Fluid therapy for the surgical patient

Birgitte Brandstrup* MD, PhD
Surgical Department, Slagelse University Hospital, Ingemannsvej 18, DK-4200 Slagelse, Denmark

Perioperative fluid therapy is the subject of much controversy, and the results of the clinical trials investigating the effect of fluid therapy on outcome of surgery seem contradictory. The aim of this chapter is to review the evidence behind current standard fluid therapy, and to critically analyse the trials examining the effect of fluid therapy on outcome of surgery. The following conclusions are reached: current standard fluid therapy is not at all evidence-based; the evaporative loss from the abdominal cavity is highly overestimated; the non-anatomical third space loss is based on flawed methodology and most probably does not exist; the fluid volume accumulated in traumatized tissue is very small; and volume preloading of neuroaxial blockade is not effective and may cause postoperative fluid overload. The trials of ‘goal-directed fluid therapy’ aiming at maximal stroke volume and the trials of ‘restricted intravenous fluid therapy’ are also critically evaluated. The difference in results may be caused by a lax attitude towards ‘standard fluid therapy’ in the trials of goal-directed fluid therapy, resulting in the testing of various ‘standard fluid regimens’ versus ‘even more fluid’. Without evidence of the existence of a non-anatomical third space loss and ineffectiveness of preloading of neuroaxial blockade, ‘restricted intravenous fluid therapy’ is not ‘restricted’, but rather avoids fluid overload by replacing only the fluid actually lost during surgery. The trials of different fluid volumes administered during outpatient surgery confirm that replacement of fluid lost improves outcome. Based on current evidence, the principles of ‘restricted intravenous fluid therapy’ are recommended: fluid lost should be replaced and fluid overload should be avoided.

Key words: fluid therapy; third space loss; perioperative fluid therapy; goal-directed fluid therapy; fluid volume; outcome of surgery.

In order to maintain a patient’s physiological functions and to replace fluid lost, intravenous fluid resuscitation is a key component in the treatment of surgical patients. The determination of the optimal fluid volume to be given is not simple, however, because both the lost volume and physiological parameters depend on preconditions that are not always fulfilled, i.e. (1) that lost fluid can be accurately measured, and (2) that changes in physiological parameters with adequate sensitivity are proportional to changes in blood volume.

* Tel. +45 5855 9000x2124.
E-mail address: bbrandstrup@hotmail.com.
In daily clinical practice a combination of measured lost volume and physiological changes is used for the assessment of the fluid status in the surgical patient, and a typical protocol for postoperative fluid management will include frequent monitoring of blood pressure, heart rate, blood pH, urinary output, fluid balance, and body weight measurements. However, during and after surgery, blood pressure is decreased by anaesthetic and analgesic drugs, urinary output is decreased by the release of stress hormones, and acidosis may be inflicted on the patient by the very administration of saline-containing fluids. Moreover, movement of fluids between body compartments, with a disappearance of intra-vascular volume into a third space, would make the replacement of only measured losses inadequate.

There is little doubt that hypovolaemia leads to poor tissue perfusion, suboptimal organ function, organ failure, and death. Fluid overload, on the other hand, may be just as harmful as hypovolaemia, but the effects of fluid overload have not attracted the same scientific attention as have the effects of hypovolaemia. Iatrogenic fluid overload has been shown to decrease pulmonary function, to hamper gut motility, and to decrease subcutaneous oxygen tension. Pulmonary oedema has been described as a consequence of fluid overload, even in patients without pre-existing cardiac disease. Associations have been shown between intra-operative fluid overload and complications as well as mortality following major surgical procedures, and recently clinical randomised trials have shown fluid overload to cause a poor outcome following gastrointestinal surgery. Currently, the volumes of fluid administered during surgery far exceed the volumes lost. The observed postoperative body weight increase of 3–7 kg following major surgery reflects this.

In order to determine the optimal fluid volume to be administered during surgery, randomised trials examining the possible effects of fluid volume on outcome of surgery have been performed. The theoretical and therapeutic approaches of the trials have, however, been contradictory. The trials of ‘goal-directed fluid therapy’ test the effects of standard fluid therapy versus standard fluid plus extra fluid given to obtain central haemodynamic parameters on target values that are thought to be beneficial for outcome (typically maximal stroke volume, oxygen delivery or oxygen consumption). The trials examining ‘restricted fluid therapy’ claim that all fluid administered in excess of measured losses (and thus increasing body weight) will result in fluid overload and may be harmful; these trials may be regarded as goal-directed trials where the goal is not maximal stroke volume but normal body weight.

This chapter reviews the existing (or missing) evidence behind the current standard fluid therapy, as well as the literature concerning the influence of administered intravenous fluid volumes on outcome of surgery.

CURRENT FLUID THERAPY IN MAJOR SURGERY: EVIDENCE AND IMPLICATIONS

Standard fluid therapy includes replacement of fluid lost (by basal fluid requirements, perspiration through the surgical wound, loss to the third space, and blood loss and exudation through the surgical wound) and maintenance of physiological functions (‘preloading’ of neuroaxial blockade).

It is generally agreed that fluid lost by the basal fluid requirements, perspiration through the surgical wound, blood loss, and exudation should be replaced. Any disagreement regarding these losses is about the timing, the route of administration,
and the type of fluid used for replacement. However, replacement of the so-called ‘loss to the third space’ and the ‘preloading of neuroaxial blockade’ are subject to much controversy, and doubts have been raised about the very existence of the third space loss.\textsuperscript{24} Replacement of such a third space loss, as well as the preloading of neuroaxial blockade, will inevitably cause a postoperative body weight gain, i.e. a postoperative fluid overload.

**Fluid lost during surgery**

*The insensible perspiration*

The insensible perspiration is approximately 10 mL/kg/day in normal conditions, and this does not change much during surgery. About two thirds of the volume is lost through the skin and one-third from the airways. The loss through the airways depends on the humidity of the inhaled air. Inhalation of (or ventilation with) 100% water-saturated air causes a loss close to zero, while inhalation of (or ventilation with) dry air causes a loss of approximately 0.5 mL/kg/hour.\textsuperscript{25} Patients are allowed to drink until 2 hours before elective surgery and should therefore be well hydrated.\textsuperscript{26} Unfortunately this is not always the case. For determination of the volume lost during fasting, an obvious approach would be to record or ask the patient about the intake. The deficit may then be replaced with approximately 80 mL/fasting hour.

Both perspiration and deficit from fasting primarily involve the loss of water, and replacement with a water preparation seems therefore logical (i.e. glucose 5%). Surgery- and disease-induced stress, however, causes a rise in blood glucose, and to avoid an enhancement of this, preoperative or intra-operative glucose infusion has previously been discouraged. However, clinical trials have shown that preoperative glucose administration—either intravenous or oral—reduces the postoperative cellular insulin resistance\textsuperscript{27,28}, increases well-being\textsuperscript{29}, and improves postoperative muscle strength.\textsuperscript{30} Preoperative rehydration with glucose-containing fluids is therefore both logical and beneficial for the fasting patient. Intra-operative glucose administration is controversial, mostly due to lack of evidence and concerns about hyperglycaemia. Two clinical randomised trials have investigated the effect of intra-operative glucose administration during outpatient gynaecological laparoscopy, with contradictory results: one trial showed intra-operative glucose infusions to improve recovery\textsuperscript{31}, but the other trial could not confirm this.\textsuperscript{32}

*Urine*

Urine in large volumes cannot be expected during surgery, both because the release of stress hormones reduces the excretion of salt and water, and because the anaesthesia may cause hypotension. It is, however, important to distinguish between the anaesthesia-induced hypotension and hypovolaemia. The first is caused by vasodilation and may reduce the glomerular filtration rate (GFR) but not the arterial blood supply to the renal stoma. Hypovolaemia, on the other hand, reduces both GFR and renal blood supply and may cause renal failure. It is not at all evident that a large urinary output is necessary to prevent postoperative renal failure, or that a small urinary output is associated with renal failure in the absence of hypovolaemia.\textsuperscript{33,34} A small diuresis is therefore acceptable during surgery as long as hypovolaemia is not the cause.
The evaporative loss

The evaporative loss from the surgical wound depends on both the size of the incision and the exposure of the intestines.\(^\text{35}\) 

- in minor incisions with slightly exposed but non-exteriorised viscera it is 2.1 g/hour;
- in moderate incisions with partly exposed but non-exteriorised viscera it is 8.0 g/hour;
- in major incisions with completely exposed and exteriorised viscera it is 32.2 g/hour.

Note that the loss is given in grams per hour, and is independent of the body weight of the patient.

The loss from completely exteriorised viscera decreases by 50% after 20 minutes, and wrapping the exteriorised viscera in plastic reduces the evaporation loss by 87.5%. There is no reason to believe that the loss from incisions in other anatomical regions is very different.

The loss to third space

The 'loss to the third space' can be divided into an anatomical and a non-anatomical loss.\(^\text{37,38}\) The anatomical third space loss represents pathological accumulations of fluid in the extracellular volume (ECV), and may be named as such to avoid confusion.

Pathological fluid accumulations. Before, during, or after surgery the disease and/or trauma may cause fluid to accumulate in a transcellular or interstitial space and cause an expansion of the ECV. Examples of this are ascites in the peritoneal cavity, pleural exudation, or other transcellular fluid sequestrations, as well as accumulations of blood or oedema in the interstitial space of traumatized tissues. A volume of ascitic or pleural fluid emptied through drains or during surgery can be accurately measured, and will cause a postoperative weight loss. In patients who are allowed to drink, regeneration of such fluid postoperatively will cause a return to preoperative weight. In case of doubt the loss may be quantified, for example by ultrasound imaging.

The volume of fluid accumulated in the interstitial space of traumatized tissue is more difficult to assess, and is highly influenced by the administration of intravenous fluid. In a study of rabbits, it was found that the formation of a small bowel anastomosis caused an increase of water in the surrounding tissue of 5–10% if no intravenous fluid was administered. The oedema doubled when 15 mL/kg/hour of intravenous fluid was given. If equivalent changes occur in humans, 2.5–5 mL may accumulate around a large bowel anastomosis if no fluid is administered, and 5–10 mL may accumulate if 15 mL/kg/hour fluid is given. If one imagines the entire colon to be oedematous, the accumulation would be 150–300 mL, depending on the volume of intravenous fluid administered.

The non-anatomical third space loss (or deficit in functional extracellular volume). It is believed that the surgical trauma per se causes a contraction of the ECV, with a volume of extracellular fluid sequestered in a compartment where it is not available for measurement with a tracer or for the regeneration of lost plasma. This phenomenon was first described in 1960 in a trial of dogs subjected to haemorrhagic shock, compared with the ECV before bleeding, the ECV measured during shock was much smaller than anticipated from the volume of lost blood. A year later the same
observation was made in patients undergoing abdominal surgery: despite correction for external losses, the measured ECV during surgery was found to be largely diminished (up to 28% or −3.7 L) compared to similar measurements before surgery. The severity of the trauma seemed to correlate with the ECV lost, so that the larger the trauma, the larger the ‘loss of ECV’. The anatomical location of the missing fluid was not clear. Sequestration in the intracellular compartment was suggested, but was not confirmed by later investigations including measurements of total body water. Sequestration in the intestinal lumen was suggested, but this hypothesis was later rejected. A last hypothesis—that the fluid was sequestered in traumatized tissue—could not be confirmed by measurement of ECV changes in American soldiers with extensive trauma and severe shock during the armed conflict of Vietnam.

A systematic review of the literature concerning measurements of ECV changes in surgery or haemorrhagic shock reveals that only trials utilizing the SO tracer and a very short equilibration time (20–30 minutes) have demonstrated this non-anatomical third space loss. All other studies—utilizing various different tracers, multiple sampling techniques, and longer equilibration times—have not been able to find a contraction of the ECV neither during surgery nor during haemorrhagic shock. Furthermore, investigators utilizing the labelled bromide tracer have found the opposite of a third space loss: corrected for the lost blood, an expansion of the ECV instead of a contraction was found following surgery.

In my opinion, a phenomenon that can only be demonstrated with one specific method of measurement is not evident, in particular not when the method used implies serious weaknesses and all other methods of measurement contradict the finding. Nevertheless, the loss to the third space is replaced according to algorithms. Volumes up to 15 mL/kg/hour are recommended in the first hour of abdominal surgery, with decreasing volumes in subsequent hours.

Replacement of lost blood

Replacement of lost blood with a crystalloid demands infusion of double or triple volume because crystalloid is dispersed throughout the entire extracellular space. This causes an expansion of the interstitial space, with postoperative oedema formation and body weight gain. This may be desirable if the surgical trauma causes a contraction of the ECV (a third space loss, see above) that needs replacement. Indeed, it was the firm belief in the third space loss that started the ‘crystalloid era’. If surgery, on the other hand, does not cause a contraction of the ECV, a colloid that stays in the vascular space for a longer time seems to be a more expedient choice for replacement of lost blood. Trials of colloid versus crystalloid have shown diverging results, and the literature has been reviewed in several publications. However, none of the trials of colloids versus colloids have used what is perhaps the most important beneficial potential of resuscitation with a colloid: avoiding postoperative fluid overload (body weight increase). Therefore, all the trials may have investigated the effects of fluid overload with a colloid versus fluid overload with a crystalloid.

Exudation from surgical wound

Exudation from the surgical wound is often lost in the surgical dressings, and its volume is therefore based on an estimate, but it will show as a postoperative weight change. In abdominal surgery with exteriorised viscera in a plastic bag, however, the loss can be
measured rather accurately. The exudate contains protein, and manipulation of the intestines increases the protein loss.91

The maintenance of physiological functions

Neuroaxial blockade causes a relaxation of the vascular bed innervated by the affected segments of the spinal cord.92 This causes a decrease in peripheral vascular resistance with a decrease in arterial blood pressure (BP). Despite the fact that cardiac output and peripheral blood flow may be unaltered, it is common to respond to this decrease in BP by giving either 500 mL of colloid or 1000 mL of crystalloid intravenously. However, this treatment has not been shown to be effective. The earliest non-randomised trials and retrospective investigations93–95 suggested fluid preloading to reduce the incidence of hypotension in 20–35% of patients, but this has not been confirmed in clinical randomised trials of preloading versus no preloading.96–104 Neither the decrease in blood pressure nor the need for pressor substances was significantly altered by the fluid preloading of the neuroaxial blockade.

TRIALS OF GOAL-DIRECTED FLUID REGIMENS (STANDARD FLUID VERSUS EXTRA FLUID)

The trials of goal-directed therapy fall into two categories: trials of fluid loading alone, and trials investigating the effect of fluid therapy in addition to different medications.

Six trials were found examining the effect of fluid therapy alone.105–110 The trials of good methodological quality (see below) are shown in Table 1. The goal of the fluid therapy was to obtain a maximal stroke volume (SV) output determined by oesophageal Doppler or a target CVP, from the theoretical point of view that maximal stroke volume is also optimal for the patient (i.e. it is optimal that the patient’s heart is working on ‘the top of the Starling curve’). As seen from the table, the study populations of these trials are small, reflecting that power was not calculated to show a difference in postoperative morbidity or mortality, but in intestinal pH107 or length of hospital stay. With the possible exception of the trial by Gan and colleagues111, who registered gastric emptying time (see below), none of the trials defined by protocol a primary endpoint of a specific complication or group of complications that may be ‘fluid-related’. Moreover, the difference in fluid volume between the groups was very small. With no control or registration of postoperative fluid therapy, it is not at all obvious that the fluid therapy is actually responsible for the differences observed. Only one trial111 attempted blinded registration of outcome measures, but none of the trials followed the patients after discharge. Even though ‘standard fluid therapy’ varies enormously between centres and doctors, none of the investigators presented a view of what the right ‘standard fluid therapy’ is, but tested ‘standard therapy’ versus ‘standard fluid plus more fluid’. As seen from Table 1, the absolute volumes given during surgery varied from 1000 mL109 to 5252 mL.106 This is, in my opinion, the greatest weakness of these trials.

The trial by Gan and colleagues106 found a shorter duration of postoperative nausea and earlier return to solid food in the intervention group. The difference in intra-operative fluid volume between groups compared was, however, only 595 mL, and pre- or postoperative fluid therapy was not recorded. The results of this trial are contradicted by those of two other trials with a much larger fluid difference between
### Table 1. Trials of goal-directed fluid therapy with extra hydroxyethyl starch (HES) to maximal stroke volume.

<table>
<thead>
<tr>
<th>Authors</th>
<th>Surgery</th>
<th>Number of patients</th>
<th>Intervention</th>
<th>Preoperative fluid</th>
<th>Intraoperative fluid</th>
<th>Postoperative fluid</th>
<th>Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sinclair et al, 1997</td>
<td>Orthopaedic surgery</td>
<td>40 in two groups</td>
<td>HES to maximal SV evaluated by ED</td>
<td>Unknown</td>
<td>1475 mL (ED) vs 1000 mL</td>
<td>Unknown</td>
<td>Hospital stay shorter in the intervention group</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>No difference for complications</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Mortality: 1 in intervention group, 2 in control group</td>
</tr>
<tr>
<td>Mythen et al, 1999</td>
<td>Thoracic surgery</td>
<td>60 in two groups</td>
<td>HES to maximal SV evaluated by ED</td>
<td>Unknown</td>
<td>2100 mL (ED) vs 1800 mL</td>
<td>Unknown</td>
<td>More patients with complications in the control group (6 vs 0)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Mortality: 1 in the control group</td>
</tr>
<tr>
<td>Venn et al, 2002</td>
<td>Orthopaedic surgery</td>
<td>90 in three groups</td>
<td>HES to maximal SV evaluated by ED or CVP</td>
<td>2051 mL (ED) vs 2000 mL</td>
<td></td>
<td></td>
<td>Hospital stay shorter in the intervention group</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>No difference in complications</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Mortality: 9 in the intervention groups and 2 in the control group</td>
</tr>
<tr>
<td>Conway et al, 2002</td>
<td>Abdominal surgery</td>
<td>57 in two groups</td>
<td>HES to maximal SV evaluated by ED</td>
<td>Unknown</td>
<td>4522 mL (ED) vs 3864 mL</td>
<td>Unknown</td>
<td>No differences for complications or hospital stay</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Mortality: 1 in the control group</td>
</tr>
<tr>
<td>Gan et al, 2002</td>
<td>General, urological or gynaecological surgery</td>
<td>100 in two groups</td>
<td>HES to maximal SV evaluated by ED</td>
<td>Unknown</td>
<td>5252 mL (ED) vs 4657 mL</td>
<td>Unknown</td>
<td>Hospital stay shorter in the intervention group</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>No difference for complications</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Mortality not reported</td>
</tr>
</tbody>
</table>

SV, stroke volume; ED, oesophageal Doppler; CVP, central venous pressure.
the groups (close to 3 L) on the day of surgery and adequate recording of postoperative administered fluid volume. In both these trials liberal fluid therapy was found to significantly delay gastric emptying time and increase postoperative complications.

The three trials of patients with fractures of the hip have been analysed in a Cochrane review. One trial was excluded due to methodological problems, but two trials were included in the meta-analysis. The conclusion of the Cochrane review was that the number of trials and patients included were few, and that fluid optimization regimens tended to increase the administered fluid volume and may have a benefit in shortening hospital stay but also a possible adverse effect of increased mortality (control versus intervention: 3/50 versus 10/80; Peto’s odds ratio 1.44, 95% CI: 0.45–4.65).

TRIALS OF AN OPTIMIZATION PROGRAMME WITH FLUID AND ADDITIONAL DRUGS

Eleven trials were found which tested 'standard fluid therapy' versus 'extra fluid, inotropic, and other-drug therapy.' Even though fluid therapy was the first treatment of choice, the fluid volume administered is described in only four trials.

In the trial by Wilson and colleagues, 138 patients undergoing major abdominal surgery were randomised into three groups. The two intervention groups received preoperative intravenous fluid in addition to intra-operative dopexamine or adrenaline. The dopexamine group had a reduction in postoperative morbidity, while the mortality was significantly reduced in both the intervention groups. It is difficult to interpret the importance of the fluid therapy for the results of this trial, mainly because all patients in the intervention groups received pressor substances.

In the trial by Boyd and colleagues, 107 patients undergoing major surgery were randomised either to an optimization programme or to a control group. The intravenous volume difference between the groups was, however, only 183 mL, and postoperative fluid administration was not controlled.

Two trials of patients undergoing vascular surgery were found. In the trial by Bender and colleagues, 104 patients were randomised either to a control group or to an optimization programme including fluid, dopamine, nitroprusside, and/or diuretics administered to obtain physiological goals measured with a pulmonary artery catheter (PAC). The control group received a PAC only if judged to be clinically necessary. The volume difference between the two groups was 5137 versus 3789 mL. Thirteen patients in the intervention group developed a complication versus seven patients in the control group, but the result was not significant. One patient in each group died.

In the trial by Bonazzi and colleagues, 100 male patients younger than 75 years and free of cardiac diseases were randomised into two groups. The patients in the treatment group were transferred to the ICU the day before surgery, and fluid, dobutamine and nitroglycerine were administered to obtain physiological goals measured with a PAC. For the two first postoperative days the optimization programme was continued on the ICU for the patients in the intervention group but not for the control group; 4500 mL fluid was given to the intervention group versus 3250 mL to the control group on the day of surgery. The differences between groups
on the first and second postoperative days were 580 and 170 mL. No significant differences in clinical outcome or hospital stay were found.

The effect of the administered fluid for the results of these trials is difficult to interpret, because it is impossible to separate effects of the fluid therapy from the effects of the additional therapy. Moreover, only one trial registered the postoperative fluid administration\(^\text{115}\), blinding of outcome measures was not attempted, and the patients were not followed after discharge in any of the trials.

Sandham and colleagues\(^\text{119}\) have recently performed the most exhaustive trial of goal-directed therapy. In a multi-centre design, 1999 ASA group 3–4 patients undergoing urgent or elective surgery were randomised to a goal-directed optimization programme using a PAC or ‘standard therapy’. The goal was optimal oxygen delivery and cardiac index in the PAC group, and the first drug of choice was intravenous fluid, but the administered fluid volumes are not given. The optimization programme, however, did not reduce postoperative mortality, morbidity or time in hospital, but the use of a PAC had significant adverse effects.

**TRIALS ON RESTRICTED INTRAVENOUS FLUID THERAPY**

As discussed above, current standard fluid therapy is not at all evidence-based; the existence of a non-anatomical third space loss is not convincing, and no effect of the preloading of the neuroaxial blockade has been shown. The postoperative weight gain of 3–7 kg in patients undergoing major elective surgery therefore seems to represent a genuine fluid overload. For a thorough review of the physiological (adverse) effects of fluid overload see Holte et al.\(^\text{125}\)

We therefore designed a clinical randomised assessor-blinded multi-centre trial to answer the following questions\(^\text{11}\):

1. Can a restricted fluid protocol improve tissue healing?
2. Can a restricted fluid protocol prevent cardiopulmonary complications?

Patients planned for colorectal resection were randomly allocated to either a restricted (R) or a standard (S) intra- and postoperative intravenous fluid regimen (86 in each group). The R regimen was designed to replace measured fluid losses but without a postoperative weight gain. During surgery, fluid preloading of the epidurals and fluids for the non-anatomical third space loss were omitted. Blood was replaced with hydroxyethyl starch (HES) 6% volume for volume (with allowance for a maximum of 500 mL extra). The same principles were followed postoperatively, and a body weight increase of more than 1 kg was treated with furosemide. The administered fluid volume on the day of surgery was a median of 2740 mL in the R group versus 5388 mL in the S group, and on the first postoperative day R versus S was 500 versus 1500 mL. Administered fluid on postoperative days 2–6 was similar. Complications were registered after 30 days of follow-up by both an unblinded (clinical) and a blinded assessment.

Postoperative complications were significantly reduced by the restricted fluid therapy (R versus S, ITT-analysis: 28 (33%) versus 44 (51%), \(P = 0.013\); per-protocol analysis: 21 (30%) versus 40 (56%), \(P = 0.003\). The two hypotheses were confirmed (R versus S: tissue healing complications 11 (16%) versus 22 (31%), \(P = 0.040\); cardiopulmonary complications 5 (7%) versus 17 (24%), \(P = 0.007\). A dose-response relation between administered fluid volume and postoperative complications was found (\(P < 0.001\)). Four patients in the standard group died, but there were no deaths in the restricted group (absolute risk
reduction 5.6, 95% CI: 0.3–10.9%). In all cases, the cause of death was a cardiopulmonary complication. Adverse effects were lower diuresis and higher creatinine (but not urea) on the day of surgery in the R group. On the other hand, patients in the S group had lower arterial pH, a lower concentration of bicarbonate, and negative base excess in the immediate postoperative period ($P < 0.01$). Furthermore, the S regimen caused haemodilution, with lower concentrations of serum albumin and total protein. The restricted regimen did not cause haemodynamically unstable patients; no significant differences in intra- and postoperative arterial blood pressures were found, and the administration of pressor substances was similar.

The results of our trial confirm the results of Lobo and colleagues who randomised 20 patients undergoing colonic resection to either a restricted postoperative fluid regimen or a standard regimen to investigate the effects on gastric emptying time and complications. The restricted group received no more than 2 L intravenous fluid and 77 mmol sodium daily. The control group received at least 3 L water and 154 mmol sodium daily. Even though the intervention did not include the intra-operative fluid therapy, the administered fluid volume between the groups on the day of operation was 3000 versus 5700 mL. Significantly shorter solid- and liquid-phase gastric emptying times and a significant reduction in postoperative complications were found in the restricted group (R versus S: 1 versus 7, $P < 0.05$).

Recently, the results of both the above trials have been confirmed by Nisanevich et al. who randomised 156 patients undergoing various major gastrointestinal procedures to either a restricted intravenous fluid protocol (R: 4 mL LR/kg/hour) or a liberal intravenous fluid protocol (L: 12 mL LR/kg/hour). In both groups lost blood was replaced by lactated Ringers solution (LR) by 1:3. Low diuresis, low blood pressure, or increased heart rate initiated the administration of a fluid bolus. The mean administered intra-operative volume was (L versus R) 3871 versus 1408 mL, and the rest of the day of operation (L versus R) 2012 versus 2170 mL was given. Thus, the total volume administered on the day of surgery was very similar to the volumes given in the two previous trials. On postoperative days 1 and 2 a similar fluid volume was given to the two groups. Blinded registration of outcome was performed. The trial showed that significantly fewer patients in the restricted group had a postoperative complication (R versus L: 13 versus 23, $P < 0.05$). Patients in the restricted group had significantly shorter time to first flatus and stool ($P < 0.001$), and hospital stay was significantly reduced. The trial has the weakness that the patients were not followed after discharge, with the consequence that late complications (for example wound infections) may have been overlooked.

In conclusion, restricted intravenous fluid therapy has consistently been shown to improve outcome in patients undergoing major gastrointestinal surgical procedures. No trials exist, however, testing the effects of restricted fluid therapy on other types of surgery.

**TRIALS OF OUTPATIENT SURGERY**

Nine randomised trials were found testing different intravenous fluid volumes on outcome of outpatient surgery (see Table 2). The outcome assessed included thirst, dizziness, drowsiness, well-being, and for some of the trials nausea, vomiting and overnight stay in hospital. Intravenous fluid was found to improve self-reported drowsiness and dizziness in seven of the trials, and in three of the trials postoperative nausea was less in the groups receiving fluid. The volume
<table>
<thead>
<tr>
<th>Author</th>
<th>Surgery</th>
<th>Number of patients</th>
<th>Blinding</th>
<th>Duration of surgery (minutes)</th>
<th>Intervention</th>
<th>Fast (hours)</th>
<th>Postoperative oral fluid intake</th>
<th>Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>Keane and Murray, 1986</td>
<td>Mixed outpatient surgery</td>
<td>212 in two groups</td>
<td>No</td>
<td>18</td>
<td>1000 mL Hartman’s solution + 1000 mL DW versus no fluid</td>
<td>?</td>
<td>?</td>
<td>Fluid reduces thirst, drowsiness and increases well-being No effect on nausea</td>
</tr>
<tr>
<td>Spencer, 1988</td>
<td>Minor gynaecological surgery</td>
<td>100 in two groups</td>
<td>No</td>
<td>8</td>
<td>1 L CSL versus no fluid</td>
<td>?</td>
<td>?</td>
<td>Fluid reduces dizziness and nausea</td>
</tr>
<tr>
<td>Cook et al, 1990</td>
<td>Gynaecological laparoscopy</td>
<td>75 in three groups</td>
<td>Yes</td>
<td>20</td>
<td>CSL 20 mL/kg versus CSL + DW 20 mL/kg versus no fluid</td>
<td>11–16</td>
<td>?</td>
<td>Fluid reduces dizziness and drowsiness Hospital stay reduced in dextrose group</td>
</tr>
<tr>
<td>Yogendran et al, 1995</td>
<td>Mixed outpatient surgery</td>
<td>200 in two groups</td>
<td>Yes</td>
<td>28</td>
<td>Plasmolyte 20 mL/kg (1215 mL) versus plasmolyte 2 mL/kg (164 mL)</td>
<td>8–13</td>
<td>?</td>
<td>Fluid reduces thirst, dizziness and drowsiness No effect on nausea</td>
</tr>
<tr>
<td>Elkahim et al, 1998</td>
<td>Day case termination of pregnancy</td>
<td>100 in two groups</td>
<td>Yes</td>
<td>12</td>
<td>1 L CSL versus no fluid</td>
<td>9.66</td>
<td>1.5–2</td>
<td>Fluid reduces nausea and vomiting</td>
</tr>
<tr>
<td>Bennet et al, 1999</td>
<td>Dental- alveolar surgery</td>
<td>90 in two groups</td>
<td>Yes</td>
<td>?</td>
<td>NS 16 mL/kg versus NS 1 mL/kg</td>
<td>8–13</td>
<td>?</td>
<td>Fluid reduces dizziness and drowsiness No effect on nausea</td>
</tr>
<tr>
<td>McCaul et al, 2003</td>
<td>Gynaecological laparoscopy</td>
<td>108 in three groups</td>
<td>Yes</td>
<td>22</td>
<td>CSL 1.5 mL/kg fasting hour (1115 mL) versus CSL + DW 1.5 mL/kg fasting hour (1148 mL) versus no fluid</td>
<td>11.5</td>
<td>?</td>
<td>No significant differences between the groups</td>
</tr>
</tbody>
</table>

(Continued on next page)
<table>
<thead>
<tr>
<th>Author</th>
<th>Surgery</th>
<th>Number of patients</th>
<th>Blinding</th>
<th>Duration of surgery (minutes)</th>
<th>Intervention</th>
<th>Fast (hours)</th>
<th>Postoperative oral fluid intake</th>
<th>Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>Magner et al, 2004</td>
<td>Gynaecological laparoscopy</td>
<td>141 in two groups</td>
<td>Yes</td>
<td>20</td>
<td>CSL 30 mL/kg versus CSL 10 mL/kg</td>
<td>13</td>
<td>?</td>
<td>Fluid reduced nausea and vomiting No effect on dizziness or thirst</td>
</tr>
<tr>
<td>Holte et al, 2004</td>
<td>Laparoscopic cholecystectomy</td>
<td>48 in two groups</td>
<td>Yes</td>
<td>68</td>
<td>LR 15 mL/kg (998 mL) versus 40 mL/kg (2928 mL)</td>
<td>2</td>
<td>Mean 600 mL</td>
<td>Fluid reduces thirst, nausea, dizziness, drowsiness, improves well-being and pulmonary function and shortens hospital stay</td>
</tr>
</tbody>
</table>

DW, dextrose in water 5%; CSL, compound sodium lactose (Na: 131, K: 5, Ca: 2, Cl: 111, lactate: 29 mmol/L); NS, normal saline 0.9%; LR, lactated Ringer’s solution.
administered, however, equates very well with the patient’s deficit from fasting, and may even be small if the fasting lasted more than 12–24 hours. Thus, the results confirm that fluid losses should be replaced, but do not assess the problem of fluid administration in excess of external losses during surgery.

**Practice points**

- Preoperative glucose-containing fluid by the oral or intravenous route improves outcome; a deficit due to fasting should not exist.
- Fluid preloading of neuroaxial blockade has not been shown to prevent or lessen the decrease in blood pressure or the need for pressor substances, but may cause fluid overload.
- The fluid volume needed for maintenance is not altered much by surgery.
- Evaporation from the surgical wound is small: 2.1–32.2 mL/hour, depending on the exposure of the intestines.
- Pathological fluid accumulation in the traumatized tissue is small in elective surgery.
- The non-anatomical third space loss is based on flawed methodology and most probably does not exist.
- The logical choice for replacement of lost blood is a colloid given on a volume-for-volume basis.
- A small urinary output during surgery is acceptable as long as vasodilatation and not hypovolaemia is the cause.
- In major surgery, trials of ‘goal-directed fluid therapy’ aiming at maximal stroke volume have shown diverging results, but not a convincingly improved outcome, most probably because the ‘standard fluid therapy’ has not been questioned or modified, causing some of the trials to test fluid overload versus even more fluid, because the volume difference between the groups has been small, and because the fluid therapy in the surgical ward has not been controlled.
- Also in major surgery, trials of ‘restricted intravenous fluid therapy’ or ‘goal-directed fluid therapy’ aiming at normal body weight have improved outcome in gastrointestinal surgery; the principles have not been tested during other surgical procedures.
- In outpatient surgery, replacement of the deficit due to fasting with approximately 1000 mL of intravenous fluid increases postoperative well-being.

**Research agenda**

- The role of glucose-containing fluid during surgery is not known.
- Possible transfer of fluid between compartments during surgery is unknown, if it occurs at all.
- The goal of intravenous fluid therapy aiming at normal body weight—i.e. ‘restricted intravenous fluid therapy’—needs testing in areas other than gastrointestinal surgery.
- Central haemodynamic changes during ‘restricted intravenous fluid therapy’ are unknown.
- The goal of fluid to maximal stroke volume has not been tested against ‘restricted intravenous fluid therapy’.
One trial examined the effect of a mean volume of 1 versus 2.9 L LR in 48 patients undergoing laparoscopic cholecystectomy. Measured 2 and 4 hours postoperatively, it was found that thirst, dizziness, drowsiness, nausea, and fatigue were decreased, while well-being, pulmonary function and exercise capacity was increased in the group receiving liberal fluid therapy. However, the fluid was not the only difference between the groups in this trial: in the recovery room significantly more patients in the low-volume group received an opiate \((P=0.011)\) in significantly larger doses \((P<0.04)\) than did the patients in the high-volume group. As all the above outcome measures are well-known morphine side-effects, not controlling the postoperative opiate administration is a major weakness, and the result of the trial is therefore difficult to interpret. Moreover, in two previous trials (one by the same group of investigators), 3 L intravenous fluid has been shown to hamper pulmonary function.4,5

The last trial—of gynaecological laparoscopy—found no significant benefits of fluid therapy compared to no fluid at all.32

RecommendaTions

With no evidence of the existence of a non-anatomical third space loss and no effect of fluid preloading of neuroaxial blockade, the ‘restricted intravenous fluid therapy’ is not at all ‘restricted’, but based on current evidence. The principle is that loss should be replaced, but fluid overload (recognized as a postoperative body weight gain) should be avoided.

This principle should be continued postoperatively (in the recovery room and in the surgical ward), with replacement of the daily requirements for nutrition, electrolytes, glucose, and water. The patients should be fed.

Body weight measurements are the most reliable tool for estimation of fluid balance in surgical patients and should consequently guide the quantity of perioperative fluid administration. Registration of fluid losses on the fluid chart should guide the quality of fluid replacements. However, clinical judgement is indispensable: body weight changes do not recognize internal loss of vascular volume. Careful examination of patients with hypotension or low diuresis should be performed and the cause treated. If the cause is loss of volume, intravenous fluids should be supplemented; if the cause is vasodilatation (e.g. due to large doses of epidural analgesia or habitual anti-hypertensive medication), the treatment is not fluid but dose adjustment of the provoking factor or vasoconstricting agents (e.g. ephedrine). If the cause is development of a surgical complication (e.g. anastomotic leakage with sepsis), action should be taken to treat the complication, etc.

References

3. Prough DS & Bidani A. Hyperchloremic metabolic acidosis is a predictable consequence of intraoperative infusion of 0.9% saline. Anesthesiology 1999; 90: 1243–1254.


