Fluid management in major surgery: when is enough enough?

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Intensive care specialists are confronted with postoperative patients on a daily basis. In a large proportion of these patients a laparotomy has been performed for various reasons. Although many textbooks and articles address their peroperative fluid management, there is no consensus on the optimal fluid therapy in patients undergoing a laparotomy.

While about 50 years ago a restricted fluid regimen was standard therapy [1,2], over the subsequent decades a more liberal regimen became common practice. This liberal regimen is once more under discussion, and over the past 15 years, a more restricted approach seems to have been regaining popularity. This discussion is important because peroperative fluid management has great potential for influencing morbidity and mortality. In this editorial we will show the main advantages and disadvantages of both regimens and, based on current literature on guiding fluid therapy, give our recommendations.

Pathophysiology

Sixty percent of total body weight is water, which is distributed between extracellular and intracellular compartments. Fluid transport between body compartments is regulated by the Starling equilibrium, the decisive variables being differences in hydrostatic and oncotic pressure and specific permeability coefficients. The cell membrane is selectively permeable while the capillary endothelium is non-selective, and freely permeable to both water and small ions but relatively impermeable to larger molecules such as proteins. Therefore the major determinant of water flux between plasma and interstitial fluid is plasma protein concentration. [3,4]

The two main components of the stress response to surgery are the endocrine and the cytokine responses. The endocrine response to surgical trauma leads to conservation of sodium and water and to excretion of potassium, the principal mediators being antidiuretic hormone (ADH) and the renin-angiotensin-aldosterone-system. [3,5,6] Several other mediators, that are enhanced by surgical stress, may influence the distribution of fluids. Increased cortisol secretion, an obligatory stress response, may be of major importance in the control of fluid homeostasis, primarily through allowing other stress responses to maintain capillary integrity. [5,6] In addition, the cortisol-induced inhibition of the inflammatory response to trauma may reduce postoperative fluid shifts. [3,5,7] The cytokine response, typically consisting of IL-1, IL-6 and TNF-α after major surgery may lead to altered endothelial permeability and vasodilatation [5,6], resulting in protein losses from the intravascular space to the extravascular compartment.

This theoretically causes an increase in interstitial oncotic pressure that further increases transcapillary flux towards the interstitium and eventually leads to the development of tissue oedema. [3,5]

Wet vs. dry

For decades anaesthesiologists and intensive care specialists have advocated a liberal fluid regimen. [3,4,6] This was based on the concept of third space losses as stated by Shires [8] and perhaps also on the fear of possible complications of inadequate fluid administration: reducing effective circulating volume, diverting blood away from non-vital areas (gut, skin, kidneys) to vital organs (brain, heart) possibly resulting in gastrointestinal ischaemia and renal insufficiency. [4,5]

Recent studies comparing liberal and restricted fluid regimens in major abdominal surgery have shown that, while for decades the effects of inadequate fluid administration were supposed to be more detrimental than with a more liberal regimen [3,4,6], the opposite might be true: more liberal fluid regimens seem to increase morbidity and mortality. [6,9,10,11,12]

Brandstrup et al allocated 141 ASA I-III patients scheduled for colorectal surgery to a restricted group (RPG) and a liberal group (LPG). In the RPG, which was aimed at unchanged body weight, external losses only were replaced using HAES 6%. Hypotension and oliguria were treated following the same algorithm in both groups. It was shown that there was a significant reduction in postoperative complications (31% vs. 55%) in the RPG. [9]

Nisanevich et al randomly assigned 152 patients undergoing elective intra-abdominal surgery, to an LPG and RPG. The ASA physical status ranged from ASA I-III (25% was classified ASA III, significantly more than the 3% in the previously mentioned study by Brandstrup et al). The LPG received a bolus of 10 ml·kg⁻¹ followed by 12 ml·kg⁻¹·h⁻¹, while the RPG received 4 ml·kg⁻¹·h⁻¹ of lactated Ringer’s solution. Patients in the LPG passed faeces significantly later (6 vs. 4 days) and their postoperative hospital length of stay (LOS) was significantly longer (9 vs. 8 days). [11]

Lobo et al included 20 patients, classified ASA I or II, undergoing a hemicolectomy. Perioperative management was the same in both groups. Postoperatively the RPG were given 77 mmol of sodium and 2 litres of water a day versus 154 mmol sodium and 3 litres of water in the LPG. Gastric emptying times and passage of flatus and faeces were significantly longer in the LPG. Patients in the LPG experienced more side-effects and their LOS was significantly longer. [12] These studies seem to favour a restricted fluid regimen during the peroperative period (Table 1).
Determining your goal

Fluid management has been based on recipes and pressure-driven protocols,[4,13], while the goal one tries to achieve is optimizing flow to various organs to ensure adequate cellular oxygenation and mitochondrial function. Several difficulties arise when trying to assess tissue flow or oxygenation. Over the past few years many investigators have tried to assess the adequacy of tissue perfusion by measuring diverse surrogate markers like central venous oxygen saturation ($S_{CV}$O$_2$), tissue partial carbon dioxide tension ($P_{CO_2}$) and tissue pH (for example gastric tonometry). However, despite technical improvements, many authors who used one of these modalities concluded that these techniques were interesting in research facilities but not yet applicable in clinical practice.[14,15]

How can we estimate the adequacy of tissue perfusion in the perioperative period? Probably still the best way to go is to use the flow variable that has been most extensively investigated i.e. cardiac output. Although a Cochrane Collaboration review showed no evidence of benefit from a pulmonary artery catheter (PAC) in patients undergoing routine major surgery[16], various less invasive methods were developed and compared to the PAC in terms of reliability. These less invasive modalities of estimating cardiac output can be categorized by the Fick principle, techniques based on the Fick principle, techniques using wave pulse contour analysis and oesophageal Doppler techniques.

**Fick principle**

The Fick equation (cardiac output equals $\Delta V_{CO_2}/\Delta T_{CO_2}$) is frequently used to measure cardiac output using the pulmonary circulation and both arterial and venous oxygen content. The main disadvantage of this technique is the fact that only the amount of blood flow that participates in gas exchange contributes to changes in the total amount of carbon dioxide ($V_{CO_2}$) and end-tidal carbon dioxide ($ET_{CO_2}$). Hence, intrapulmonary shunting can influence cardiac output estimation. To eliminate this bias, patient monitoring devices based on this technique are used to estimate the shunting fraction by peripheral pulsoximetry combined with the inhaled fraction of oxygen ($F_{O_2}$) and oxygen arterial content ($P_{O_2}$) measured in arterial blood gases. In order to use this technique, the patient must be mechanically ventilated and arterial blood gases are required.[17,18]

The most extensively studied monitor that uses the above mentioned principles is the NICO (Novametrix Medical Systems Inc.). While some studies have shown fair agreement between thermodilution and NICO cardiac output, other studies have shown that, especially in haemodynamic instability, lung disease or atelectasis (which is not uncommon in patients presenting for major surgery), agreement was poor.[19,20] Cuschieri et al described an easily applicable approach to the Fick principle using only central venous and arterial $P_{CO_2}$.

Table 1: Studies comparing a restricted (RPG) and liberal (LPG) fluid regimens in major surgery (LOS=length of stay)

<table>
<thead>
<tr>
<th>Researchers</th>
<th>No. of patients</th>
<th>Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>Brandstrup et al</td>
<td>141</td>
<td>Reduction complications in RPG</td>
</tr>
<tr>
<td>Nisanovich et al</td>
<td>152</td>
<td>Return bowel function earlier, LOS shorter in RPG</td>
</tr>
<tr>
<td>Lobo et al</td>
<td>20</td>
<td>Reduction side-effects, return bowel function earlier, LOS shorter in RPG</td>
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</tbody>
</table>

Table 2: Studies comparing Doppler guided fluid therapy (group 1) versus standard fluid protocol (group 2) in major surgery (LOS=length of stay)

<table>
<thead>
<tr>
<th>Researchers</th>
<th>No. of patients</th>
<th>Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sinclair et al</td>
<td>40</td>
<td>39% Reduction LOS in group 1</td>
</tr>
<tr>
<td>Gan et al</td>
<td>100</td>
<td>Return bowel function earlier, LOS 2 days (523 vs. 733) shorter in group 1</td>
</tr>
<tr>
<td>Noblett et al</td>
<td>108</td>
<td>86% Reduction complications in group 1, LOS 2 days (7 vs. 9) shorter in group 1</td>
</tr>
<tr>
<td>Wakeling et al</td>
<td>128</td>
<td>Return bowel function earlier, LOS 1.5 days (10 vs. 11.5) shorter in group 1</td>
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[21] The venous-arterial difference was shown to be inversely correlated with the cardiac index following a simple regression equation with a correlation coefficient squared ($R^2$) of 0.892. Using this approach only central venous and arterial access are mandatory for estimating cardiac output.

**Pulse wave contour analysis**

Pulse contour analysis was first described by Wesseling et al[22] It is as accurate as thermodilution cardiac output monitoring as was shown by Mielck, Goedje and Linton et al[23,24,25] Even in patients with septic shock receiving catecholamines, Linton et al showed fair agreement between thermodilution and pulse wave contour cardiac output measurements.[26] A recent study by Solus-Biguenet evaluated potential predictors of fluid responsiveness during major hepatic surgery.[27] The respiratory variation in pulse pressure was assessed using an arterial waveform (PPV$ART$), the pulse oxymetry waveform (PPV$SAT$) and the Finapres® method (PPV$Fina$), which uses measurements of arterial pressure by an inflatable finger cuff in combination with an infrared plethysmograph. This study showed that PPV$ART$ and PPV$Fina$ correlated well with the fluid challenge-induced changes in stroke volume. The authors concluded that measuring fluid responsiveness during major surgery may be implemented simply and non-invasively.[27]

**Oesophageal Doppler**

Oesophageal Doppler-techniques use a Doppler-transducer at the tip of a flexible probe which is situated facing the descending aorta. A characteristic aortic velocity signal is obtained in which the magnitude is determined by the velocity of the moving red blood cells passing through the aorta. Cardiac output is being determined by multiplying the area under the curve with the cross-sectional area of the aorta.[18,28,29] Additionally, these monitors provide a derived parameter called corrected flow time ($FT_C$) which is the systolic flow time in the descending aorta corrected for heart rate.

In a meta-analysis, Dark et al (21 studies involving 2,400 paired measurements) concluded that Doppler-based monitors showed a high validity for monitoring changes in cardiac output, but there was limited clinical agreement between thermodilution and Doppler-techniques when comparing absolute cardiac output values.[30]

Taking into account the current state of technology, it seems reasonable to use some form of cardiac output measurement in determining the optimal fluid strategy during major surgery. Also, during surgery it would be useful to predict fluid responsiveness before administration of quantities of fluid. Sinclair et al, Gan et al and Noblett et al assigned different patient groups to a standard care and to a protocol group.
All studies used a similar protocol in which a fluid challenge was given if the FT_{C} (see above) was shorter than 350 ms. Wakeling et al performed a prospective randomized-controlled trial comparing an oesophageal Doppler-guided fluid protocol to routine central venous pressure monitoring. These studies all showed a reduction in postoperative morbidity and length of stay (Table 2).

**Conclusion**

Over the last decade there seems to have been a shift from liberal fluid regimens to the more restricted protocols that are being used during major surgery. In many cases standard protocols of fluid management are pressure driven and based on formulas; hyper- and hypovolaemia can easily occur. In order to have more control over tissue oxygenation and optimal intravascular fluid status, other techniques are being studied. Measuring tissue flow and oxygenation seems unattainable in clinical practice, but guiding fluid management using some form of cardiac output monitoring has been shown to be feasible and sometimes quite simple and non-invasive. It is noteworthy that, while several studies using Doppler monitoring have shown a reduction in length of hospital stay and postoperative morbidity, this modality has found its way in the management of critically ill patients in the ICU whereas it is still sparsely used in the operating room. Although it is impossible to write an evidence based fluid management guideline based on the results of the studies performed in this area to date, until more evidence comes available it seems reasonable to implement some of the results from these studies into clinical practice.

Based on these studies, we think it is justified, to reduce the amount of peroperative fluids administered by using oesophageal Doppler-monitoring and only giving fluid challenges when FT_{C} drops below 350 ms or stroke volume decreases by more than 10% of the last value. When there is no response to a fluid challenge in terms of increments in stroke volume and FT_{C} is less than 350 ms, further fluid challenges should be withheld and other treatments considered (e.g. inotropic support). This approach has been shown to reduce the postoperative complication rate and length of hospital stay and is easily applicable in clinical practice, while the advantages of a liberal fluid regimen have not been proven in terms of clinical outcomes.

But perhaps the crux is not the total amount of fluid but ‘just the right amount of fluid for this patient at this time in these circumstances’.

**References**

1. Moore FD. Metabolic care of the surgical patient 1999
3. Morgan GE. Clinical anesthesiology 2002