rate of infusion of fluid with additional replacement of observed losses. Although it seems logical that some fluid is better than none, as the magnitude of surgical insult becomes greater, choosing what fixed dose to give become harder (16). Several studies have compared different "restrictive" and liberal" strategies based on a "recipe book" approach (Table 1). They vary in the type and the duration of the surgical procedure, the timing of fluid administration (pre-, intra- or post-operative) and the volume of crystalloid infused. Overall, it appears that for patients having fasted and undergoing minor surgical procedure, fluid administration to compensate preoperative dehydration improves outcome. For patients undergoing more severe surgical procedure, and in particular major abdominal procedure, administration of very large amount of crystalloids in the per- and the postoperative period appear to be associated with increased postoperative complications and prolonged hospital stay. However, a recent randomized double-blind study in patients undergoing fast-track colonic surgery reported that a very restrictive fluid strategy might be associated with increased morbidity.

When significant amounts of fluid are required, an alternative approach based on potential physiological end-points is more effective. There is no evidence that tissue under-perfusion could be avoided through the use of static measurements of intravascular pressures. Indeed, arterial blood pressure measurements do not reflect blood flow and hypovolemia may be present despite adequate filling pressures. Cardiac filling pressures (central venous pressure (CVP) and pulmonary occlusion pressure (PAOP)) are often misleading for assessing optimal left ventricular loading, as they may be influenced by several factors other than blood volume including those affecting cardiac performance, vascular compliance, and intrathoracic pressure (6).

Several studies suggest that variations in systolic pressure and pulse pressure (systolic-diastolic) during positive pressure ventilation could be a useful method of predicting circulatory responses to a "fluid challenge" (22, 23). In a prospective observational study, PREISMAN *et al.* (24) compared different static indicators of cardiac preload and functional parameters, derived from the arterial pressure waveform analysis in predicting the response to fluid administration. All functional parameters predicted fluid responsiveness better than the static one. Studies in patients with sepsis who required mechanical ventilation demonstrated that a decrease in systolic pressure of 5 mmHg or more during one positive pressure mechanical breath was strongly predictive of a positive response to a subsequent colloid volume challenge (25). Studies in surgery, however have been less conclusive (26).

Information may be gained by assessing the response of CVP or PAOP to a "fluid challenge" (i.e. a fixed volume of fluid is infused in 10 to 15 min). This approach has been shown to improve outcome when compared to "routine" practice in orthopedic surgery (27). Monitoring blood flow instead of intravascular pressure when performing a "fluid challenge" may be an even more efficient approach. Fluid challenge with monitoring of blood flow allows maximization of stroke volume without inappropriate excessive fluid infusion. Several studies have used oesophageal Doppler monitoring to gain information on blood flow in the perioperative period (7, 27-34) (Table 1). They developed algorithms with the aim of maximizing stroke volume through infusion of repeated bolus of colloids and compared this with "standard" fluid management. Among the nine studies pertaining to fluid optimization during the intra- and the post-operative period with this approach, seven (n = 725) found a reduced hospital stay (35). Complications were decreased in four studies, and postoperative nausea and vomiting and ileus were reduced in three. Interestingly, similar results were obtained while different kind of synthetic colloids were used : gelatin, high and low "in vivo" molecular weight hydroxyethyl starches. Of importance, using such a goal-oriented approach did not always result in an increased administration of colloids. As suggested by Noblet *et al.* (31), not only the volume, but also the timing of fluid boluses administration in order to prevent hypovolemia rather than to treat it might be important. All these studies have used oesophageal Doppler for perioperative maximization of cardiac stroke volume with fluid challenges, so-called goal-directed therapy, other flow-related

Table 1
 Perioperative fluid strategy

Authors	Procedure	Duration (min)	Timing	Strategy	Crystalloids : volume (ml)	Colloids : volume (ml)	Outcome
YOGENDRAN (39) 1995	Ambulatory 200	29 ± 2	Pre	"recipe book"	Restrictive : 164 ± 28 Liberal : 1215 ± 30		↓ thirst, drowsiness and dizziness lower in the liberal group
MAHARAJ (40) 2005	Ambulatory 80	22 ± 3	Pre	"recipe book"	Restrictive : 213 ± 7 Liberal : 1799 ± 53		↓ postoperative nausea, vomiting and pain in the liberal group
MAGNER (41) 2004	Gynecologic 141	22 ± 12	Pre+ intra	"recipe book"	Restrictive : 10 ± 1 ml/kg Liberal : 28 ± 6 ml/kg		↓ postoperative nausea and vomiting in the liberal group
HOLTE K. (42) 2007	Colonic 32	77-198	Intra	"recipe book"	Restrictive : 580-1500 Liberal : 2722-6500	Restrictive : 350-750 Liberal : 341-850	Transient improvement in pulmonary function, but tendency of increased morbidity in the restrictive group.
HOLTE K. (43) 2007	Orthopedic 48	41-127	Intra	"recipe-book"	Restrictive : 500-980 Liberal : 2400-4000	Restrictive : 500 Liberal : 500	Hypercoagulability and ↓ vomiting in the liberal group. No difference in hospital stay
HOLTE K. (8) 2004	Cholecystec 48	28-215	Intra	"recipe book"	Restrictive : 722-1455 Liberal : 1950-3920		↑ postoperative organ function and ↓ hospital stay in the liberal group
BRANDSTRUP (4) 2003	Colo-rectal 172	90-390	Intra	"recipe book"	Restrictive : 1100-8050 Liberal : 2700-11080	Similar volume of HES 200/0.5 in both groups	↓ postoperative complications in the restrictive group
NISANEVICH (5) 2005	Abdominal 152	268 ± 112	Intra	"recipe book"	Restrictive : 1408 ± 946 Liberal : 3878 ± 1170	NA	Earlier return in bowel function, ↓ post-operative complications and hospital stay in the restrictive group
NOBLETT (31) 2006	Colo-rectal 108	167 ± 55	Intra	GDT guided fluid management	Control : 2625 ± 1004 Protocol : 2298 ± 863	Control : 1209 ± 824 Protocol : 1340 ± 838	↓ complications and hospital stay
CONWAY (29) 2002	Bowel 57	140 ± 60	Intra	GDT : SV optimization through OD	Control : ± 36 ml/kg Protocol : ± 36 ml/kg	Control : 19 ± 15 ml/kg Protocol : 28.0 ± 16 ml/kg	↑ cardiac output in the protocol group 5 patients in the control group required ICU
GAN (28) 2002	Uro/Gyneco 100	250 ± 115	Intra	GDT : SV optimization through OD	Control : 4375 ± 2452 Protocol : 4405 ± 2650	Control : 282 ± 470 Protocol : 847 ± 373	Earlier return in bowel function and ↓ hospital stay in the protocol group
WAKELING (30) 2005	Bowel 128	157 ± 68	Intra	GDT : SV optimization through OD	Control : 3000 Protocol : 3000	Control : 1500 Protocol : 2000	↓ postoperative complications and hospital stay in the protocol group
SINCLAIR (32) 1997	Orthopedic 40	60-92	Intra	GDT : SV optimization through OD	Control : 700-1250 Protocol : 500-1000	Control : 0-450 Protocol : 550-950	Faster medically fit and ↓ hospital stay in the protocol group
VENN (27) 2002	Orthopedic 90	48-80	Intra	GDT : SV optimization through OD	Control : 1100-1473 Protocol : 983-1257	Control : 319-476 Protocol : 1077-1336	Faster fit for discharge in the protocol group
MYTHEN (7) 1995	Cardiac 60	150-330	Intra	GDT : SV optimization through OD	Control : 800-3000 Protocol : 200-1800	Control : 0-1800 Protocol : 200-1800	↑ Gut mucosal perfusion, ↓ complications, ICU & hospital stay in the protocol group
LOBO (3) 2002	Colonic 20	NA	Post	"recipe book"	Restrictive : 116000 Liberal : 18000		Earlier return in bowel function and ↓ hospital stay in the restrictive group
McKENDRY (33) 2004	Cardiac	NA	Post	GDT : SV optimization through OD*	Control : 328 ± 99 Protocol : 353 ± 95	Control : 1042 ± 620 Protocol : 1667 ± 464	↓ postoperative complications, ICU and hospital stay in the protocol group
PEARSE (34) 2005	General 122	NA	Post	GDT : SV optimization through LiDCO**	Control : 960 ± 335 Protocol : 930 ± 221	Control : 1204 ± 898 Protocol : 1907 ± 878	↓ postoperative complications and hospital stay in the protocol group

Data are reported as ranges, mean ± SD or median, as presented in the original article ; GDT : goal-directed therapy ; SV : stroke volume ; OD : esophageal Doppler ; LiDCO : lithium indicator dilution cardiac output ; * In addition, glyceryl trinitrate or adrenaline administration were guided by the mean arterial pressure ; ** In addition, dopexamine administration was guided by LiDCO to obtain an oxygen delivery index > 600 ml/min.m².

techniques are available and they are potentially easier to apply in clinical practice (35). However, their efficacy remains to be demonstrated (36, 37).

Finally, as the ultimate goal of fluid therapy is the maintenance of tissue perfusion and cellular oxygenation, the use of tissue perfusion indices appeared very appealing (16). Several technologies have been developed, to monitor local or general tissue perfusion perioperatively. Although no interventional study using one of these monitors to guide fluid therapy has demonstrated an improvement in outcome (38), this approach requires further clinical investigation.

CONCLUSIONS

Adequate fluid therapy improves patient's outcome after surgery, while a "wet" or a "dry" approach may be associated, depending on the situation, with an increased rate of postoperative complications. Compensation of preoperative dehydration appears rational. For major surgery, fluids should be administered through a goal-directed approach based on the dynamic evaluation of arterial pressure, cardiac filling pressure, or better, blood flow in response to fluid challenges, and not through a "recipe book" approach. The type of fluid to be administered should depend on the specific space that needs to be restored (intracellular, extracellular or intravascular) and on the pharmacokinetic properties of the different solutions. In the setting of repeated "fluid challenges", synthetic colloids appear more efficacious than crystalloids. Further studies must focus on specific patients' population who may benefit from a particular kind of fluid and on the improvement of monitoring measures to recognize volume deficits and to guide fluid therapy.

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