A pivotal trial of fluid therapy for major abdominal surgery: need and equipoise

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Anaesthetists typically manage perioperative hypotension in the first instance with an intravenous (IV) fluid bolus of a balanced salt crystalloid solution, or sometimes with one of several colloids. If persistent or more profound hypotension occurs, particularly in the intraoperative period, an IV vasoconstrictor (typically a metaraminol bolus) is used. Similar approaches are used in the surgical wards and intensive care unit, but in the latter there is the option of commencing a vasoactive drug infusion to support blood pressure and/or limit IV fluid administration.

We simply do not know whether using a "liberal" fluid strategy based primarily on supplemental IV fluids, or a "restrictive" strategy based on altered haemodynamic goals and/or vasopressor drug therapy, is best for most patients undergoing major surgery. The evidence base for fluid management in the postoperative setting is poor and is insufficient to guide our practice.[1-4] Anaesthetists, intensivists and surgeons differ in their approaches to perioperative fluid therapy.[5,6]

Colloids and crystalloids are both used for fluid resuscitation and maintenance, but the amount of fluids administered and the goals of resuscitation need re-evaluation. There are many reasons why clinicians administer generous amounts of IV fluids during and after surgery. Common reasons include concern about preoperative dehydration; efforts to support circulation after general and regional anaesthesia, avoid gut hypoperfusion and promote tissue oxygen delivery; attempts to avoid blood transfusion; and maintenance of urine output.[7-9] Optimising tissue perfusion typically requires more fluid than indicated by normal clinical criteria or with invasive monitoring.[9]

Occult hypovolaemia and intraoperative gut hypoperfusion occur in around 60% of major surgery patients; both of these complications are linked to increases in morbidity and mortality.[8] Further support for a liberal fluid strategy comes from some studies showing that in patients undergoing minor surgery, mostly in an ambulatory setting, it improves early recovery measures, such as dizziness, nausea and thirst, and may improve pulmonary function and exercise capacity, and shorten hospital stay.[10] Similarly in the intensive care setting, small trials suggest fluid supplementation and optimised haemodynamics reduce organ dysfunction, postoperative morbidity and death.[11,12]

If fluid administration is restricted, it is likely to increase the risk of hypotension, which can otherwise only be treated with vasopressor therapy. Vasopressors can impair organ perfusion, threaten local tissues at the site of IV administration, cause arrhythmias, or be used mistakenly when hypovolaemia is the underlying cause.

Conversely, excess fluid administration causes oedema, with increased pulmonary morbidity,[13] impaired coagulation,[14] increased bacterial translocation and sepsis,[15] and poor wound healing.[16] In contrast to the above, other small trials of patients undergoing abdominal surgery found that fluid restriction led to reduced morbidity and hospital stay.[9,10] This conflicting evidence explains why there are diverse and varied practices around the world. Several expert guideline or consensus statements have been published, with most supporting restrictive fluid administration.[2,17] But all come to similar conclusions — high-grade evidence regarding the optimal fluid regimen is currently lacking.[17]

Liberal or restrictive intravenous fluid resuscitation

Traditional perioperative IV fluid regimens in abdominal surgery can lead to patients receiving 3–7 L of fluid on the day of surgery and more than 3 L/day for the following 3 to 4 days, causing a 3–6 kg weight gain.[18,19]

Several small trials have reported faster return of bowel function, reduced hospital stay and fewer complications among patients managed with a restrictive fluid regimen.[12,14,20] Similar benefits were found in recent trials in colorectal and abdominal aortic surgery.[21,22] However, other trials were not able to replicate these findings.[19,23] A meta-analysis of the fluid trials up to 2007 found restrictive regimens reduced overall complications (odds ratio, 0.41; 95% CI, 0.22–0.77; $P = 0.005$), but the authors noted the heterogeneity of fluid regimens and definitions of outcomes.[3] Another two recent small trials found either no benefit[24] or harm.[25]

The optimal fluid regimen, haemodynamic (or other) targets and fluid choice (colloid or crystalloid) for patients undergoing major surgery are based on rationales that are not supported by strong evidence. Practices vary substantially, guidelines are vague, small trials and meta-analyses are contradictory. The strongest and most consistent evidence, and biological plausibility because of tissue oedema, supports a restrictive fluid strategy. But other evidence supports goal-directed therapy, requiring addi-

Table 1. What do you think is the highest acceptable maintenance intravenous fluid rate to test in a clinical trial?*

	Anaesthetists ($n = 115$)	Intensivists ($n = 123$)
⩾ 160 mL/h	63	53
120 mL/h	46	57
100 mL/h	6	11
80 mL/h	1	2

* *P* for trend, 0.053.

Table 2. What do you think is the lowest acceptable maintenance intravenous fluid rate to test in a clinical trial?*

	Anaesthetists ($n = 115$)	Intensivists ($n = 123$)
80 mL/h	30	20
70 mL/h	8	7
60 mL/h	41	41
⩽ 50 mL/h	36	54

* *P* for trend, 0.023.

tional IV fluid. There is no good evidence that use and choice of colloids improves outcome. We are therefore planning a large pragmatic trial to test both restrictive and liberal fluid strategies in major abdominal surgery.

A survey of anaesthetists and intensivists

One of the contentious issues in designing such a trial is how far most clinicians are prepared to limit or maximise IV fluid therapy in a trial setting. We therefore surveyed 238 trial group members and collaborators from both the Australian and New Zealand College of Anaesthetists (response rate, 115/123 [93%]), and the Australian and New Zealand Intensive Care Society (ANZICS) Clinical Trials Groups (response rate, 123/≈480 [26%]). The response rate suggests strong interest in such a trial and that it is sufficiently representative so that valid generalisations could be made.

Respondents were asked to consider maintenance fluid therapy in the first 24 hours after major abdominal surgery, such as a bowel resection or Whipple procedure. The median maximal IV fluid rate was 120 mL/h, but 48% were prepared to administer 160 mL/h or more (Table 1). The median minimum rate was 60 mL/h (Table 2). Interestingly, anaesthetists appeared prepared to give more fluid than intensivists; the median values were ⩾ 160 mL/h and 120 mL/h, respectively.

These findings highlight discipline-specific differences, and probably reflect the different experiences anaesthetists and intensivists are confronted with on a daily basis. Anaesthetists spend most of their clinical practice focusing on haemodynamic stability and avoiding hypotension in the intraoperative and immediate postoperative periods, whereas intensivists are exposed to patients recovering from major surgery over a longer period — this probably includes greater appreciation of the adverse effects of fluid overload and tissue oedema, as well as the ease of administration of IV vasoactive drugs (rather than additional IV fluid) to manage hypotension. These findings are highly relevant to a perioperative fluid trial in patients undergoing major surgery, in which ICU admission or ICU–ward liaison review is commonly required.

Conclusions

There is strong evidence that we need to perform a pivotal phase IV trial to determine whether a fluid-restrictive or a fluid-liberal approach best serves the need of patients undergoing major abdominal surgery. Our survey indicates strong interest in such a trial in the relevant specialty communities (anaesthesia and intensive care) as well as sufficient variation in people's self-reported preferences for perioperative fluid therapy. While individuals may have strong preferences, our survey also indicates that, at group level, there is equipoise with regard to these two approaches. The lack of evidence, the importance of this issue, the broad and strong interest in conducting a large trial and presence of equipoise all suggest that the time for a pivotal trial is now.

Competing interests

None declared.

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