

## Clinical update: perioperative fluid management

In a recent randomised trial in 1000 patients, the ARDS Clinical Trials Network concluded that a balanced fluid regimen (conservative management) over the first 7 days was beneficial in patients with acute lung injury.<sup>1</sup> Despite the primary outcome of 60-day mortality not being significantly different compared with a cumulative fluid excess of 7 L, conservative management shortened the duration of intensive care (14·6 vs 16·8 days) and improved lung function, leading to a shorter period of mechanical ventilation (13·4 vs 15·9 days).

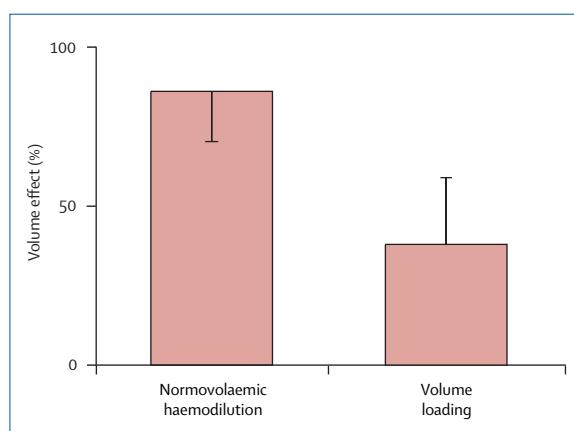
The study draws attention to the debate on perioperative fluid management. Although fluid restriction is accepted in thoracic surgery,<sup>2</sup> the situation differs in the general surgical population. Many believe that liberal fluid use is appropriate perioperatively to prevent anaesthesia-induced hypotension and, therefore, to protect organ function, especially in the kidneys.<sup>3</sup> The background is an assumed large intravascular volume-deficit after preoperative fasting, an increased evaporative fluid loss, and an inevitable shift towards the third space (ie, an ill-defined compartment thought to reflect otherwise unexplainable perioperative fluid losses) during major surgery.<sup>4</sup>

The belief is that vasoconstriction enables the awake and fasted adult to maintain adequate blood pressure despite hypovolaemia. This mechanism is thought to fail during induction of anaesthesia, because of decreased sympathetic tone. The resulting decrease in blood

pressure, as well as use of vasoconstrictors, is blamed as the trigger for perioperative acute renal failure.<sup>3</sup> Thus, preoperative volume loading is considered indispensable and fluid boluses are part of most recommendations for perioperative treatment.<sup>3,5</sup> Other widely used guides to fluid therapy are cardiac filling pressures and even peripheral venous pressure, qualitatively assessed by infusion flow rate, as well as end-tidal carbon dioxide pressure and central venous oxygen saturation.

However, fluid preloading and liberal intraoperative fluid substitution are not evidence-based procedures. Preoperative deficits and insensible losses are highly overestimated<sup>6</sup> and prophylactic fluid boluses have no major effect on the incidence or severity of anaesthesia-related hypotension.<sup>7</sup> Furthermore, volume effects are context-sensitive: a simultaneous infusion of iso-oncotic colloids during acute bleeding (ie, when carefully maintaining intravascular normovolaemia) led to volume effects of over about 90%.<sup>8</sup> By contrast, about two-thirds of an additional bolus in a normovolaemic patient leaves the vasculature towards the interstitial space within minutes (figure).<sup>9</sup>

A liberal fluid regimen has not previously been shown to decrease the incidence of acute renal failure. Nor is there evidence that kidney function deteriorates postoperatively in normovolaemia when urinary output was moderately reduced perioperatively. Rather, protection of fluid compartments is a physiological reaction to surgical stress.<sup>10</sup> In contrast with general opinion, cardiac filling pressures are poor predictors of volume state,<sup>11,12</sup> and a changing peripheral venous pressure can have many causes, most of them trivial. A decreasing end-tidal carbon dioxide pressure can, among other causes, indicate low cardiac output, which is, however, not necessarily related to hypovolaemia. As a commonly used alternative for the more invasively obtainable pulmonary arterial oxygen saturation, detection of central venous oxygen saturation can indicate a change in tissue oxygen supply. However, global volume is an indirect measure, one that only partly affects direct measures such as cardiac output or haemoglobin concentration. Consequently, these traditional variables, despite being widely used because of lack of an alternative in practice, are not suitable to justify any fluid regimen.



**Figure:** Context-sensitivity of volume effects of iso-oncotic colloids in normovolaemic individuals

Experiment used 5% human albumin. Normovolaemic haemodilution=removal of mean 1150 (SD 196) mL blood and simultaneous replacement by 1333 (204) mL colloid ( $n=15$ ).<sup>8</sup> Volume loading=infusion of 1379 (128) mL colloid ( $n=10$ ).<sup>9</sup> Bar=SD, difference  $p<0.05$ .

There are two main, partly competing, efforts to update traditional perioperative infusion: fluid substitution with a fixed regimen and estimations of actual fluid losses, and fluid optimisation with secondary circulatory variables. The idea behind optimisation is to obtain supranormal values of tissue-oxygen delivery.<sup>13</sup> With this concept transferred to the general surgical patient, a maximum stroke volume, achieved by oesophageal doppler-monitored fluid boluses, was considered to represent the optimum fluid load. Indeed, compared with fluid substitution at the discretion of the anaesthetist, this goal-directed approach led to a significantly reduced hospital stay (7 vs 9 days) and fewer intermediate and major postoperative complications (2% vs 15%) after elective colorectal surgery.<sup>14</sup> Additionally, patients treated intraoperatively with colloid boluses (7 mL/kg at first, then 3 mL/kg), to maintain a predefined minimum aortic flow and to optimise stroke volume individually, tolerated diet significantly earlier (2 vs 4 days after intervention).<sup>14</sup> The beneficial effect of doppler-guided fluid-optimisation seems to rise with age and frailty, and obviously it is advantageous to avoid crystalloids in such procedures.<sup>15</sup> Also, several indirect variables were tested as predictors of fluid responsiveness. Less invasive measurements, such as variation in the systolic arterial or pulse pressure (on the principle that intrathoracic pressure changes cyclically during mechanical ventilation, decreasing venous backflow and consequently stroke volume, preferentially in hypovolaemic patients) strongly distinguish between responders and non-responders to fluid challenge. Therefore, they are increasingly replacing the unreliable static cardiac-filling pressures.<sup>16</sup>

Nevertheless, circulatory optimisation, achieved by optimising these easily applicable surrogate variables, has not yet been reliably translated into improved outcomes and, for practical reasons, oesophageal doppler cannot be routine. Interestingly, protocol-based fluid restriction reduces the incidence of perioperative complications, cardiopulmonary events and disturbances of bowel motility, while improving wound and anastomotic healing.<sup>5,17-19</sup>

Whereas many studies of major non-abdominal surgery are underpowered, the findings for major abdominal surgery are promising. In 2002, Lobo and co-workers investigated 20 adults after elective colonic resection.<sup>19</sup> Intraoperatively, fluid use was similar in all patients, but

|                                     | Lobo et al <sup>19</sup> |             | MacKay et al <sup>20</sup> |              |
|-------------------------------------|--------------------------|-------------|----------------------------|--------------|
|                                     | Standard                 | Restrictive | Standard                   | Restrictive  |
| <b>Daily intravenous intake (L)</b> |                          |             |                            |              |
| Day of operation                    | 5.6*‡                    | 3.0*‡       | 2.8†                       | 2.0†         |
| 1st postoperative day               | 3.0*‡                    | 1.6*‡       | 2.6†                       | 2.0†         |
| 2nd postoperative day               | 2.7*‡                    | 1.3*‡       | 2.5†                       | 0.0†         |
| 3rd postoperative day               | 2.7*‡                    | 1.0*‡       | 0.5†                       | 0.0†         |
| <b>Daily oral intake (L)*‡§</b>     |                          |             |                            |              |
| 1st postoperative day               | 0.1                      | 0.2         | Not reported               | Not reported |
| 2nd postoperative day               | 0.2                      | 0.6         | Not reported               | Not reported |
| 3rd postoperative day               | 0.4                      | 0.8         | Not reported               | Not reported |
| <b>Weight change (kg)*‡§</b>        |                          |             |                            |              |
| 1st postoperative day               | 2.7                      | 0.7         | 1.1                        | -0.5         |
| 2nd postoperative day               | 3.3                      | 0.0         | 1.2                        | -0.4         |
| 3rd postoperative day               | 2.7                      | -0.7        | 1.1                        | -0.7         |
| <b>Endpoints (days)†</b>            |                          |             |                            |              |
| Time to first flatus                | 4.0                      | 3.0         | 2.9                        | 2.9          |
| Postoperative hospital stay         | 9.0                      | 6.0         | 7.2                        | 7.2          |

Values are \*mean or †median. ‡Values are estimated from graphs. §Cumulative values vs preoperative state.

Table: Semiquantitative comparison of two studies on postoperative fluid handling

postoperatively they were randomised to a restrictive ( $\leq 2$  L a day) or a standard ( $\geq 3$  L a day) protocol. The standard protocol caused a significant weight gain of 3 kg, a later return of bowel function, and a longer hospital stay. In a larger trial in 80 patients undergoing colorectal surgery, MacKay and colleagues did not confirm these findings, despite their protocols for postoperative fluid management seeming, at first sight, to be similar to Lobo's (table).<sup>20</sup> But patients in MacKay's randomised groups were intraoperatively managed with relative fluid restriction (basal rate 10 mL/kg per h) compared with that in Lobo's study (about 18 mL/kg per h). The resulting different postoperative starting points are reflected by the respective values of perioperative weight change and total fluid intake on the day of operation. A sufficient postoperative fluid balance was not possible, because oral fluid intake was only "encouraged", but not reported by MacKay. Nevertheless, with no patient receiving more than 3 L of intravenous fluid a day, even perioperatively, MacKay's standard group was actually treated too restrictively to cause measurable harm.

Rather, MacKay's findings underline the importance of a rational concept for perioperative treatment. In a multicentre study in a homogeneous group of 141 patients undergoing major colorectal surgery, perioperative intravenous fluid restriction (mean 2740 vs 5388 mL) significantly reduced the incidence of

major and minor complications.<sup>17</sup> Despite limited fluid application and a perioperative decrease in urine output, acute renal failure did not occur in any restrictively treated patient. Others found similar results, including a decreased hospital stay under fluid restriction, in a more heterogeneous group of 152 patients scheduled for mixed-abdominal surgery.<sup>5</sup> In 2006, a systematic review of 80 randomised trials recommended to avoid fluid overload in major surgical procedures.<sup>18</sup>

But what, exactly, is overload? Despite the beneficial effects of restrictive fluid management in major abdominal surgery, extrapolations to the perioperative treatment for an individual remain difficult. There are large differences in the definitions of liberal or standard and restrictive (table), which reflect the lack of standardisation and make any pooling of data impossible. In most previous investigations with a strict protocol, a locally used regimen was simply entitled the liberal protocol, and the investigators compared this with their own restrictive idea. But, when comparing these restrictive regimens to measured values of preoperative blood volume after overnight fasting and insensible perspiration, fluid restriction in those studies was only "less liberal". Preoperative fasting does not normally cause intravascular hypovolaemia,<sup>8,9</sup> and the measured basal evaporative water loss is only about 0.5 mL/kg per h, increasing to a maximum of 1 mL/kg per h during major surgery.<sup>6</sup> In addition, a measurable weight gain even in restricted study groups<sup>5,17</sup> indicates that there is still potential for improvement.

Adequate substitution of fluid needs before, during, and after major abdominal surgery can improve outcome. The same is true for doppler-guided achievement of supranormal predefined goals for cardiac output. Future studies should compare these two approaches, erroneously called fluid restriction and optimisation, respectively, to make a decision about which is the better choice. However, we should also be able to provide a rational fluid regimen to the many patients in whom extended monitoring is not possible for logistical or financial reasons. To achieve this end, more well-powered trials are needed, comparing the current standard to a fluid regimen that is based on scientific data about perioperative losses.

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