RELIEF study; what does it mean for fluid management?

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Introduction

Use of intravenous fluids during and after major surgery is ubiquitous and done for a variety of valid physiological reasons including to correct for preoperative fasting and other fluid deficits, anesthesia-induced vasodilation, hemorrhage, 'third space' losses, enhance tissue oxygen delivery and to maintain urine output. Traditional IV fluid regimens in abdominal surgery deliver up to 7 liters of fluid on the day of surgery which can lead to oedema and a 3- to 6-kg weight gain and may be associated with pulmonary, renal and wound complications. [1-4] Several small trials have shown that a more restrictive fluid regimen led to fewer complications and shorter hospital stay [5,6] and these have resulted in consensus statements that recommend a restrictive approach to fluid administration, particularly as a component of Enhanced Recovery after Surgery (ERAS) programs.[7-8]

To address the lack of high quality evidence in this area we conducted the Restricted versus Liberal Fluid Therapy for Major Abdominal Surgery (RELIEF) Trial[9] which compared a restrictive with a more traditional (liberal) fluid regimen for abdominal surgery. Our primary hypothesis was that a restrictive fluid regimen for adults undergoing major abdominal surgery leads to reduced complications and improved disability-free survival when compared with a liberal fluid regimen.

Methods

In a pragmatic, international, trial, we randomly assigned 3000 at-risk patients undergoing major abdominal surgery to a restrictive or liberal intravenous fluid regimen during and up to 24 hours after surgery. The primary outcome was disability-free survival through to 1 year after surgery. Secondary outcomes included 30-day acute kidney injury (AKI), a composite of septic complications, surgical site infection or death, and 90-day renal replacement therapy. Patients were eligible to be included if they were undergoing major abdominal surgery with an expected duration of at least 2 hours and a hospital length of stay of at least 3 days. At least one patient-level risk factor had to be present (including age>70yrs, diabetes, heart disease, renal impairment or obesity)

Results

3000 patients were randomised at 47 centres in 7 countries between May 2013 and September 2016 of these 2983 were included in the analysis and we had outcome data at 1 year available in 2901.

During and up to 24 hours after surgery, 1493 patients in the restrictive group received a median (IQR) 3.7 (2.9 to 4.9) litres compared with 6.1 (5.0 to 7.4) litres in 1490 patients in the liberal group (P<0.001). Disability-free survival at 1 year was 81.9% in the restrictive fluid group and 82.3% in the liberal fluid group (hazard ratio for death or disability 1.05, [95% CI, 0.88 to 1.24], P=0.61). The rate of AKI was 8.6% in the restrictive group and 5.0% in the liberal group (P<0.001). The rate of septic complications or death was 21.8% in the restrictive group and 19.8% in the liberal group (P=0.19). Rates of surgical site infection (16.5% versus 13.6%, P=0.024) and renal replacement therapy (0.9% versus 0.3%, P=0.048) were higher in the restrictive group.

Discussion

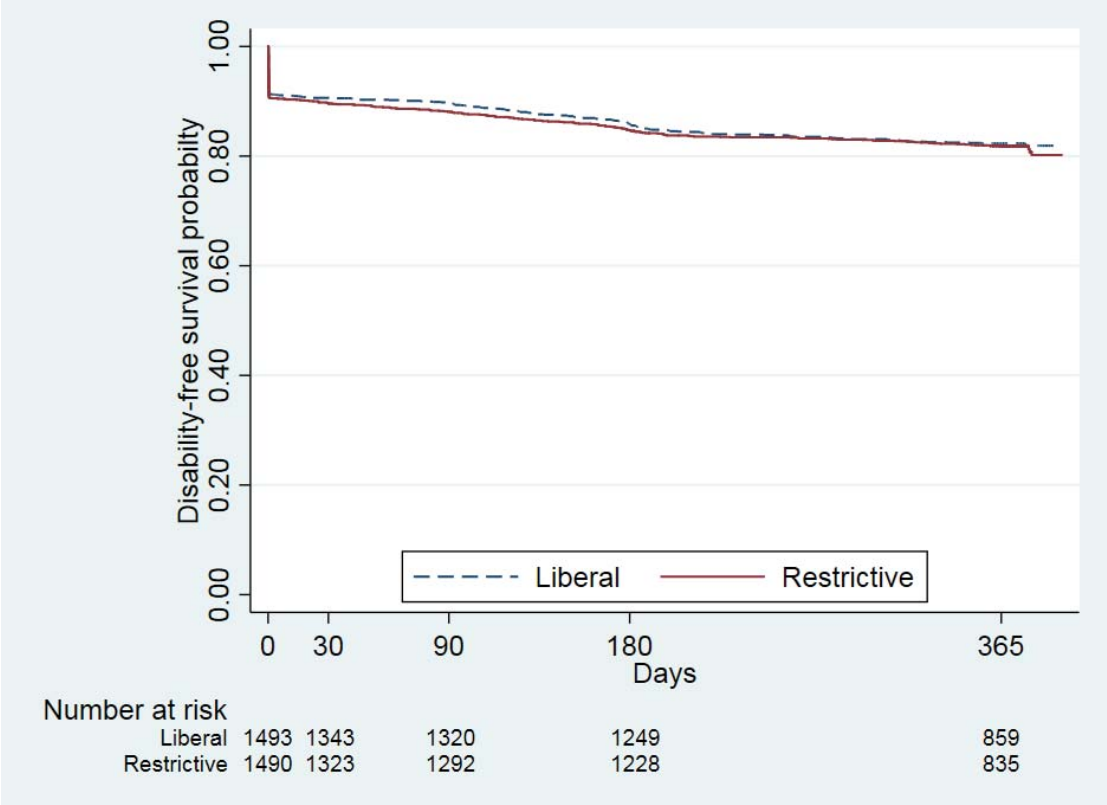
IV fluid regimens for abdominal surgery have been classified into restrictive (less than 1.74 litres per day), balanced (1.75 to 2.75 litres per day), and liberal (greater than 2.75 litres per day).[10] RELIEF study patients assigned to restrictive fluid therapy received a median 1.7 litres intraoperatively and a further 1.9 litres in the first 24 postoperative hours.[9] Patients in the liberal fluid group received 3.0 litres during surgery, and a further 3.0 litres in the first 24 postoperative hours. In previous studies intraoperative 'restrictive' fluid replacement varied from 1.0 to 2.7 liters compared with 2.8 to 5.4 liters in 'liberal' regimens.[11] Current recommendations suggest avoiding a greater than 2.5 kg weight gain – this was achieved in a majority of patients in our study, including those in the liberal fluid group. [12-14]

The RELIEF study findings should not be used to support excessive IV fluid administration. Rather, they show a modestly liberal fluid regimen is safer than a restrictive regimen. There is a belief that fluid-induced edema impairs wound healing. In contrast, we identified a higher rate of surgical site infection in the restrictive group, possibly because of wound and/or anastomotic hypoperfusion.

New Zealand patients included in the restrictive arm of the trial faired particularly badly if managed with a restrictive fluid approach, with a hazard ratio for death or disability of 5.59 (1.61-19.5, p=0.007). This is possibly a spurious result due to the low numbers of patients included (94 in total), although it is interested to reflect that the reason for low patient numbers from New Zealand was a lack of clinician (both anaesthetist and surgeon) equipoise with many stating that the liberal arm was "too wet".

Conclusions

In patients having major abdominal surgery, a restrictive fluid regimen did not improve disability-free survival through to 1 year after surgery. However, a restrictive fluid regimen increased the rates of AKI, renal replacement therapy use, and surgical site infection. Accordingly, our findings support the preferential use of a moderately liberal approach to perioperative fluid therapy.



Probability of freedom from death or persistent disability in the restrictive and liberal fluid groups through to 1 year after surgery.

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