Original Article

Renal water conservation determines the increase in body weight after surgery: A randomized, controlled trial

ABSTRACT

Background: The present study was undertaken to identify factors that correlate with the gain in body weight after surgery.

Methods: Twenty-one patients (median age of 49 years) were randomized to receive either Ringer × s acetate or 6% dextran 70 as their first infusion fluid during cholecystectomy or hysterectomy. Each patient's body weight was measured before the surgery and on the first postoperative morning. Blood and urine samples were analyzed for signs of stress, inflammation, and kidney injury. The fluid retention index (FRI), which reflects how strongly the kidneys excrete or retain fluid, was also calculated.

Results: The body weight increased by a median of 0.4 kg in the crystalloid fluid group and by 1.0 kg in the colloid fluid group (maximum 2.5 kg, $P < 0.01$). This difference was due to less urinary excretion after surgery in the colloid group ($P < 0.03$). The increase in body weight did not correlate with the infused fluid volume, the plasma concentrations of C-reactive protein or cortisol, or the urinary excretion of albumin, cortisol, or neutrophil gelatinase-associated lipocalin. However, the body weight increased with the postoperative FRI score ($r = 0.64$; $P < 0.003$) and with the surgery-induced change in FRI score ($r = 0.72$; $P < 0.002$).

Conclusion: How strongly the kidneys excrete or retain fluid, which can be assessed by urine sampling, was the strongest indicator of the increase in body weight during the day of surgery. The amount of fluid alone did not correlate with the gain in body weight.

Key words: C-reactive protein; fluid balance; fluid retention; neutrophil gelatinase-associated lipocalin; surgery

Introduction

An increase in body weight is a common finding after major abdominal surgery. The gain might last for several days and has been attributed to liberal fluid administration.[1] This extra fluid can also impair gastrointestinal recovery[2] and wound healing[3] and if severe, it can increase the incidence of pulmonary edema.[1,4] However, the degree of weight gain after moderate, rather than major, surgery has not been studied. In particular, it is unclear whether the amount and the type of fluid, being crystalloid or colloid, govern the increase in body weight. In this type of surgery, other factors than the amount of infused fluid may also be of importance.

In the present study, we measured the change in body weight before and on the day after surgeries that required only modest amounts of intravenous (i.v.) fluid (1–2 L). Patients were randomized to receive either a crystalloid or a colloid as their first i.v. fluid. Consideration was given to the stress and inflammatory responses to the surgery and how strongly the kidneys excrete the retain fluid, which was analyzed in

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sampled urine.[5-8] The hypothesis was that the increase in body weight correlates with the use of crystalloid fluid, high cortisol excretion, inflammation, and/or renal fluid retention.

Methods

The participants of this prospective, open, controlled clinical trial were 27 patients who underwent an elective surgery under general anesthesia scheduled to last for >30 min at Södertälje Hospital in Södertälje, Sweden, between May 2012 and August 2015 (there was a temporary arrest of recruitment during 2013). The protocol was approved by the Ethics Committee of Stockholm on June 29, 2011 (number 2011657-31/3, Officer in charge: Hans Glaumann), and informed consent was obtained from each case. The study was registered at controlled-trials.com as ISRCTN72860921. Exclusion criteria were age below 18 years, endocrine disorders, kidney disease, dementia, and heart disease that caused physical restraint.

Procedure

The patients arrived at the ward between 7 and 10 a.m. on the day of surgery. They had not ingested solid food since midnight but had been allowed to drink clear fluids up to 2 h before the surgery. Premedication was then given according to the departmental routines and consisted of 1 g of paracetamol, 120 mg of etoricoxib 120 mg (Arcoxia, MSD), 5 mg of oxycodone (OxyNorm, Mundipharma), and 25 mg of meclizine (Postafen, Terali) by mouth.

The patients were randomized by the closed envelope method to receive either Ringer's acetate (Baxter Healthcare) or 6% dextran 70 in isotonic saline (Macrodex, Meda, Sweden) in a proportion of 3:1 as their first perioperative i.v. fluid. Anaphylactic reactions were prevented by always preceding dextran 70 with an i.v. injection of 20 ml of 15% dextran 1 kD (Promiten, Meda).

The randomization scheme included 500 ml of dextran or 1500 ml of Ringer's acetate, but the staff could give less volume if not indicated by clinical needs or continue with a fluid of their own choice if more volume was indicated. The infusion was initiated upon arrival at the operating theater and covered the volume load given during the induction of general anesthesia and during most of the intraoperative period. The original intention had been to randomize patients to crystalloid fluid or hydroxyethyl starch, but the colloid was changed to dextran because the use of starch was abandoned in our hospital when the study was about to begin.

General anesthesia was induced with remifentanil and propofol and intubation facilitated with rocuronium. The anesthesia was maintained using sevoflurane and iterated doses of remifentanil and rocuronium. The arterial pressure was measured with an automatic cuff monitor every 5 min, both during the surgery and in the postoperative care unit.

During surgery, the mean arterial pressure (MAP) and cardiac index were also recorded continuously with a noninvasive hemodynamic monitor (Nexfin, BMEYE, Amsterdam, The Netherlands).[9] These recordings were managed by a research nurse, and the results were not revealed to the clinical staff. One patient undergoing a hysterectomy also received epidural analgesia and two others a transversus abdominis plane block.

On the morning after the surgery, thirst was assessed again using the visual analog scale (VAS) and the body weight was measured on the same electronic scale as before the surgery. Blood samples for the measurement of plasma cortisol and C-reactive protein concentrations were taken, along with notes on surgical complications. The blood samples were analyzed at the certified clinical laboratory at Karolinska University Hospital in Stockholm. One month after the surgery, all patients were interviewed by telephone and notes on late complications were taken.

Urine sampling and analysis

Urine was sampled on three occasions. First, a spot sample was taken when the patients were asked to empty their bladders just before entering the operating theater. Second, the patients voided or else had their bladder emptied with a catheter when leaving the postoperative care unit. Finally, the urine excreted on the surgical ward up to 8 a.m. was collected, measured, and sampled on the next day.

All three urine samples were used to analyze the excretion of albumin, cortisol, and neutrophil gelatinase-associated lipocalin (NGAL), as well as the four components of the fluid retention index (FRI). Albuminuria is a measure of damage to the glycocalyx layer in the glomeruli, cortisol excretion is an index of the glucocorticoid activity, NGAL is an indicator of tubule-interstitial inflammation, and FRI is a 6-graded scale that provides a summary measure of four metabolic waste products that appear in higher concentrations when the kidneys conserve fluid [Table 1].

The urinary albumin and albumin/creatinine ratio were measured in our research laboratory on a DCA Vantage Analyzer (Siemens Healthcare Diagnostics, Tarrytown, NY, USA). The cortisol and NGAL excretions were quantified at the clinical chemistry laboratory at Karolinska University Hospital. The lower limit for detection of NGAL was 35 μg/l, which was set to zero in the calculations.

Table 1: Scheme for calculating the fluid retention index, which is the mean of the fluid retention scores for four urinary markers

Fluid retention score	1	2	3	4	5	6
Color (shade)	1	2	3	4	5	6
Specific gravity	≤1.005	1.010	1.015	1.020	1.025	1.030
Osmolality (mOsmol/kg)	<250	250-450	450-600	600-800	800-1000	>1000
Creatinine (mmol/)	<4	4-7	7-12	12-17	17-25	>25

The FRI is a composite index of four markers that all indicate fluid retention.[5-8] To create this index, urine color was assessed immediately by holding a 10 ml tube of urine next to a color scale, which is available at www.hydrationcheck.com. The urine-specific gravity was measured by Multistix® reagent strips inserted into a Clinitek Status® Analyzer (Siemens Healthcare Diagnostics). The osmolality and the creatinine concentration were measured within 24 h at Karolinska University Hospital. Previous work has found that ranges of each marker correspond to a range of the other three markers.[5] Therefore, each of the four markers (urine color, specific gravity, osmolality, and creatinine) was given a score according to Table 1. The FRI is the mean of these four scores. A detailed description of the FRI concept is given elsewhere.[5]

Body weight, thirst, and fluid balance

The body weight was measured on an electronic scale to the nearest 10 g on arrival to the operating theater and also at 8 a.m. on the first postoperative day. The weight of any resected tissue (median 430 g, $N = 10$) was subtracted from the preoperative weight. On the same occasions, the patients were asked to estimate their thirst on a VAS graded from 0 (no thirst) to 100 (maximum thirst).

The fluid balance was calculated for the same period of time and taken as the sum of the infused and orally ingested fluid minus the sum of blood loss and the urinary excretion.

Complications

On the morning of the first postoperative day and 30 days after surgery, a research nurse interviewed the patient and read the medical records to register postoperative adverse events. This was done by filling in a checklist of 18 complications based on the surveys by Brandstrup *et al*.[1] and Bennett-Guerrero *et al*.[10] The checklist included all complications arising from the respiratory, gastrointestinal, cardiovascular, neurological systems, any pain requiring opiates, and systemic and local infection.

Statistics

The study was powered to detect a difference in the surgery-induced change in body weight depending on infusion fluid, based on the notion that crystalloid fluid can increase the body weight by 4 kg after abdominal surgery.[1] The originally planned number of patients was sixty, but the study was concluded earlier because of slow recruitment and by the recognition that of the futility of trying to demonstrate that the use of colloid fluid versus a crystalloid would result in less of an increase in body weight.

Data were presented as the median and interquartile range. Group comparisons were performed with the Mann-Whitney´s U test and changes analyzed by the Wilcoxon´s matched-pair test. Correlations between parameters were studied by simple linear regression where r = correlation coefficient. $P < 0.05$ was statistically significant.

Results

Six patients from the originally included 27 patients were excluded from the study because of canceled or rescheduled operations or because of practical problems encountered during data collection [Figure 1]. Demographics and the types of surgery for the 21 analyzed patients are shown in Table 2.

The hemodynamic parameters did not differ significantly between the crystalloid and colloid group during the operations, but the colloid group had a smaller urinary excretion during the first postoperative night and a higher plasma cortisol concentration on the first postoperative morning [Table 2].

Body weight, fluid balance, and fluid retention index

The median change in body weight from before surgery to the day after surgery was + 0.7 kg (0.3–1.6), after correction for resected tissue. The lowest and highest values were − 0.7 and + 2.5 kg, respectively.

No significant relationship was apparent between the change in body weight and the postoperative C-reactive protein or serum cortisol concentrations, the cortisol excretion, the amount of fluid infused during the surgery, or the amount of fluid received up to the first postoperative morning. However, the body weight increased more in the colloid group (+1.0 vs. +0.4 kg, $P < 0.01$; [Table 3]).

A statistically significant linear relationship existed between the change in body weight and the FRI score before surgery [Figure 2a] and the FRI score on the first postoperative morning [Figure 2b], as well as the difference between these

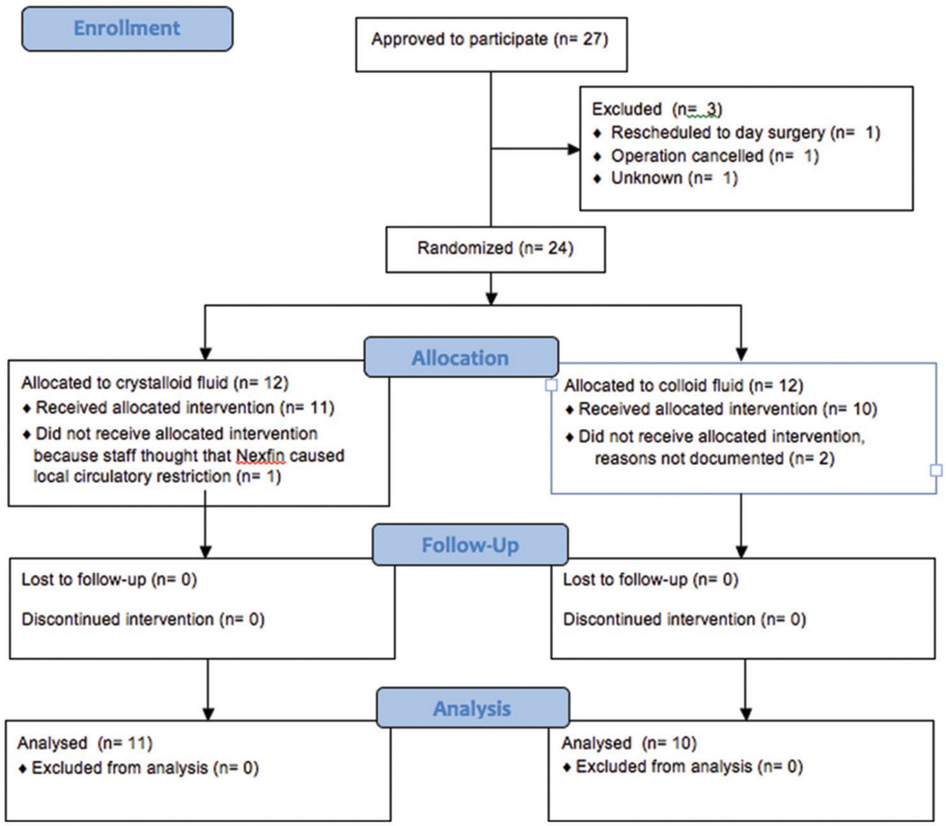

Figure 1: Consort flow diagram for the study

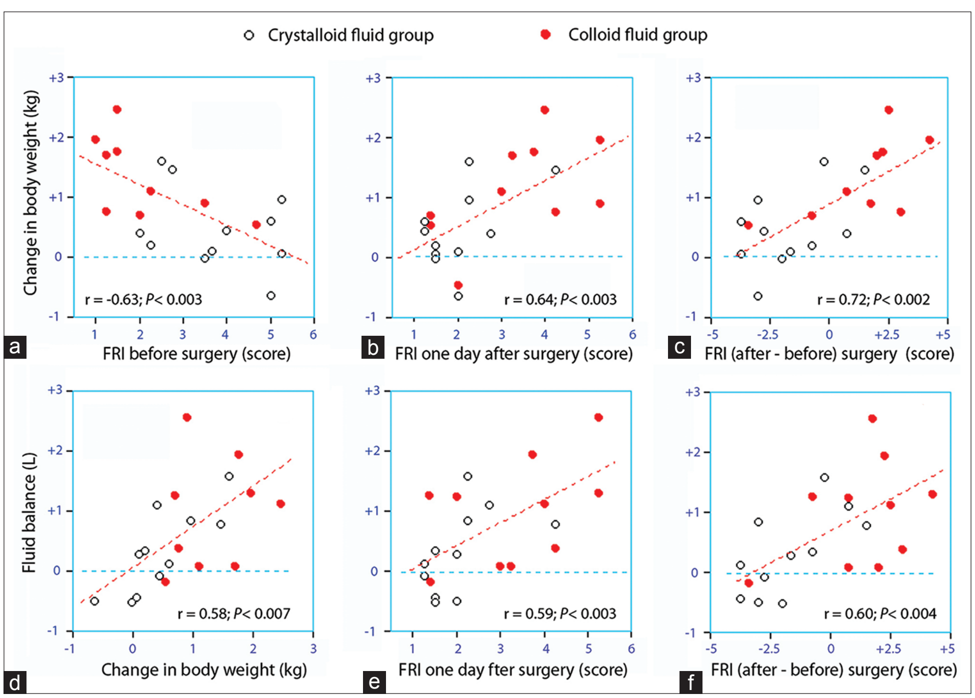

Figure 2: Upper row - The change in body weight from before surgery to the first morning after surgery (after correction for resected tissue) versus (a) the fluid retention index (FRI) before the surgery, (b) fluid retention index in the first morning after the surgery, and (c) the change in fluid retention index from before surgery to the first morning after surgery. Lower row - The fluid balance from before surgery to the first morning after the surgery versus (d) the change in body weight (e) fluid retention index in the first morning after the surgery, and (f) the change in fluid retention index from before surgery to the first morning after surgery

Table 2: Demographics, hemodynamics, and postoperative complications

	Crystalloid group	Colloid group
n	11	10
Females/males (*n*)	10/1	10/0
Age (years)	50 (36-59)	48 (45-51)
Body weight (kg)	72 (59-79)	64 (62-69)
Morbidity (*n*)		
Hypertension	2	1
Asthma	1	0
Depression	0	1
Type of surgery (*n*)		
Open hysterectomy	3	6
Laparoscopic cholecystectomy	5	2
Ovarian cyst	1	1
Cystocele	1	0
Incisional hernia	1	1
Operating time (min)	70 (56-92)	86 (68-129)
Fluid during surgery, total (ml)	1000 (700-1075)	1300 (1000-1750)
Colloid	0	500 (500-500)
Urinary excretion during surgery (ml)	50 (31-90)	219 (90-300)[a]
Blood loss (only hysterectomies)	175 (75-225)	400 (225-700)
Hemodynamics[b]		
Arterial pressure (mmHg)		
Systolic	103 (96-110)	101 (94-108)
Diastolic	64 (62-71)	60 (57-64)
Mean	78 (69-85)	74 (70-79)
Heart rate (bpm)	63 (58-68)	64 (60-67)
Cardiac index (ml/min/m^2)	2.9 (2.3-3.1)	3.0 (2.7-3.2)
Pulse pressure variation (%)	10 (9-12)	8 (7-12)
Stroke volume variation (%)	8.5 (7.0-11.0)	7.5 (7.0-11.0)
Systolic pressure ≤70 mmHg[c], (*n*)	4	2
Day after surgery		
Postoperative fluid given (ml)	1100 (825-1100)	1275 (600-1500)
Postoperative urine volume (ml)	1400 (912-1813)	700 (375-960)[a]
Complications (*n*)		
Nausea and vomiting	2	6[d]
Pain requiring opiates	2	6[d]
Nasal oxygen needed	3	1

Differences between the groups were not statistically significant except where noted. [a]$P<0.03$, [b]Mean values during surgery, [c]At least one event, [d]$P<0.05$ with the Chi-square test. Data are total number (*n*) or the median (25-75th percentile range)

two FRI scores [Figure 2c]. The volumetric fluid balance also correlated with the gain in body weight [Figure 2d], with the FRI 1 day after surgery [Figure 2e], and with the change in FRI [Figure 2f].

Urinary biomarkers

All patients with an FRI score >4.0 had albuminuria. The albumin excretion increased during the surgical period [$P < 0.003$; Table 3] and the rise correlated with the FRI value in the first postoperative morning ($P < 0.04$) but not with any of the other urinary biomarkers.

Table 3: Biochemical parameters measured before, during, and after moderate surgery

	Crystalloid group	Colloid group
FRI (score)		
Before surgery	3.7 (2.6-5.0)	1.5 (1.3-2.2)[a]
Postoperative unit	2.3 (1.5-3.0)	2.4 (1.5-4.0)
Day after surgery	2.0 (1.5-2.3)	3.5 (2.9-4.3)
Change from before to the day after surgery		
FRI (score)	−2.0 (−3.0-−0.4)	+1.9 (0.8-2.5)[a]
Body weight (kg)	+0.4 (0.1-0.9)	+1.0 (0.7-1.8)[b]
Thirst (VAS score)		
Before surgery	36 (34-58)	24 (18-41)
Day after surgery	46 (15-66)	61 (35-66)
Serum creatinine (μmol/L)		
Before surgery	64 (61-69)	62 (59-68)
After surgery	57 (53-65)	61 (52-64)
Plasma C-reactive protein (mg/l)	5 (4-22)	14 (10-19)
Urinary albumin/creatinine (mg/mmol)		
Before surgery	0.5 (0.1-1.2)	0.0 (0.0-0.6)
Postoperative unit	3.2 (0.4-24.5)	3.9 (1.7-7.5)
Day after surgery	1.6 (0.0-3.5)	2.2 (1.1-6.4)
Serum cortisol (nmol/l), after surgery	23 (20-29)	141 (38-369)[b]
Urine cortisol/creatinine (nmol/mmol)		
Before surgery	23 (18-35)	30 (20-43)
Postoperative unit	14 (2-29)	5 (3-34)
Day after surgery	2 (1-27)	13 (1-50)

Differences between the groups were not statistically significant except where noted. [a]$P<0.01$; [b]$P<0.035$. Data are the median (25-75th percentile range). FRI: Fluid retention index; VAS: Visual analog scale

The albumin excretion during surgery (log-transformed data) increased with lower diastolic ($r = -0.57$; $P < 0.03$) and MAPs ($r = -0.54$; $P < 0.04$). There was also a trend for the FRI score to increase for lower arterial pressures, but these correlations were not statistically significant.

The cortisol excretion before surgery correlated inversely with the FRI score measured at the same time ($r = -0.54$; $P < 0.02$). Overall, the cortisol excretion decreased during the surgery [$P < 0.05$; Table 3] but was relatively higher in the first postoperative morning in those who had undergone hysterectomy ($P < 0.04$).

NGAL was only above the limit of detection in 22% of the urine samples, and the concentrations were most often reduced during the course of surgery. No pattern related to fluid balance or the indices of inflammation and stress was found.

Complications

The colloid group had a higher incidence of postoperative nausea and vomiting, as well as more pain requiring opiates, during the postoperative follow-up [Table 2]. These differences could not be statistically attributed to the increase in body weight or to inequality in the number of hysterectomies between the fluid groups.

The follow-up at 30 days showed that one patient in the crystalloid group had developed deep vein thrombosis and that two patients in the colloid group had suffered from an infection in the surgical wound. One patient from the colloid group developed transient joint pains 4–5 days after the surgery that required treatment with antiphlogistics and a period of absence from work.

Discussion

The increase in body weight occurring during the perioperative period varied from being slightly negative to an increase of 2.5 kg. The gain correlated poorly with the amount of infused fluid, which was unexpected. The use of colloid instead of a crystalloid did not reduce either the perceived need for fluid among the staff or the surgery-induced increase in body weight. The increase was even greater in the colloid group despite the fact that the differences in fluid volumes infused during the surgery matched the blood loss. The fluid volumes given postoperatively were also quite similar in the two groups. Therefore, the greater increase in body weight for those who received the colloid must be explained by their much smaller postoperative urinary excretion (700 ml vs. 1,400 ml; [Table 2]).

The reduced urinary excretion in the colloid group is mirrored by a gradual increase in the FRI score. This urine analysis actually correlated more clearly with the overall increase in body weight than did any of the other biomarkers, and it was even slightly better than a calculation of the fluid balance that included measurement of all excreted urine, as well as the weight of any resected tissue. A perioperative increase in body weight even appeared to be unlikely if the FRI score was low in the first postoperative morning.

Only marginal fluctuations were noted in serum creatinine and urinary NGAL, which suggests that the kidney function was largely unaffected although the kidneys retained fluid. However, a modest increase occurred in the albumin excretion, which is a sign of glomerular glycocalyx damage of inflammatory origin. An infusion of crystalloid fluid in preoperative patients is more readily excreted in the presence of albuminuria[11] after which the FRI probably rises as a counter-response. In the present study, a high FRI was always accompanied by albuminuria, which has a long-term prognostic value in cardiovascular and metabolic disease, such as heart failure, hypertension, and diabetes.[12] The albuminuria was most apparent when the arterial pressure was low during the surgery. However, the albumin excretion was already markedly lower during the first postoperative night, which makes long-term harm unlikely.

More postoperative symptoms occurred in the colloid group, which we could not statistically link to any fluid balance parameter. The perceived thirst tended to increase after the surgery, despite the fact that most patients developed some degree of overhydration. Thirst is difficult to interpret as it is elicited by multiple mechanisms including dry mouth, hyperosmolality, and hypovolemic stress.[13] Therefore, the thirst score is a patient comfort issue more than a useful guide to the state of hydration.

The difference in postoperative urinary excretion between the patients who received crystalloid and colloid fluid is consistent with volunteer experiments showing that the diuretic response is effective following infusion of colloid fluid alone while a subsequently infused crystalloid is poorly excreted,[14] probably due to translocation of colloid molecules to the interstitial fluid space.[15] Our statistical analysis did not support the view that the distribution of hysterectomies between the groups accounted for the higher serum cortisol, and the greater fluid retention in patients randomized to colloid.

An unexpected finding was that a low FRI score before surgery indicated a subsequent large increase in body weight during the surgery [Figure 2a]. This suggests that the renal fluid conservation response to surgery operates in a nonlinear fashion and is most effective when the kidneys are initially set to excrete fluid. The difference between the post- and pre-operative FRI even provided the most linear relationship with the change in body weight. Figure 2c shows that an unchanged FRI corresponds to an average weight gain of approximately 1 kg, while a marked reduction of the FRI score was needed to avoid an increase in body weight.

Urine sampling has previously been used to diagnose dehydration in recreational[5] and elite sports.[16,17] FRI is a recently developed composite index of metabolic waste products that are excreted at a fairly stable rate and therefore appear in higher urinary concentrations when the kidneys retain fluid. Four markers are used to reduce the potentially confounding influences of diet, disease, medication, and occasional outliers on the results. The ranges of agreement between them have been published for participants over the age of 17–69 years.[5] These ranges were assigned a score, where a higher value indicated stronger fluid retention [Table 1]. An index value of ≥4.0 corresponds to the degree of renal water conservation that accompanies dehydration of ≥3% of the body weight.[5]

In hospital care, a high urinary content of metabolic waste products is associated with a greater plasma volume expansion in response to crystalloid fluid[18] and a greater need for fluid optimization before abdominal surgery.[19] In hip fracture surgery, a high preoperative FRI has been associated with a greater rise in NGAL[7] and a greater number of postoperative complications.[20] In acute geriatric care, an admission FRI of ≥4.0 was associated with a higher 30-day mortality.[8] The present study is the first to show that a single postoperative FRI score can be used to indicate weight gain in the perioperative period.

Limitations of the present study include the inclusion of a smaller number of patients than had been originally planned. A perfect match between open and laparoscopic surgeries also could not be achieved. The study was also about to start at a time when the safety of hydroxyethyl starch in the operating theater was in question. Therefore, starch was replaced with dextran 70, which is not widely used internationally. Moreover, colloid fluids should only be used to treat hypovolemia, while we randomized patients to receive this fluid as their first infusion during the surgery, regardless of whether hypovolemia had been diagnosed. Halfway into the study, the marketing of the Nexfin hemodynamic monitor was abandoned and replaced with an updated apparatus, ClearSight, but we continued to use the Nexfin to maintain the integrity of our data collection.

Conclusion

The study suggests that the increase in body weight after surgery of moderate extent is indicated by the FRI score, which is a urine-based analysis of how the kidneys are set to excrete or conserve fluid. The use of a colloid (dextran 70) did not allow a reduction in the amount of fluid infused during surgery. Dextran infusion was followed by less postoperative urinary excretion, a greater increase in body weight, and an increasing FRI score.

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Conflicts of interest
There are no conflicts of interest.

References

1. Brandstrup B, Tønnesen H, Beier-Holgersen R, Hjortsø E, Ørding H, Lindorff-Larsen K, *et al.* Effects of intravenous fluid restriction on postoperative complications: Comparison of two perioperative fluid regimens: A randomized assessor-blinded multicenter trial. Ann Surg 2003;238:641-8.
2. Li Y, He R, Ying X, Hahn RG. Ringer's lactate, but not hydroxyethyl starch, prolongs the food intolerance time after major abdominal surgery; an open-labelled clinical trial. BMC Anesthesiol 2015;15:72.
3. Voldby AW, Brandstrup B. Fluid therapy in the perioperative setting – A clinical review. J Intensive Care 2016;4:27.
4. Arieff AI. Fatal postoperative pulmonary edema: Pathogenesis and literature review. Chest 1999;115:1371-7.
5. Hahn RG, Waldréus N. An aggregate urine analysis tool to detect acute dehydration. Int J Sport Nutr Exerc Metab 2013;23:303-11.
6. Hahn RG, Bahlmann H, Nilsson L. Dehydration and fluid volume kinetics before major open abdominal surgery. Acta Anaesthesiol Scand 2014;58:1258-66.
7. Hahn RG. Renal injury during hip fracture surgery: An exploratory study. Anaesthesiol Intensive Ther 2015;47:284-90.
8. Johnson P, Waldreus N, Hahn RG, Stenström H, Sjöstrand F. Fluid retention index predicts the 30-day mortality in geriatric care. Scand J Clin Lab Invest 2015;75:444-51.
9. Fischer MO, Avram R, Cârjaliu I, Massetti M, Gérard JL, Hanouz JL, *et al.* Non-invasive continuous arterial pressure and cardiac index monitoring with Nexfin after cardiac surgery. Br J Anaesth 2012;109:514-21.
10. Bennett-Guerrero E, Welsby I, Dunn TJ, Young LR, Wahl TA, Diers TL, *et al.* The use of a postoperative morbidity survey to evaluate patients with prolonged hospitalization after routine, moderate-risk, elective surgery. Anesth Analg 1999;89:514-9.
11. Hahn RG. Why crystalloids will do the job in the operating room. Anaesthesiol Intensive Ther 2014;46:342-9.
12. Jackson CE, Solomon SD, Gerstein HC, Zetterstrand S, Olofsson B, Michelson EL, *et al.* Albuminuria in chronic heart failure: Prevalence and prognostic importance. Lancet 2009;374:543-50.
13. Waldréus N, Hahn RG, Engvall J, Skoog J, Ewerman L, Lindenberger M. Thirst response to acute hypovolaemia in healthy women and women prone to vasovagal syncope. Physiol Behav 2013;120:34-9.
14. Hahn RG, Bergek C, Gebäck T, Zdolsek J. Interactions between the volume effects of hydroxyethyl starch 130/0.4 and Ringer´s acetate. Crit Care 2013;17:R104.
15. Hahn RG, Lyons G. The half-life of infusion fluids: An educational review. Eur J Anaesthesiol 2016;33:475-82.
16. Casa DJ, Armstrong LE, Hillman SK, Montain SJ, Reiff RV, Rich BS, *et al.* National athletic trainers' association position statement: Fluid replacement for athletes. J Athl Train 2000;35:212-24.
17. Popowski LA, Oppliger RA, Patrick Lambert G, Johnson RF, Kim Johnson A, Gisolf CV. Blood and urinary measures of hydration status during progressive acute dehydration. Med Sci Sports Exerc 2001;33:747-53.

18. Hahn RG, Isacson MN, Fagerström T, Rosvall J, Nyman CR. Isotonic saline in elderly men: An open-labelled controlled infusion study of electrolyte balance, urine flow and kidney function. Anaesthesia 2016;71:155-62.
19. Li Y, He R, Ying X, Hahn RG. Dehydration, hemodynamics and fluid volume optimization after induction of general anesthesia. Clinics (Sao Paulo) 2014;69:809-16.
20. Ylinenvaara SI, Elisson O, Berg K, Zdolsek JH, Krook H, Hahn RG. Preoperative urine-specific gravity and the incidence of complications after hip fracture surgery: A prospective, observational study. Eur J Anaesthesiol 2014;31:85-90.