
Fluid therapy for the surgical patient

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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.

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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.^{1–3} 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^{4,5}, to hamper gut motility^{6,7}, and to decrease subcutaneous oxygen tension.⁸ Pulmonary oedema has been described as a consequence of fluid overload^{9,10}, even in patients without pre-existing cardiac disease.^{11–15} Associations have been shown between intra-operative fluid overload and complications^{16–19} as well as mortality following major surgical procedures²⁰, and recently clinical randomised trials have shown fluid overload to cause a poor outcome following gastrointestinal surgery.^{7,11} 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.^{6,21–23}

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.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.²⁵ Patients are allowed to drink until 2 hours before elective surgery and should therefore be well hydrated.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^{27,28}, increases well-being²⁹, and improves postoperative muscle strength.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 recovery³¹, but the other trial could not confirm this.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 vasodilatation 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.^{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 intestines³⁵.

- 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 minutes³⁵, and wrapping the exteriorised viscera in plastic reduces the evaporation loss by 87.5%.³⁶ 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.^{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.³⁸ 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.³⁹ This phenomenon was first described in 1960 in a trial of dogs subjected to haemorrhagic shock⁴⁰; 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.⁴¹ The severity of the trauma seemed to correlate with the ECV lost⁴², 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.^{43–46} Sequestration in the intestinal lumen was suggested, but this hypothesis was later rejected.⁴⁷ 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.^{48,49}

A systematic review of the literature concerning measurements of ECV changes in surgery or haemorrhagic shock reveals that only trials utilizing the SO³⁵ tracer and a very short equilibration time (20–30 minutes) have demonstrated this non-anatomical third space loss.²⁴ 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.^{43–86} 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.^{44,46,54–56,73–76}

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^{46,78,87,88} and all other methods of measurement contradict the finding. Nevertheless, the loss to the third space is replaced according to algorithms.^{39,89,90} Volumes up to 15 mL/kg/hour are recommended in the first hour of abdominal surgery, with decreasing volumes in subsequent hours.⁹⁰

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 crystalloids 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 investigations^{93–95} 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 I. 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 I, 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.

Authors	Surgery	Number of patients	Intervention	Preoperative fluid	Intraoperative fluid	Postoperative fluid	Results
Sinclair et al, 1997	Orthopaedic surgery	40 in two groups	HES to maximal SV evaluated by ED	Unknown	1475 mL (ED) versus 1000 mL	Unknown	Hospital stay shorter in the intervention group No difference for complications Mortality: 1 in intervention group, 2 in control group
Mythen et al, 1999	Thoracic surgery	60 in two groups	HES to maximal SV evaluated by ED	Unknown	2100 mL (ED) versus 1800 mL	Unknown	More patients with complications in the control group (6 versus 0) Mortality: 1 in the control group
Venn et al, 2002	Orthopaedic surgery	90 in three groups	HES to maximal SV evaluated by ED or CVP	2051 mL (ED) 1850 (CVP) 2000 mL	2300 mL (ED) versus 2300 (CVP) versus 1700 mL	Volumes include fluid given in the recovery room. Unknown on the surgical ward	Hospital stay shorter in the intervention group No difference in complications Mortality: 9 in the intervention groups and 2 in the control group
Conway et al, 2002	Abdominal surgery	57 in two groups	HES to maximal SV evaluated by ED	Unknown	4522 mL (ED) versus 3864 mL	Unknown	No differences for complications or hospital stay Mortality: 1 in the control group
Gan et al, 2002	General, urological or gynaecological surgery	100 in two groups	HES to maximal SV evaluated by ED	Unknown	5252 mL (ED) versus 4657 mL	Unknown	Hospital stay shorter in the intervention group No difference for complications Mortality not reported

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.^{6,7} 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.¹¹² One trial was excluded due to methodological problems¹⁰⁸, but two trials were included in the meta-analysis.^{109,110} 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'.^{113–123} Even though fluid therapy was the first treatment of choice, the fluid volume administered is described in only four trials.^{113,115,116,122}

In the trial by Wilson and colleagues¹²², 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 colleagues¹¹⁶ 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 colleagues¹¹³, 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 1348 mL (intervention versus control: 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 colleagues¹¹⁵, 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 administration¹¹⁵, blinding of outcome measures was not attempted, and the patients were not followed after discharge in any of the trials.

Sandham and colleagues¹¹⁹ 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.¹²⁵

We therefore designed a clinical randomised assessor-blinded multi-centre trial to answer the following questions¹¹:

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 ($P < 0.01$).¹²⁶ 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.¹²⁶

The results of our trial confirm the results of Lobo and colleagues⁶ 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.⁷ 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).^{31,32,127–133} 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^{31,127–131,133}, and in three of the trials postoperative nausea was less in the groups receiving fluid.^{128,130,131} The volume

Table 2. Trials of outpatient surgery.								
Author	Surgery	Number of patients	Blinding	Duration of surgery (minutes)	Intervention	Fast (hours)	Postoperative oral fluid intake	Results
Keane and Murray, 1986	Mixed outpatient surgery	212 in two groups	No	18	1000 mL Hartman's solution + 1000 mL DW versus no fluid	?	?	Fluid reduces thirst, drowsiness and increases well-being No effect on nausea
Spencer, 1988	Minor gynaecological surgery	100 in two groups	No	8	1 L CSL versus no fluid	?	?	Fluid reduces dizziness and nausea
Cook et al, 1990	Gynaecological laparoscopy	75 in three groups	Yes	20	CSL 20 mL/kg versus CSL + DW 20 mL/kg versus no fluid	11–16	?	Fluid reduces dizziness and drowsiness Hospital stay reduced in dextrose group
Yogendran et al, 1995	Mixed outpatient surgery	200 in two groups	Yes	28	Plasmolyte 20 mL/kg (1215 mL) versus plasmolyte 2 mL/kg (164 mL)	8–13	?	Fluid reduces thirst, dizziness and drowsiness No effect on nausea
Elkahim et al, 1998	Day case termination of pregnancy	100 in two groups	Yes	12	1 L CSL versus no fluid	9.66	1.5–2	Fluid reduces nausea and vomiting
Bennet et al, 1999	Dent-alveolar surgery	90 in two groups	Yes	?	NS 16 mL/kg versus NS 1 mL/kg	8–13	?	Fluid reduces dizziness and drowsiness No effect on nausea
McCaul et al, 2003	Gynaecological laparoscopy	108 in three groups	Yes	22	CSL 1.5 mL/kg/feeding hour (1115 mL) versus CSL + DW 1.5 mL/kg/feeding hour (1148 mL) versus no fluid	11.5	?	No significant differences between the groups

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Table 2 (continued)

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

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 have 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.^{1,32} 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 ($P=0.01$) 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

1. Scheingraber S, Rehm M, Sehmisch C & Finsterer U. Rapid saline infusion produces hyperchloremic acidosis in patients undergoing gynaecologic surgery. *Anesthesiology* 1999; **90**: 1265–1270.
2. Waters JH, Miller LR, Clalk S & Kim JV. Cause of metabolic acidosis in prolonged surgery. *Crit Care Med* 1999; **27**: 2142–2146.
3. Prough DS & Bidani A. Hyperchloremic metabolic acidosis is a predictable consequence of intraoperative infusion of 0.9% saline. *Anesthesiology* 1999; **90**: 1243–1254.
4. Collins JV, Cochrane GM, Davis J et al. Some aspects of pulmonary function after rapid saline infusion in healthy subjects. *Clin Sci Mol Med* 1973; **45**: 407–410.
5. Holte K, Jensen P & Kehlet H. Physiologic effects of intravenous fluid administration in healthy volunteers. *Anesth Analg* 2003; **96**: 1504–1509.

6. Lobo DN, Bostock KA, Neal KR et al. Effect of salt and water balance on recovery of gastrointestinal function after elective colonic resection: a randomised controlled trial. *Lancet* 2002; **359**: 1812–1818.
7. Nisanevich V, Felsenstein I, Almogy G et al. Effect of intraoperative fluid management on outcome after intra-abdominal surgery. *Anesthesiology* 2005; **103**: 25–32.
8. Lang K, Boldt J, Suttner S & Haisch G. Colloids versus crystalloids and tissue oxygen tension in patients undergoing major abdominal surgery. *Anesth Analg* 2001; **93**: 405–409.
9. Cooperman LH & Price HL. Pulmonary edema in the operative and postoperative period: a review of 40 cases. *Ann Surg* 1970; **172**: 883–891.
10. Stein L, Beraud J, Morissette M et al. Pulmonary edema during volume infusion. *Circulation* 1975; **52**: 483–489.
11. Brandstrup B, Tønnesen H, Beier-Holgersen R et al. The danish study group on perioperative fluid therapy. Effects of intravenous fluid restriction on postoperative complications: comparison of two perioperative fluid regimens. A randomized assessor blinded multi centre trial. *Ann Surg* 2003; **238**: 641–648.
12. Arief Al. Fatal postoperative pulmonary edema. Pathogenesis and literature review. *Chest* 1999; **115**: 1371–1377.
13. Mills M. The clinical syndrome. *J Trauma* 1968; **8**: 651–655.
14. Simmons RL, Heisterkamp III. CA, Moseley RV & Doty DB. Post resuscitative blood volumes in combat casualties. *Surg Gynecol Obstet* 1969; **128**: 1193–1201.
15. Stein L, Beraud J, Cavanilles J et al. Pulmonary edema during fluid infusion in the absence of heart failure. *J Am Med Assoc* 1974; **229**: 65–68.
16. Bennett-Guerrero E, Feerman DE, Barclay GR et al. Preoperative and intraoperative predictors of postoperative morbidity, poor graft function, and early rejection in 190 patients undergoing liver transplantation. *Arch Surg* 2001; **136**: 1177–1183.
17. Calligaro KD, Azurin DJ, Dougherty MJ et al. Pulmonary risk factors of elective abdominal aortic surgery. *J Vasc Surg* 1993; **18**: 914–920.
18. Møller AM, Pedersen T, Svendsen P-E & Engquist A. Perioperative risk factors in elective pneumonectomy: the impact of excess fluid balance. *Eur J Anaesth* 2002; **19**: 57–62.
19. Patel RL, Townsend ER & Fountain SW. Elective pneumonectomy: factors associated with morbidity and operative mortality. *Ann Thorac Surg* 1992; **54**: 88.
20. Lowell JA, Schifferdecker C, Driscoll DF et al. Postoperative fluid overload: not a benign problem. *Crit Care Med* 1990; **18**: 728–733.
21. Perco MJ, Jarnvig I, Højgaard-Rasmussen N et al. Electric impedance for evaluation of body fluid balance in cardiac surgical patients. *J Cardiothorac Vasc Anesth* 2001; **15**: 44–48.
22. Sun X, Iles M & Weissman C. Physiologic variables and fluid resuscitation in the postoperative intensive care unit patient. *Crit Care Med* 1993; **21**: 555–561.
23. Rasmussen LA, Rosenberg J, Crawford ME & Kehlet H. Perioperativ væskebehandling en kvalitetsundersøgelse. *Ugeskr Laeger* 1996; **158**: 5286–5290.
24. Brandstrup B, Svendsen C, Engquist A. Hemorrhage and surgery cause a contraction of the extra cellular space needing replacement—evidence and implications. A systematic review. *Surgery*; in press.
25. Reithner L, Johansson H & Strouth L. Insensible perspiration during anaesthesia and surgery. *Acta Anaesthesiol Scand* 1980; **24**: 362–366.
26. A report by the American society of anesthesiologists task force on preoperative fasting, practice guidelines for preoperative fasting and the use of pharmacologic agents to reduce the risk of pulmonary aspiration: application to healthy patients undergoing elective procedures. *Anesthesiology* 1999; **90**: p. 896–905.
27. Ljungqvist O, Thorell A, Gutniak M et al. Glucose infusion in stead of preoperative fasting reduces postoperative insulin resistance. *J Am Coll Surg* 1994; **178**: 329–336.
28. Nygren J, Soop M, Thorell A et al. Preoperative oral carbohydrates and postoperative insulinresistance. *Clin Nutr* 1999; **18**: 117–120.
29. Hausel J, Nygren J, Almström C et al. Perioperative oral carbohydrate improve well being after elektive colorectal surgery. *Clin Nutr* 1999; **18**(supplement 1): 21.
30. Henriksen MG. Effects of preoperative oral carbohydrates and peptides on postoperative endocrine response, mobilization, nutrition and muscle function in abdominal surgery. *Acta Anaesthesiol Scand* 2003; **47**: 191–199.

31. Cook R, Anderson S, Riseborough M & Blogg CE. Intravenous fluid load and recovery. A double-blind comparison in gynaecological patients who had day-case laparoscopy. *Anaesthesia* 1990; **45**: 826–830.
32. McCaul C, Moran C, O’Cronin D et al. Intravenous fluid loading with or without supplementary dextrose does not prevent nausea, vomiting and pain after laparoscopy. *Can J Anaesth* 2003; **5**: 440–444.
33. Alpert RA, Roizen MF, Hamilton WVK et al. Intraoperative urinary output does not predict postoperative renal function in patients undergoing abdominal aortic revascularization. *Surgery* 1984; **95**: 707–711.
34. Priano LL, Smith JD, Cohen JJ & Everts EE. Intravenous fluid administration and urine output during radical neck surgery. *Head Neck* 1993; **15**: 208–215.
35. Lamke LO, Nielsson GE & Reithner HL. Water loss by evaporation from the abdominal cavity during surgery. *Acta Chir Scand* 1977; **143**: 279–284.
36. Roe CF. Effect of bowel exposure on body temperature during surgical operations. *Am J Surg* 1971; **122**: 13–15.
37. Carrico CJ, Canizaro PC & Shires GT. Fluid resuscitation following injury: rationale for the use of balanced salt solutions. *Crit Care Med* 1976; **4**: 46–54.
38. Chan STF, Kapadia CR, Johnson AW et al. Extracellular fluid volume expansion and third space sequestration at the site of small bowel anastomosis. *Br J Surg* 1983; **70**: 36–39.
39. Kaye AD & Grogono AW. Fluid and electrolyte physiology. In Miller RD, Cucchiara RF, Miller ED, Reves JG, Roizen MF & Savarese JJ (eds.) *Anesthesia*. Philadelphia: Churchill Livingstone, 2000, pp. 1606–1607.
40. Shires T, Brown FT, Canizaro PC & Summerville N. Distributional changes in extra cellular fluid during acute hemorrhagic shock. *Surg Forum* 1960; **11**: 115–117.
41. Shires T, Williams J & Brown F. Acute changes in extracellular fluids associated with major surgical procedures. *Ann Surg* 1961; **154**: 803–810.
42. Carrico CJ, Coln CD & Shires GT. Salt administration during surgery. *Surg Forum* 1966; **17**: 59–61.
43. Beall AC, Johnson PC, Shirkey AL et al. Effects of temporary cardiopulmonary bypass on extracellular fluid volume and total body water in man. *Circulation* 1964; **29**: 59–62.
44. Gumpert JRW, Zollinger RM & Moore FD. Extracellular fluid volume changes following major surgery. *Br J Surg* 1968; **55**: 382.
45. Gutelius JR, Shizgal HM & Lopez G. The effect of trauma on extracellular water volume. *Arch Surg* 1968; **97**: 206–214.
46. Kragelund E. Changes of the apparent $^3\text{H}_2\text{O}$, ^{82}Br , ^{125}I human albumin and ^{51}Cr red blood cell dilution volumes before, during and after operation in human subjects. *Ann Surg* 1970; **172**: 116–124.
47. Nielsen OM. Extracellular fluid and colloid osmotic pressure in abdominal vascular surgery. A study of volume changes. *Dan Med Bull* 1991; **38**: 9–21.
48. Anderson RV, James PM, Bredenberg CE et al. Extracellular fluid and plasma volume studies on casualties in The Republic of Viet Nam. *Surg Forum* 1967; **18**: 32–34.
49. Doty DB, Hufnagel HV & Moseley RV. The distribution of body fluids following hemorrhage and resuscitation in combat casualties. *Surg Gynecol Obstet* 1970; **130**: 453–458.
50. Albert SN, Shibuya J, Custeau P et al. A simplified method for measuring the volume of extracellular fluid by radioactive sulphur (^{35}S). *South Med J* 1967; **60**: 933–939.
51. Ariel IM. Metabolic alterations induced by intra-abdominal operations. *Ann Surg* 1953; **138**: 186–202.
52. Aronstam EM, Schmidt CH & Jenkins E. Body fluid shifts, sodium and potassium in patients undergoing thoracic surgical procedures. *Ann Surg* 1953; **137**: 316–324.
53. Bock JC, Barker BC & Clinton AG. Post-traumatic changes in, and effect of colloid osmotic pressure on the distribution of body water. *Ann Surg* 1989; **210**: 395–403.
54. Breckenridge IM, Digerness SB & Kirklin JW. Validity of concept of increased extracellular fluid after open heart surgery. *Surg Forum* 1969; **20**: 53–56.
55. Breckenridge IM, Digerness SB & Kirklin JW. Increased extracellular fluid after open intracardiac operation. *Surg Gynecol Obstet* 1970; **131**: 53–56.
56. Cleland J, Pluth JR, Tauxe WN et al. Blood volume and body fluid compartment changes soon after closed and open intracardiac surgery. *Thorac Cardiovasc Surg* 1966; **52**: 698–705.
57. Cohn LH & Angell WW. Relative extracellular fluid deficits in patients undergoing coronary artery bypass. *Surg Forum* 1971; **22**: 151–152.
58. Crystal RG & Baue AF. Influence of hemorrhagic hypotension on measurements of the extracellular fluid volume. *Surg Gynecol Obstet* 1969; **129**: 576–582.

59. Crystal RG & Baue AF. Effects of nephrectomy and urethral occlusion on extracellular fluid measurements during shock. *Surg Gynecol Obstet* 1970; **131**: 1109–1114.
60. DeGosse JJ, Randall HT, Habif DV & Roberts KE. The mechanism of hyponatremia and hypotonicity after surgical trauma. *Surgery* 1956; **40**: 27–36.
61. Furneaux RW & Tracy GD. The validity of the isotope dilution method of measuring extracellular fluid volume after acute haemorrhage. *Aust J Exp Biol Sci* 1970; **48**: 407–415.
62. Gilder H, Cortese AF, Loehr WJ et al. Dilution studies in experimental hemorrhage and endotoxic shock: a critical look at the excessive deficits in shocked dogs. *Ann Surg* 1970; **171**: 42–50.
63. Hoye RC, Voightlander V, Plantin LO & Birke G. Changes in total circulating albumin, plasma volume and extracellular fluid volume with haemorrhage and the response to hydrocortisone. *Acta Chir Scand* 1971; **137**: 299–304.
64. Ladegaard-Pedersen HJ & Engell HC. A comparison between the changes in the distribution volumes of Inulin and ⁵¹Cr-EDTA after major surgery. *Scand J Clin Lab Invest* 1975; **35**: 109–113.
65. Larsson M, Nylander G & Öhman U. Post hemorhagic changes in plasma water and extracellular fluid volumes in rat. *J Trauma* 1981; **21**: 870–877.
66. Lyon RP, Stanton JR, Freis ED & Smithwick RH. Blood and 'available fluid' (thiocyanate) volume studies in surgical patients. Part I. Normal patterns of response of the blood volume, available fluid, protein, chloride and hematocrit in the postoperative surgical patient. *Surg Gynecol Obstet* 1949; **89**: 9–19.
67. McNeill IF, Dixon JP & Moore FD. The effects of haemorrhage and hormones on the partition of body water II. The effects of acute single and multiple haemorrhage and adrenal corticosteroids in the dog. *J Surg Res* 1963; **3**: 332–343.
68. Middleton ES, Mathews R & Shires T. Radio sulphate as a measure of the extracellular fluid in acute hemorrhagic shock. *Ann Surg* 1969; **170**: 174–186.
69. Moore FD, Ball MR & Codding MB. *The Metabolic Response to Surgery*. Illinois: Springfield; 1952.
70. Moore FD, Dagher FJ, Boyden CM et al. Hemorrhage in normal man: I. Distribution and dispersal of saline infusions following acute blood loss: clinical kinetics of blood volume support. *Arch Surg* 1966; **163**: 485–504.
71. Newton WT, Pease HD & Butcher HR. Sodium and sulphate space as a measure of extracellular fluid. *Surg Forum* 1969; **20**: 1–2.
72. Nielsen OM & Engell HC. Extracellular fluid volume and distribution in relation to changes in plasma colloid osmotic pressure after major surgery. *Acta Chir Scand* 1985; **151**: 221–225.
73. Pacifico AD, Digerness S & Kirklin JW. Acute alterations of body composition after open intracardiac operations. *Circulation* 1970; **41**: 331–341.
74. Pluth JR, Cleland J, Meador CK et al. Effect of surgery on volume distribution. Compartments pools and spaces in medical physiology. In Bregner PE, Lusbauch CC & Anderson EB (eds.) *Proceedings of a Symposium Held at the Oak Ridge Institute of Nuclear Studies*. Oak Ridge: US Atomic Energy Commission, USA, 1966, pp. 217–240.
75. Reid DJ, Digerness S & Kirklin JW. Intracellular fluid volume in surgical patients measured by the simultaneous determination of total body water and extracellular fluid. *Surg Forum* 1967; **18**: 29–30.
76. Reid DJ. Intracellular and extracellular fluid volume during surgery. *Br J Surg* 1968; **55**: 596.
77. Roberts JP, Roberts JD, Skinner C et al. Extracellular fluid deficit following operation and its correction with Ringer's lactate. *Ann Surg* 1985; **202**: 1–8.
78. Roth E, Lax LC & Maloney JV. Ringer's lactate solution and extracellular fluid volume in the surgical patient: a critical analysis. *Ann Surg* 1969; **169**: 149–164.
79. Shizgal HM, Lopez GA & Gutelius JR. Extracellular fluid volume changes following hemorrhagic shock. *Surg Forum* 1967; **18**: 35–36.
80. Shizgal HM, Lopez GA & Gutelius JR. Effects of experimental haemorrhagic shock on extracellular water volume. *Ann Surg* 1972; **176**: 736–741.
81. Shizgal HM, Solomon S & Gutelius JR. Body water distribution after operation. *Surg Gynecol Obstet* 1977; **144**: 35–41.
82. Stahl WM. Intraoperative volume support by sodium infusion: an approach to quantitation. *Surg Forum* 1967; **18**: 30–32.
83. Stewart JD & Rourke GM. Changes in blood and intestinal fluid resulting from surgical operation and ether anaesthesia. *J Clin Invest* 1938; **17**: 413–416.
84. Vineyard GC & Osborne DP. Simultaneous determination of extracellular water by ³⁵-sulphate and ⁸²-bromide in dogs, with a note on the acute effects of hypotensive shock. *Surg Forum* 1967; **18**: 37–39.

85. Virgilio RW, Homer LD, Herman CM et al. The effect of hemorrhagic shock on the extracellular fluid space in the nephrectomized baboon. *Ann Surg* 1970; **171**: 261–268.
86. Virtue RW, Levine DS & Aikawa JK. Fluid shifts during the surgical period: RISA and 35S determinations following glucose, saline, or lactate infusions. *Ann Surg* 1966; **163**: 523–528.
87. Anderson RV, Simmons RL, Collins JA et al. Plasma volume and sulphate spaces in acute combat casualties. *Surg Gynecol Obstet* 1969; **128**: 719–724.
88. Kragelund E & Dyrbye MO. Sulphate space in the human organism after intravenous administration of radio sulphate. *Scand J Clin Lab Invest* 1967; **19**: 319–324.
89. Barash PG, Cullen BF & Stoelting RK. *Handbook of Clinical Anesthesia*. Philadelphia, PA: Lippincott, Williams & Wilkins; 1999.
90. Engquist A. *Stress inducerede væske- og elektrolyt forandringer Rationel Væske-Elektrolytbehandling og Ernæring*, 1993. København: Munksgaard; 1993 p. 218–23.
91. Kragelund E. Loss of fluid and blood to the peritoneal cavity during abdominal surgery. *Surgery* 1971; **69**: 284–287.
92. Kleinman W. Spinal, epidural, & caudal blocks. In Morgan Jr. GE, Mikhail MS & Murray MJ (eds.) *Clinical Anesthesiology, International*, 3rd edn. NY, USA: Lange medical books/McGraw-Hill medical publishing division, 2002.
93. Clark RB, Thompson DS & Thompson CH. Prevention of spinal hypotension associated with caesarean section. *Anesthesiology* 1976; **45**: 670–674.
94. Fanelli G, Casati A, Berti M & Rossignoli L. Incidence of hypotension and bradycardia during integrated epidural/general anaesthesia. An epidemiological observational study on 1200 consecutive patients. Italian study group on integrated anaesthesia. *Minerva Anestesiologica* 1998; **64**: 313–319.
95. Wollman SB & Marx GF. Acute hydration for prevention of hypotension of spinal anesthesia in parturients. *Anesthesiology* 1968; **29**: 374–380.
96. Hahn RG. Haemoglobin dilution from epidural-induced hypotension with and without fluid loading. *Acta Anaesthesiol Scand* 1992; **36**: 241–244.
97. Jackson R, Reid JA & Thorburn J. Volume preloading is not essential to prevent spinal-induced hypotension at Caesarean section. *Br J Anaesth* 1995; **75**: 262–265.
98. Kinsella SM, Pirlet M, Mills MS et al. Randomized study of intravenous fluid preload before epidural analgesia during labour. *Br J Anaesth* 2000; **85**: 311–313.
99. Park GE, Hauch MA, Curlin F et al. The effects of varying volumes of crystalloid administration before caesarean delivery on maternal haemodynamics and colloid osmotic pressure. *Anesth Analg* 1996; **83**: 299–303.
100. Rout CC, Rocke DA, Levin J et al. A re-evaluation in the role of crystalloid preload in the prevention of hypotension associated with spinal anesthesia for elective cesarean section. *Anesthesiology* 1993; **79**: 262–269.
101. Hawthorne L, Slaymaker A, Bamber J & Dresner M. Effect of fluid preload on maternal haemodynamics for low-dose epidural analgesia in labour. *Int J Obstet Anesth* 2001; **10**: 312–315.
102. Cheek TG, Samuels P, Miller F et al. Normal saline i.v. fluid load decreases uterine activity in active labour. *Br J Anaesth* 1996; **77**: 632–635.
103. Nishimura N, Kajimoto Y, Kabe T & Sakamoto A. The effect of volume loading during epidural analgesia. *Resuscitation* 1985; **13**: 31–39.
104. Kubli M, Shennan AH, Seed PT & O'Sullivan G. A randomised controlled trial of fluid pre-loading before low dose epidural analgesia for labour. *Int J Obstet Anesth* 2003; **12**: 256–260.
105. Conway DH, Mayall R, Abdul-Latif MS et al. Randomised controlled trial investigating the influence of intravenous fluid titration using oesophageal doppler monitoring during bowel surgery. *Anaesthesia* 2002; **57**: 845–849.
106. Gan TJ, Soppitt A, Maroof M et al. Goal-directed intraoperative fluid administration reduces length of hospital stay after major surgery. *Anesthesiology* 2002; **97**: 820–826.
107. Mythen MG & Webb AR. Perioperative plasma volume expansion reduces the incidence of gut mucosal hypoperfusion during cardiac surgery. *Arch Surg* 1995; **130**: 423–429.
108. Schultz RJ, Whitfield GF, Lamura JJ et al. The role of physiologic monitoring in patients with fractures of the hip. *J Trauma* 1985; **25**: 309–316.
109. Sinclair S, James S & Singer M. Intraoperative intravascular volume optimisation and length of hospital stay after repair of proximal femoral fracture: randomised controlled trial. *Br Med J* 1997; **315**: 909–912.

110. Venn R, Steele A, Richardson P et al. Randomized controlled trial to investigate influence of the fluid challenge on duration of hospital stay and perioperative morbidity in patients with hip fractures. *Br J Anaesth* 2002; **88**: 65–71.
111. Gan TJ, Soppitt A, Maroof M et al. Intraoperative volume expansion guided by esophageal doppler improves postoperative outcome and shortens hospital stay. *Anesthesiology* 1999; **91**: A537.
112. Price J, Sear J, Venn R. Perioperative fluid volume optimization following proximal femoral fracture (cochrane review). The Cochrane Library; 2002.
113. Bender JS, Smith-Meek MA & Jones CE. Routine pulmonary artery catheterization does not reduce morbidity and mortality of elective vascular surgery. Results of a prospective, randomized trial. *Ann Surg* 1997; **226**: 229–236.
114. Berlauck JF, Abrams JH, Gilmour JI et al. Perioperative optimization of cardiovascular hemodynamics improves outcome in peripheral vascular surgery. A prospective randomized trial. *Ann Surg* 1991; **214**: 297.
115. Bonazzi M, Gentile F, Biasi GM et al. Impact of perioperative haemodynamic monitoring on cardiac morbidity after major vascular surgery in low risk patients. A randomised pilot trial. *Eur J Vasc Surg* 2002; **445–451**.
116. Boyd O, Grounds RM & Bennet ED. A randomized clinical trial of the effect of deliberate perioperative increase of oxygen delivery on mortality in high risk surgical patients. *J Am Med Assoc* 1993; **270**: 2699–2707.
117. Lobo SMA, Salgado PF, Castillo VGT et al. Effects of maximizing oxygen delivery on morbidity and mortality in high-risk surgical patients. *Crit Care Med* 2000; **28**: 3396–3404.
118. Pölonen P, Ruokonen E, Hippeläinen M et al. A prospective, randomized study of goal oriented hemodynamic therapy in cardiac surgical patients. *Anesth Analg* 2000; **90**: 1052–1059.
119. Sandham JD, Hull RD, Brant RF et al. A randomized, controlled trial of the use of pulmonary-artery catheters in high-risk surgical patients. *New Engl J Med* 2003; **348**: 5–14.
120. Shoemaker WC, Appel PL & Kram HB. Prospective trial of supranormal values of survivors as therapeutic goals in high risk surgical patients. *Chest* 1987; **94**: 1176–1186.
121. Takala J, Meier-Hellmann A, Edelston J et al. Effect of dopexamine on outcome after major abdominal surgery: a prospective randomized, controlled multicenter study. *Crit Care Med* 2000; **28**: 3417–3423.
122. Wilson J, Woods I, Fawcett J et al. Reducing the risk of major elective surgery: randomised controlled trial of preoperative optimisation of oxygen delivery. *Br Med J* 1999; **318**: 1099–1103.
123. Ziegler DW, Wright JG, Choban PS & Fancbaum L. A prospective randomized trial of preoperative 'optimization' of cardiac function in patients undergoing elective peripheral vascular surgery. *Surgery* 1997; **122**: 584–592.
125. Holte K, Sharrock N & Kehlet H. Pathophysiology and clinical implications of perioperative fluid excess. *Br J Anaesth* 2002; **89**: 622–632.
126. Brandstrup B. Restricted intravenous fluid therapy in colorectal surgery, results of a clinical randomised multi centre trial. University of Copenhagen. 27-6-2003 (Thesis/Dissertation); 2003.
127. Bennett J, McDonald T, Lieblich S & Piecuch J. Perioperative rehydration in ambulatory anesthesia for dent alveolar surgery. *Oral Surg Oral Med Oral Pathol* 1999; **88**: 279–284.
128. Elhakim M, el-Sebiae S, Kaschef N & Essawi GH. Intravenous fluid and postoperative nausea and vomiting after day-case termination of pregnancy. *Acta Anaesthesiol Scand* 1998; **42**: 216–219.
129. Keane PW & Murray PF. Intravenous fluids in minor surgery. Their effect on recovery from anaesthesia. *Anaesthesia* 1986; **41**: 635–637.
130. Spencer EM. Intravenous fluids in minor gynaecological surgery. Their effect on postoperative morbidity. *Anaesthesia* 1988; **43**: 1050–1051.
131. Yogendran S, Asokumar B, Cheng DC & Chung F. A prospective randomized double-blinded study of the effect of intravenous fluid therapy on adverse outcomes on outpatient surgery. *Anesth Analg* 1995; **80**: 682–686.
132. Holte K, Klarskov B, Christensen DS et al. Liberal versus restrictive fluid administration to improve recovery after laparoscopic cholecystectomy—a randomized, double blind study. *Acta Anaesthesiol Scand* 2003; **47**(supplement): 79.
133. Magner JJ, McCaul C, Carton E et al. Effect of intraoperative intravenous crystalloid infusion on postoperative nausea and vomiting after gynaecological laparoscopy: comparison of 30 and 10 mL/kg. *Br J Anaesth* 2004; **93**: 381–385.