'Liberal' vs. 'restrictive' perioperative fluid therapy – a critical assessment of the evidence

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Background: Several studies have assessed the effect of a 'liberal' vs. a 'restrictive' perioperative fluid regimen on post-operative outcome. The literature was reviewed in order to provide recommendations regarding perioperative fluid regimens.

Methods: A PubMed search identified randomized clinical trials and cited studies, comparing two different fixed fluid volumes on post-operative clinical outcome in major surgery. Studies were assessed for the type of surgery, primary and secondary outcome endpoints, the type and volume of administered fluid and the definition of the perioperative period. Also, information regarding perioperative care and type of anaesthesia was assessed.

Results: In the seven randomized studies identified, the range of the liberal intraoperative fluid regimen was from 2750 to 5388 ml compared with 998 to 2740 ml for the restrictive fluid regimen. The period for fluid therapy and outcome endpoints were inconsistently defined and only two studies reported perioperative care principles and discharge criteria. Three studies found an improved outcome (morbidity/hospital stay) with a restrictive fluid regimen whereas two studies found no difference and two studies found differences in the selected outcome parameters.

Conclusion: Liberal vs. restrictive fixed-volume regimens are not well defined in the literature regarding the definition, methodology and results, and lack the use of or information on evidence-based standardized perioperative care-principles (fast-track surgery), thereby precluding evidence-based guidelines for procedure-specific perioperative fixed-volume regimens. Optimization of perioperative fluid management may include a combination of fixed crystalloid administration to replace extravascular losses and avoiding fluid excess, together with individualized goal-directed colloid administration to maintain a maximal stroke volume.

Accepted for publication 24 April 2009

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Fluid administration is an integrated part of care for almost any surgical procedure and consequently an everyday issue for most anaesthesiologists. Perioperative fluid therapy has received increased interest in recent years because several studies have demonstrated that the strategy for fluid therapy may influence the post-operative outcome.1–6 Obviously, hypovolaemia is recognized as a risk factor leading to adverse effects ranging from minor organ dysfunction to multi-organ failure and even death. Conversely, liberal administration of fluid may impair pulmonary, cardiac and gastro-intestinal functions, contributing to post-operative complications and prolonged recovery.1,4,6 Yet, with no established definition of normovolaemia, it has been difficult to monitor how much volume is required to ensure an optimal outcome. Attention has been directed towards different volume regimens referred to as 'liberal' or 'high' vs. 'restricted' or 'low'. In minor ambulatory/semi ambulatory procedures, more than 18 randomized trials have investigated the effect of administering more or < than ~ 11 of fluid and conclude that more than 11 of crystalloid results in reduction of symptoms related to dehydration.2,4,7 However, the data comparing crystalloid regimens in major procedures have not provided similar clear recommendations.

Therefore, the purpose of this review was to assess the randomized trials comparing a liberal vs. a restricted fixed-volume crystalloid regimen in major surgery in order to establish information for clinical practice and guidelines for future studies.

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Methods

A PubMed search identified randomized clinical trials comparing the effect of two different fixed fluid volumes on one or more post-operative clinical outcome parameters in adults undergoing major surgery. Search terms 'fluid therapy' and 'outcome' were combined and limited to randomized human studies published in English and with patients >18 years in the period 1966–2008, May 22. Additional studies were identified from review articles and papers cited in original papers.

Analysis

Studies were assessed for information regarding the type of surgery, number of patients and primary and secondary outcome endpoints. Moreover, the type and volume of administered and lost fluid, weight before and after surgery and the definition of the perioperative period were registered. Finally, information regarding perioperative management, type of anaesthesia and the use of epidural analgesia was assessed.

Results

From the 187 identified studies, only seven randomized studies were selected according to the search strategy (Table 1). Six studies included major abdominal surgery and one study included knee arthroplasty. Studies addressing abdominal surgery included colorectal procedures or a variety of abdominal procedures.

‘Liberal’ vs. ‘restrictive’ fluid regimen

Two studies reported pre-operative fluid administration and then only in the liberal groups (Table 2). The definition of a liberal vs. a restrictive intraoperative fluid regimen differed between studies. The range of a liberal intraoperative fluid regimen was from 2750 to 5388 ml compared with 998 to 2740 ml for the restrictive fluid regimen (Fig. 1). Consequently, a restrictive fluid regimen in one study differed only 10 ml from what was defined as liberal in another trial. Post-operatively, the studies reported a volume that ranged from 1500 to 2900 ml in the liberal group and between 500 and 2170 ml in the restricted group. However, post-operative volume administration was only reported in four studies. Five studies provided data on fluid intake/administration vs. fluid losses expressed as a change in body weight (Table 2).

Only two of these studies reported a conventional fluid balance of 3.71 in the liberal group and 0.21 in the restricted group at day 4 and 2.31 in the liberal group and 1.21 in the restricted group at day 0.

Indications for additional fluid administration

Five studies provided additional fluid besides the fixed-volume regimen. In the study by Brandstrup et al., the restricted group was provided with a synthetic colloid (HAES 6%) 1:1 according to blood loss; the liberal group received 1000–1500 ml of saline with a blood loss ≤500 ml, and additional blood loss was replaced with additional HAES. In the study by MacKay et al. blood products were provided; however, no indication of these or other colloid products was given. In the two studies by Holte et al. a fixed volume of colloid of 7 mg/kg was given.

In the study by Nisanovich et al. a CVP <15 mmHg was an indication of colloid administration or pharmacologic support, and blood was transfused with a haematocrit <24% (<30% in patients with cardiac morbidity). Kabon et al. provided additional fluid if diuresis was <1 ml/kg/h or if MAP <70% of preinduction.

The intra- vs. the post-operative period

When assessing the fluid volume administered intraoperatively, different periods were reported ranging from ‘intraoperative’ to ‘intraoperative including PACU stay’ to ‘day of operation’, which was not further specified. The post-operative period was defined from 1 h post-operatively to ‘to midnight’ or as the first post-operative day.

One study primarily evaluated the post-operative period. In the fast-track studies by Holte et al. intravenous fluids were not provided post-operatively and fluid needs were managed by oral intake.

Outcome endpoints

Wound infection, gastric emptying time, pulmonary function, post-operative complications and death were used in six studies as the primary outcome parameters (Table 1). In one study, no primary endpoint was defined but gastrointestinal function, complications and fitness for discharge were evaluated. Five studies reported length of hospital stay (LOS), but only three studies reported well-defined discharge criteria. Finally, gastrointestinal recovery was
<table>
<thead>
<tr>
<th>Study and year</th>
<th>Procedure/pt (n)</th>
<th>ASA I/II/III/IV (%)</th>
<th>Fast-track</th>
<th>Blinding</th>
<th>Epi intraop</th>
<th>Epi post-op</th>
<th>Anaesthesia</th>
<th>Outcome</th>
<th>Result</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lobo 2002</td>
<td>Hemi colectomy/20</td>
<td>–</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>–</td>
<td>Gastric emptying time</td>
<td>Low: ↑ GI recovery ↓ LOS: High 9 days, low 6 days</td>
</tr>
<tr>
<td>Brandstrup 2003</td>
<td>Colorectal resection/141</td>
<td>47/51/2/0</td>
<td>No</td>
<td>Assessor</td>
<td>Yes</td>
<td>Yes</td>
<td>–</td>
<td>Complications</td>
<td>Low: ↓ complications</td>
</tr>
<tr>
<td>Kabon 2005</td>
<td>Colon resection/253</td>
<td>10/75/15/0</td>
<td>No</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>i.v.: thio/ fentanyl, vola: iso/NO</td>
<td>Wound infection</td>
<td>→ Wound infection</td>
</tr>
<tr>
<td>Nisanovich 2005</td>
<td>Major abdominal surgery/142</td>
<td>22/52/26/0</td>
<td>Yes</td>
<td>Assessor</td>
<td>No</td>
<td>Yes</td>
<td>i.v.: thio/ fentanyl, vola: iso/NO</td>
<td>Death and complications</td>
<td>Low: ↑ GI recovery ↓ complications, LOS (High 9 days, low 8 days). → death</td>
</tr>
<tr>
<td>Mackay 2006</td>
<td>Colorectal resection/69</td>
<td>5/70/24/1</td>
<td>No</td>
<td>Assessor</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>Recovery</td>
<td>→ GI recovery, LOS (7.2 days), complications</td>
</tr>
<tr>
<td>Holte 2007</td>
<td>Arthroplasty/48</td>
<td>29/48/23/0</td>
<td>Yes</td>
<td>Double</td>
<td>Yes</td>
<td>Yes</td>
<td>Epi/spinal</td>
<td>Perioperative physiology and organ function</td>
<td>High: ↑ vomiting ↓ coagulation, pulmonary function → exercise capacity, pain, nausea, appetite, well-being, fatigue, ileus, post-op hypoxaemia, LOS</td>
</tr>
<tr>
<td>Holte 2007</td>
<td>Colonic surgery/32</td>
<td>22/25/53/0</td>
<td>No</td>
<td>Double</td>
<td>Yes</td>
<td>Yes</td>
<td>i.v.: prop/ remi</td>
<td>Physiological recovery</td>
<td>High: ↓ pulmonary function, vasoactive hormones, total complications → exercise capacity, ileus, pain, well-being, thirst, headache, dizzy/drowsiness, fatigue, LOS</td>
</tr>
</tbody>
</table>

↑, increased/improved; →, no change; ↓, decreased/reduced; vola, volatile anaesthetic; prop, propofol; remi, remifentanil; Low, low fluid regimen; High, high fluid regimen; GI, gastro-intestinal; i.v., intravenous.
reported in one trial\textsuperscript{13} and a battery of physiological recovery variables was utilized as secondary outcome variables in two studies\textsuperscript{11,14}

\textbf{Outcome result}

\textit{Studies with improved outcome following a restricted fluid regimen (Table 2).} Three of seven studies found that a restrictive fluid regimen improved outcome after major abdominal surgery, with two studies showing improved gastro-intestinal recovery and a reduced LOS from 9 to 6 days\textsuperscript{8} and from 9 to 8 days, respectively.\textsuperscript{13} Two studies also showed an overall reduced incidence of complications (Table 1).\textsuperscript{5,13} However, the two trials reporting LOS did not define any criteria for discharge.\textsuperscript{8,13} All three studies reported use of crystalloid, of which one study used a balanced solution (Ringers lactate)\textsuperscript{13} and two studies used saline and dextrose/glucose\textsuperscript{8,9} (Table 2). Two studies reported additional use of colloid (HAES 6\%, HES 200/0.5)\textsuperscript{8,9}. One study did not provide ASA classes\textsuperscript{8} and one study included only a small number of ASA III patients (2\%).\textsuperscript{9} In the remaining study, ASA ranged from I to III (18\%).\textsuperscript{13}

Patients with impaired renal function, congestive cardiac failure, hepatic disease, diabetes mellitus, ascites, peritoneal metastasis, impaired mobility, anaemia or those taking drugs affecting gastrointestinal mobility were excluded in the study by Lobo et al.,\textsuperscript{8} whereas pregnancy, lactation, mental disorders, alcohol consumption >35 U/week, diabetes mellitus, renal insufficiency, disseminated cancer, secondary cancer, inflammatory bowel disease or disease hindering epidural analgesia were the exclusion criteria in the study by Brandstrup et al.\textsuperscript{9} In the study by Nisanевич et al.\textsuperscript{13} hepatectomy, age <18 years, pregnancy, coagulopathy, renal or hepatic dysfunction and congestive heart failure were the exclusion criteria.

One study reported that epidural analgesia was not used perioperatively\textsuperscript{8} and one study used epidural analgesia both intra- and post-operatively\textsuperscript{9} and the last study only used epidural analgesia post-operatively.\textsuperscript{12} However, no information was provided with regard to the site (thoracic vs. lumbar) or the dose/composition of the epidural regimen. Two studies were assessor blinded,\textsuperscript{9,13} and one study was not blinded.\textsuperscript{8} Updated perioperative evidence-based care principles including pre-operative information, optimized opioid-reduced epidural and systemic analgesia, avoidance of bowel preparation, early post-operative mobilization and oral nutrition,\textsuperscript{15-17} were not described in any of the three studies recommending a restrictive fluid regimen.\textsuperscript{8,9,13}

\textit{Studies with no difference in outcome (Table 2).} Two studies in colonic surgery showed no difference between the liberal and the restrictive fluid regimen with outcome expressed as wound infection\textsuperscript{12} or gastro-intestinal recovery and LOS (7.2 days).\textsuperscript{10} Patients with fever, infection, susceptibility to malignant hyperthermia, congestive heart failure, use of diuretics, renal failure and a history of pulmonary oedema were excluded in the study by Kabon et al.\textsuperscript{12} For MacKay et al.\textsuperscript{10} renal impairment, physical disability requiring long-term care, insulin-dependent diabetes mellitus, total colectomy,
Table 2

Perioperative fluid administration and losses in millilitres.

<table>
<thead>
<tr>
<th>Study</th>
<th>Pre</th>
<th>Intra</th>
<th>Pre</th>
<th>Intra</th>
</tr>
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<tbody>
<tr>
<td></td>
<td>H</td>
<td>L</td>
<td>H</td>
<td>L</td>
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<tr>
<td></td>
<td>H</td>
<td>L</td>
<td>H</td>
<td>L</td>
</tr>
<tr>
<td></td>
<td>H</td>
<td>L</td>
<td>H</td>
<td>L</td>
</tr>
<tr>
<td>Lobo⁸</td>
<td>–</td>
<td>–</td>
<td>Intra</td>
<td>2800</td>
</tr>
<tr>
<td>Brandstrup⁹</td>
<td>500</td>
<td>–</td>
<td>To midnight</td>
<td>5388</td>
</tr>
<tr>
<td>Kabon¹²</td>
<td>700</td>
<td>0</td>
<td>Intra</td>
<td>–</td>
</tr>
<tr>
<td>Nisanovich¹³</td>
<td>–</td>
<td>Intra</td>
<td>3878</td>
<td>1408</td>
</tr>
<tr>
<td>Mackay¹⁹</td>
<td>–</td>
<td>Day of OP</td>
<td>2750</td>
<td>2000</td>
</tr>
<tr>
<td>Holte¹⁴</td>
<td>–</td>
<td>Intra</td>
<td>4250</td>
<td>1740</td>
</tr>
<tr>
<td>Holte¹¹</td>
<td>–</td>
<td>Intra</td>
<td>5050</td>
<td>1640</td>
</tr>
</tbody>
</table>

Pre, pre-operative; Intra, intraoperative; Post, post-operative; All, all administered volume; Cryst, crystalloid; Definition, definition of period; H, high volume group; L, low volume group; Post-op, post-operative; OP, operation; PACU, post-anaesthetic care unit; –, no information; S + D, saline and dextrose; S + G, saline and glucose; RL, ringers lactate; HES, hydroxyl ethyl starch 130/0.4; HAES, hydroxyl ethyl starch 200/0.5.
abdominoperineal resection and low-anterior resection requiring a defunctioning stoma were the exclusion criteria. Both studies reported the use of crystalloid but the type was only stated in one study (saline and dextrose). The use of colloid was not reported. Details regarding anaesthesia were only provided in one of the studies, and information on epidural analgesia was not given. Updated perioperative evidence-based care principles including pre-operative information, optimized opioid-reduced analgesia, avoidance of bowel preparation, early post-operative mobilization and oral nutrition were not described in the two studies without a difference in outcome.

Studies with differences in outcome (Table 2). The two blinded studies regarding knee arthroplasty and colonic surgery showed benefit from a restrictive or a liberal fluid regimen in different functional parameters. For both studies, age <50 years, weight >110 kg, BMI >10, inability to perform the pre-operative test programme, ASA IV, insulin-dependent diabetes mellitus, NYHA class IV or MI <3 month, FEV1 <11, psychiatric disorder, alcohol consumption >5 U/day, glucocorticoid and anticoagulant therapy or inability to provide informed consent were the exclusion criteria. In the colonic surgery study, additional exclusion criteria were inflammatory bowel disease, and in the knee arthroplasty study, a contraindication to tranexamic acid/epidural catheter, chronic opioid treatment and morphine intolerance were also the exclusion criteria for participation. The study in knee arthroplasty found reduced vomiting, improved pulmonary function and enhanced coagulation with the liberal regimen, but no difference between groups in exercise capacity, pain, nausea, appetite, well-being, fatigue, ileus, post-operative hypoxaemia or LOS (4 days). The study in colonic surgery found an improvement in pulmonary function and post-operative hypoxaemia and a reduced vasoactive hormonal response (aldosterone, renin and AT-II concentration) on administering a liberal fluid regimen. Although the total number of complications was reduced \( (P < 0.01) \), the number of patients with complications was not significantly reduced \( (P = 0.08) \). In addition, exercise-capacity, pain, nausea, thirst, headache, dizzy/drowsiness, fatigue, ileus and LOS ('high': 2.5 days; 'low': 3 days) were not different \( (P = 0.52) \). Both studies used a balanced crystalloid (Ringer's lactate) and a colloid (HES 140/0.4). Also, both studies were double-blinded and with updated perioperative evidence-based care principles including pre-operative information, optimized opioids-reduced analgesia, avoidance of bowel preparation, early post-operative mobilization and oral nutrition. In both studies, well-described epidural anaesthesia was used intra- and post-operatively and the type of general anaesthesia was provided in the colonic surgery study.

Discussion

Inconsistent outcome results and study designs have been reported with the use of a liberal vs. a restrictive fluid regimen. These inconsistencies relate both to the amount of administered fluid volume in the liberal vs. restrictive fluid regimens, indications for additional fluid, and to the defined intra- and post-operative period as well as information on perioperative care principles hindering direct comparison and interpretation. Accordingly, it is recommended to abandon the terms liberal and restrictive when referring to the size of a fixed-volume fluid regimen. Although changes in body weight were reported in most studies, a conventionally calculated fluid balance was only provided in two studies. Nevertheless, the studies suggest that the perioperative crystalloid excess impairs the post-operative outcome.

Study design

Exclusion criteria were extensive in most trials. In order to apply the study findings to daily clinical practice, we consider that the patients included need to be representative for the procedure-specific population. In this context, the study by Brandstrup et al. only included a limited number of ASA III patients (ASA I/II/III: 47/51/2%) and did not represent the general population undergoing colorectal resection. Nevertheless, the worse outcome demonstrated by this relatively 'healthy' population by a liberal fluid regimen leading to a weight gain suggests that fluid excess should be avoided.

Standardized evidence-based perioperative care principles

The majority of identified studies, except for the two double-blinded studies, did not describe perioperative care principles and discharge criteria in detail. This is unfortunate because pre-operative information, optimized non-opioid analgesia, avoidance of bowel preparation, early post-operative mo-
bilization and oral nutrition improve post-operative outcome per se. Thus, the study in abdominal surgery applying the 'fast-track' methodology had a median hospital stay of ~3 days in both groups in contrast to the studies reporting a reduction in LOS from 9 to 6 days and 9 to 8 days with a 'restricted' regimen. Consequently, perioperative care needs to be defined and evidence-based care principles should be adopted in order to evaluate the effect of fluid management per se. The same applies to semi-ambulatory procedures where application of evidence-based perioperative care and a liberal fluid regimen (∼3 l) improved the post-operative outcome in the context of exercise capacity, balance function, thirst, dizzy/drowsiness and the hormonal stress response compared with a restricted regimen (∼1 l), probably reflecting functional hypovolaemia with the restricted regimen.

**Outcome parameters**

In elective surgery, perioperative death is a rare event and studies with death as an outcome variable require large sample sizes. Only one study used death as a primary outcome variable, while LOS has been widely used as a secondary outcome variable. The LOS depends on multiple factors and when precise discharge criteria are not defined, interpretation of LOS remains elusive. Thus, the two studies using LOS as an outcome parameter and advocating a restrictive fluid regimen did not describe discharge criteria. A reduction in post-operative surgical complications is a tempting evaluation of the benefit of one fluid regimen over another, provided that the registered complication is related to fluid therapy. Thus, the role of fluid management in urinary tract infections may be questioned, when exact criteria for use and removal of a urinary bladder catheter are not provided. Therefore, in studies addressing the role of fluid therapy, it would be of interest to evaluate functional outcome variables with a known or at least theoretically assumed relationship with the amount of fluid administration.

**Type of fluid**

The relative role of the optimal administration of crystalloid vs. colloid ratio has not been resolved. However, there is evidence favouring balanced solutions with an electrolyte concentration similar to that found in plasma and large volumes of e.g. saline should be avoided because they induce hyperchloaemic acidosis.

**Clinical and research strategies**

Because differences in surgical trauma, pre-operative hydration, anaesthetic technique, co-morbidity, gender and age are likely to influence the fluid needs, a fixed-volume regimen is unlikely to both prevent hypovolaemia and the risk of hypervolaemia for every patient (Fig. 2). Therefore, rather than using a fixed volume of crystalloids as the main strategy of perioperative volume handling, it should be used as a background fluid regimen to replace extra-vascular fluid losses and with a focus on avoiding undesirable fluid excess and maintaining bodyweight. A more rational strategy for perioperative fluid therapy could also include a tailored individualized treatment optimizing the intravascular volume by providing maximization of cardiac stroke volume with colloid boluses, the so-called individualized 'goal-directed therapy' concept. This strategy has improved outcome in 10 randomized trials and may, in contrast to the fixed-volume regimens, offer a definition of 'normovolaemia'. Thus, rather than choosing between a fixed-volume regimen and a goal-directed concept, an approach is to combine the two strategies because they replace losses from the extra- and intravascular fluid compartments, respectively.

**Conclusion**

It is of concern that the literature pertaining to a liberal vs. a restrictive fixed-volume regimen is inconsistent regarding the definitions, methodology and defined outcome parameters, and most studies are hampered by the lack of information on evidence-based standardized perioperative care principles (fast-track surgery). Therefore, evidence-based guidelines for optimal procedure-specific perioperative fixed-volume regimens cannot be formulated. Rational perioperative fluid management may include a combination of fixed crystalloid administration to replace extra-vascular losses and individualized goal-directed colloid administration to maintain a maximal cardiac stroke volume. Yet, we consider that such an approach needs to be examined in procedure-specific studies combined with evidence-based principles for perioperative care (fast-track surgery) in order to define optimal perioperative fluid management.
Finally, we consider it important to evaluate the role of fluid therapy in outcome in high-risk patients, rather than excluding such patients in future studies.

References


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