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Liberal or restrictive fluid administration in fast-track colonic surgery: a randomized, double-blind study†

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Background. Evidence-based guidelines on optimal perioperative fluid management have not been established, and recent randomized trials in major abdominal surgery suggest that large amounts of fluid may increase morbidity and hospital stay. However, no information is available on detailed functional outcomes or with fast-track surgery. Therefore, we investigated the effects of two regimens of intraoperative fluids with physiological recovery as the primary outcome measure after fast-track colonic surgery.

Methods. In a double-blind study, 32 ASA I–III patients undergoing elective colonic surgery were randomized to 'restrictive' (Group 1) or 'liberal' (Group 2) perioperative fluid administration. Fluid algorithms were based on fixed rates of crystalloid infusions and a standardized volume of colloid. Pulmonary function (spirometry) was the primary outcome measure, with secondary outcomes of exercise capacity (submaximal exercise test), orthostatic tolerance, cardiovascular hormonal responses, postoperative ileus (transit of radio-opaque markers), postoperative nocturnal hypoxaemia, and overall recovery within a well-defined multimodal, fast-track recovery programme. Hospital stay and complications were also noted.

Results. 'Restrictive' (median 1640 ml, range 935–2250 ml) compared with 'liberal' fluid administration (median 5050 ml, range 3563–8050 ml) led to significant improvement in pulmonary function and postoperative hypoxaemia. In contrast, we found significantly reduced concentrations of cardiovascularly active hormones (renin, aldosterone, and angiotensin II) in Group 2. The number of patients with complications was not significantly different between the groups (1 *vs* 6 patients, $P=0.08$).

Conclusions. A 'liberal' fluid regimen led to a transient improvement in pulmonary function and postoperative hypoxaemia but no other differences in all-over physiological recovery compared with a 'restrictive' fluid regimen after fast-track colonic surgery. Since morbidity tended to be increased with the 'restrictive' fluid regimen, future studies should focus on the effect of individualized 'goal-directed' fluid administration strategies rather than fixed fluid amounts on postoperative outcome.

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Perioperative fluid management and its implications for outcome in elective surgery are controversial and there is a large variability in fluid regimens in daily practice.[1–4] In laparoscopic cholecystectomy (medium-size procedure), a recent randomized study found that intraoperative administration of 40 ml kg^{-1} (~3 litre) compared with 15 ml kg^{-1} (~1 litre) Ringer's lactate (RL) reduced the cardiovascular hormonal responses [antidiuretic hormone

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(ADH), aldosterone, and angiotensin II], improved perioperative organ function (pulmonary function, exercise capacity, and balance function), improved recovery (nausea, dizziness, drowsiness, general well-being), and reduced hospital stay.[5] This 'high' fluid volume probably compensated for 'hidden' functional hypovolaemia, presumably caused by insufficient intake of fluid before operation combined with fluid shifts induced by surgery. However, during major surgical procedures with a pronounced surgical stress response inducing larger perioperative fluid shifts, the physiological effects of a given volume of fluid may differ substantially from those seen in minor surgical procedures with smaller perioperative fluid shifts. Four recent randomized clinical trials have assessed liberal *vs* restrictive fluid management in major surgery. In colorectal surgery, >5 *vs* <3 litre fluid on the day of surgery led to significantly more major complications in the patients given the high volume.[4] Similar results occurred in where ~5.9 *vs* ~3.6 litre of fluid led to increased duration of ileus, postoperative complications, and hospital stay after major abdominal surgery.[3] In the largest study, 253 patients undergoing colorectal surgery received ~5.7 *vs* ~3.1 litre of crystalloid up to 2 h after operation, with no differences in wound infection/wound healing (primary outcomes) or hospital stay.[6] In a small study of 20 patients undergoing colonic surgery, gastric emptying and postoperative ileus were prolonged in patients receiving >3 litre water and 150 mmol sodium per day compared with <2 litre water and 75 mmol sodium per day after operation.[7] One of the main problems relating to perioperative fluid administration is the difficulty of adequately assessing normovolaemia, with traditional measurements such as static intravascular pressures being unreliable.[8] Recent randomized studies with individualized fluid therapy (goal-directed fluid therapy) consisting primarily of colloid infusions guided by oesophageal Doppler-derived measurements suggest benefits in the intervention groups who generally received more fluid.[8–13] In two studies of mixed abdominal/colorectal surgery, the intervention group (5–5.5 *vs* 4.5–4.7 litre) had significantly decreased postoperative ileus and a significantly decreased hospital stay.[11 12] In cardiac surgery, plasma volume expansion to achieve maximal ventricular stroke volume, assessed by oesophageal Doppler, led to significantly better perfusion of the gastrointestinal mucosa and a significant decrease in major postoperative complications.[9] In contrast, in 57 patients undergoing bowel surgery, no differences in postoperative ileus and hospital stay were found in the intervention group receiving goal-directed fluid therapy compared with standard fluid infusions (4.5 *vs* 3.7 litre perioperatively).[13] However, none of these studies was of fast-track surgery[14–16] which has implications for perioperative fluid management as patients are allowed to eat and drink freely immediately after operation, thus minimizing the use of postoperative i.v. fluid administration. As a component of fast-track colonic surgery at our institution, intraoperative fluid management has consisted of approximately 1500 ml of saline and 500 ml of colloid, an amount chosen on an empiric basis to avoid perioperative fluid overload.[14]

We therefore performed a randomized, controlled, double-blind trial in 32 consecutive patients undergoing colonic surgery within the concept of fast-track surgery with 'liberal' *vs* 'restrictive' perioperative fluid management. We hypothesized that 'restrictive' fluid administration aiming at maintaining body weight and normovolaemia would result in an improved physiological outcome with pulmonary function (spirometry) as the primary outcome measure and secondary outcome measures of exercise capacity (submaximal exercise test), orthostatic tolerance, cardiovascular hormonal responses, postoperative ileus (transit of radio-opaque markers), postoperative nocturnal hypoxaemia, and overall recovery.

Methods

In a randomized, double-blind trial, we studied 32 consecutive patients undergoing elective colonic surgery (right- and left-side hemicolectomy and sigmoid resections) from January 7, 2003 to September 27, 2004. The regional ethics committee approved the study, and the subjects gave written, informed consent before inclusion.

Exclusion criteria were: age<50 yr, weight>100 kg, or BMI>35, inability to perform the preoperative test programme (except the treadmill test), ASA grade IV, insulin-dependent diabetes, inflammatory bowel disease, no thoracic epidural, severe cardiac (NYHA IV, MI<3 months) or pulmonary insufficiency (FEV_1<1 litre), psychiatric illness (intake of psychiatric medication other than selective serotonin re-uptake inhibitors), and alcohol intake >5 units daily. Planned resections of the transverse colon were not included; however, an intraoperative change of procedure to a transverse colonic resection did not lead to exclusion. During the study period, 103 patients underwent elective colonic surgery (right/left/sigmoid resections). Sixty-one patients did not meet the inclusion criteria (20 patients <50 yr, 15 refused participation, seven were not able to give informed consent due to dementia and 19 fulfilled one or more of the above exclusion criteria). Of the remaining 42 patients, nine were excluded due to unavailability of the investigators, leaving 33 patients for randomization. Exclusion after randomization occurred only if the intraoperative intervention was changed due to unexpected intraoperative findings to a procedure incompatible with a 2-day hospital stay (e.g. creation of a stoma) or turned out to be an unexpected emergency procedure. One patient was excluded after randomization, according to these criteria, as small bowel obstruction was discovered at the start of surgery (unexpected emergency procedure). Another patient was randomized in the place of this excluded patient using a new

number. All other randomized patients completed the study.

The perioperative management followed the principles of 'fast-track' colonic surgery with a planned 2-day hospital stay. These are standard at our institution and have been described in detail elsewhere.[14] Preoperative fluid status was standardized by ensuring that all patients fasted from midnight before the operation and drank 400 ml of a sugary drink, the evening before and on the morning of surgery (PreOp®, Nutricia, Holland—electrolyte contents in 400 ml of PreOp®: 50.4 g carbohydrate, 8.8 mmol sodium, and 12.4 mmol potassium) and all operations were done in the morning. Bowel preparation was not used.[17] On arrival in the operating room, patients were randomized by the sealed envelope method (serially numbered, externally generated, and computer-generated random numbers) to the 'restrictive' or 'liberal' fluid infusion group (Table 1). The randomization code was kept separately and the investigators were blinded to it until the study was completed. Double blinding was achieved by covering the fluid infusion bags with opaque sacks, ensuring blinding of the surgeons, the patients, and the investigators obtaining the data (K.H. and L.V.). The fluid administration was controlled and administered by an anaesthetist (N.B.F. and C.L.) not involved in patient assessments. After stopping the fluid infusion, the fluid bags were discarded and the peripheral venous line capped.

All patients received a standardized combined epidural-general anaesthesia and epidural analgesia for postoperative pain management. Immediately before operation, an epidural catheter was inserted at the T_{7-8} (right-side hemicolectomy) or T_{9-10} (left-side hemicolectomy and sigmoid resection) level and tested with lidocaine 2%, 3 ml with epinephrine 1:200.000 followed by bupivacaine 0.5%, 5+5 ml, and morphine (2 mg <70 yr, 1 mg >70 yr). During surgery, bupivacaine 0.5%, 5 ml was administered every 2 h and a continuous infusion of bupivacaine 0.25% with morphine 0.05 mg ml^{-1} was administered at a fixed rate of 4 ml h^{-1}. After assessment of the epidural blockade, general anaesthesia was induced with remifentanil (0.5 μg $kg^{-1}min^{-1}$), propofol (1.5 mg kg^{-1}), and cisatracurium (0.1 mg kg^{-1}) for tracheal intubation. Anaesthesia was maintained with continuous infusion of propofol (0.3–0.4 ml $kg^{-1}h^{-1}$) and remifentanil (0.5 μg kg^{-1} min^{-1}) (reduced by 25% in patients >70 yr). Ventilation (O_2/air: 1:2) was adjusted to keep end-tidal CO_2 4.5–5.5%. Ephedrine 10 mg i.v.+40 mg i.m. was administered to all patients after induction of general anaesthesia. At the end of surgery, ketorolac (30 mg) and ondansetron (4 mg) were administered i.v. Intraoperative normothermia was maintained with a Bair-Hugger® (Augustine Medical, Eden Praire, MN, USA). Hypotension was treated with ephedrine 10 mg i.v. Patients were monitored continuously intraoperatively with non-invasive arterial pressure and heart rate. Fluid guidelines (Table 1) were followed strictly. Diuretics were not used. All patients were operated or supervised by senior surgeons, according to departmental guidelines. Nasogastric tubes were removed at the end of anaesthesia. The day of the operation was defined as day 0.

After surgery, continuous epidural analgesia with bupivacaine 0.25%+morphine 0.05 mg ml^{-1} was maintained at 4 ml h^{-1} for 48 h. Oral acetaminophen was given (2 g per 12 h) after surgery. Break-through pain was treated with bupivacaine 0.125%, 6 ml epidurally as first choice and celecoxib 200 mg as second choice.

In the recovery room, the personnel were unaware of the fluid regimen. Patients were allowed to drink fluids after surgery to a maximum of 1000 ml on the day of surgery.

On the surgical ward, the bladder catheter was removed after 24 h and the epidural catheter after 48 h; patients were allowed free solid food intake, were subjected to enforced mobilization (minimum of 8 h out of bed per day), and discharge was planned about 48 h after operation (second postoperative day).[14] Discharge criteria were sufficient pain relief on oral analgesics, sufficient oral intake, passage of flatus, and patient acceptance of discharge.

Before operation and at 6, 24, and 48 h after surgery, the patients were weighed in standard hospital clothing, and pulmonary function (FEV_1, FVC, and PEF) was measured with the patient in the sitting position as described earlier.[5]

A submaximal treadmill exercise test was performed on a Quinton Club Track 612 (Bothell, WA, USA) treadmill

Table 1 Protocol of fluid administration and patient management

	Group 1 (restrictive fluid)	**Group 2 (liberal fluid)**
Bowel preparation	Not used	
Before operation	400+400 ml glucose drink the evening before and 2 h before surgery	
Preload (at placement of epidural)	None	10 ml kg^{-1} RL
Fluid protocol during surgery	7 ml kg^{-1} h^{-1} RL first hour	18 ml kg^{-1} h^{-1} RL
	5 ml kg^{-1} h^{-1} RL subsequent hours Voluven®: 7 mg kg^{-1}	Voluven®: 7 mg kg^{-1}
After operation (PACU) on the day of surgery	No i.v. fluids	10 ml kg^{-1} RL
After operation (ward) on the day of surgery	Two protein drinks+600 ml of water=1 litre oral intake. No i.v. fluids on the ward without specific indication (hypotension, systolic pressure<90 mm Hg on two repeated measurements)	
Postoperative day 1	Free solid food intake+four protein drinks. Oral fluid intake aimed at 2–2.5 litre Removal of bladder catheter	
Postoperative day 2	Removal of epidural catheter Free solid food intake Discharge according to departmental guidelines (sufficient pain relief on oral analgesics, sufficient oral intake, passage of flatus, and patient acceptance)	

before operation and 48 h after surgery.[5] A functional exercise test modified from the previously validated 6 min walking test (using 3 min of the 6 min due to the expected limited functional capacity of our patients) was performed before operation, and 24 and 48 h after surgery.[18]

Postoperative hypoxaemia was measured by pulse oximetry (23.00–07.00) on the preoperative, first and second postoperative nights as previously described.[19 20] Outcome measures were mean and minimum Sp_{O_2}, numbers of desaturations (<90% or decrease of 5% from baseline for ≥10 s), time spent with Sp_{O_2}<90%, and heart rate. Data were subsequently downloaded from the monitor, analysed, and reported as median for each patient. All patients were given oxygen 2 litre min^{-1} on the two postoperative nights.

Orthostatic tolerance was measured before, and at 24 and 48 h after surgery by rapidly raising the patient from supine to the vertical position with measurements of systolic and diastolic arterial pressure in the supine position, after 1, 2, 3, 4, and 5 min in the vertical position, and finally after 6 min in the supine position. Clinical orthostatic reaction was also noted.

Immediately before surgery, all patients ingested 20 radio-opaque markers with 100 ml of water. The position of the markers was then determined by abdominal radiography 48 h after surgery[21] dividing the position of the markers into five intestinal sites adjusting for the type of surgery performed. Episodes of vomiting were counted in the study period. Time to flatus and defaecation was noted. Intra-abdominal pressure was measured 6 and 24 h after operation via bladder catheter.[22]

The concentrations of aldosterone, ADH, atrial natriuretic protein (ANP), angiotensin-II, and renin were measured before operation, and 6 and 24 h after operation.[5 23–25]

Balance function was assessed with a 'Basic Balance Master®' system (NeuroCom International Inc., Clackamas, USA) including 15 tests (three static and 12 dynamic) before operation and 24 and 48 h after surgery as previously described and validated.[26]

Self-reported episodes of pain, nausea, vomiting, appetite, general well-being, thirst, headache, dizziness, drowsiness, and fatigue were evaluated with standardized scales as previously described.[5]

Time to discharge, re-admission within 30 days, and complications within 30 days were recorded. Major complications were defined as:

- Cardiovascular: acute myocardial infarction (chest pain, ECG signs, and elevated enzyme levels), angina (symptoms with appropriate ECG changes), arrhythmia (ECG-verified cardiac arrhythmia requiring treatment), and cardiac failure (need for postoperative inotropic treatment).
- Respiratory: pneumonia [temperature >38°C, clinical signs of pneumonia, positive X-ray (two of three criteria)], respiratory failure [mechanical ventilation after operation (re-intubation or mechanical ventilation >24 h after operation)], and pulmonary oedema (clinical and radiological signs and need for treatment).
- Thromboembolic: thrombosis/embolus (clinical signs of thrombosis and positive scintigraphy, bleeding; requiring re-operation).
- Renal: kidney failure (requiring dialysis).
- Infectious: wound infection requiring drainage, anastomotic leakage requiring laparotomy, and wound dehiscence requiring re-operation.

Data were analysed on an intention to treat basis using non-parametric statistical methods. Data are presented as median (range). $P<0.05$ was considered significant. Continuous data were compared with Mann–Whitney's or Wilcoxon's tests. Categorical data were compared using Fisher's exact test. Outcome assessments, including multiple measurements [balance function and visual analogue scales (VAS)], were analysed with summary measures to avoid multiple comparisons [area under the curve (AUC) for VAS values and Friedman's ANOVA for hormone data].

Calculation of sample size was based on the hypothesis that liberal fluid administration may lead to a decrease in pulmonary function.[2] Data on 14 previous patients from our institution[19] found a reduction in pulmonary function (FVC) after colonic surgery by a mean of 17.5% (SD 17) 48 h after operation. We considered a decrease in postoperative pulmonary function from a clinically relevant 17.5% to 35%. With a power to detect a minimal relevant difference (MIREDIF) between the two groups of 80% and a level of significance of 0.05, 16 patients were needed in each group. CONSORT guidelines were followed for the report of this study.

Results

Thirty-two patients were recruited (Table 2). Duration of anaesthesia, surgery, and doses of propofol and remifentanil did not differ between the groups (Table 3). Patients in the restrictive group received 1640 ml (median, range 935–2250 ml) of fluid intraoperatively compared with 5050 ml

Table 2 Patient characteristics

	Restrictive fluid	Liberal fluid	*P*-value
Sex (F/M)	10/6	7/9	0.32
Age (yr)	73.5 (56–87)	76.5 (53–93)	0.25
Weight before operation	73.3 (47–98)	69.7 (49–90)	0.52
BMI (kg m^{-2})	26 (20–33)	24 (20–34)	0.45
ASA class I/II/III	5/3/8	2/5/9	0.74
Preoperative cardiovascular disease (+/−)	7/9	8/8	0.74
Preoperative haemoglobin (mmol $litre^{-1}$)	7.5 (5.6–9.3)	7.6 (5.2–9.5)	0.76
Right/transverse/left resection	7/2/7	11/0/5	0.50
Malign/benign histology	13/3	12/4	1.00

Table 3 Intraoperative data. Data presented as median (range). Composition of RL: Na^+ 130 mmol $litre^{-1}$, K^+ 4 mmol $litre^{-1}$, chloride 109 mmol $litre^{-1}$, lactate 28 mmol $litre^{-1}$, calcium 1.4 mmol $litre^{-1}$. RL, Ringers lactate; PACU, postoperative care unit; HES, hydroxyethyl starch

	Restrictive fluid	Liberal fluid	*P*-value
Duration of surgery (min)	119 (77–198)	121 (88–182)	0.36
Duration of anaesthesia (min)	166 (116–262)	174 (142–228)	0.21
Propofol (mg)	872 (330–1241)	780 (370–1756)	0.72
Remifentanil (mg)	5.90 (2.48–9.31)	5.41 (2.54–9.32)	0.90
Systolic pressure (average)	110 (85–140)	110 (100–150)	0.52
Heart rate (average)	60 (60–80)	60 (50–80)	0.99
Periods of systolic pressure <90 mm Hg (*n*)	1 (0–5)	2 (0–3)	0.64
Systolic pressure <90 mm Hg (min)	10 (0–120)	10 (0–45)	0.96
Ephedrine (total dose mg)	50 (30–95)	50 (10–105)	0.99
Ephedrine (patients requiring 'extra' doses) (+/−)	7/9	9/7	0.51
Intraoperative RL	1140 (580–1500)	3900 (2722–6500)	<0.01
Intraoperative HES	500 (350–750)	500 (341–850)	1.00
RL (PACU)	0 (0–0)	675 (500–900)	<0.01
Total fluid (intraoperatively+PACU)	1640 (935–2250)	5050 (3563–8050)	<0.01
Blood loss	200 (10–980)	305 (0–1600)	0.27
Blood transfusion intraoperatively	0 (0–876)	0 (0–558)	0.78
Blood transfusion PACU	0 (0–600)	0 (0–600)	0.41
Diuresis intraoperatively	700 (200–1700)	1150 (300–3050)	0.01
Time spent in PACU (min)	93 (55–575)	113 (60–450)	0.49
Systolic pressure PACU (average)	115 (100–145)	130 (110–150)	0.06
Heart rate (average)	70 (60–90)	70 (50–90)	0.96

(3563–8050 ml) in the liberal group ($P<0.01$) (Table 3). Fluid guidelines were followed in all patients and no other i.v. fluids were given. There was a significant weight gain in Group 2 compared with Group 1 [1.6 and 0 kg 6 h after operation ($P=0.01$), 2 and −0.2 kg 24 h after operation ($P<0.01$), and 2.9 and 0.8 kg 48 h after operation, respectively ($P<0.01$)]. Intraoperative haemodynamic data did not differ between the groups, although a trend ($P=0.06$) towards lower systolic arterial pressure was seen in the post-anaesthetic care unit (PACU) with restrictive fluid administration (Table 3). Intraoperative urine output was greater in Group 2, but did not differ at 24 h (Tables 3 and 4). Postoperative fluid intake and mobilization did not differ between the groups (Table 4).

Table 4 Postoperative data: physiological recovery

	Restrictive fluid	Liberal fluid	*P*-value
Total oral intake first 24 h after operation	875 (125–1200)	1000 (200–1300)	0.12
Haemoglobin 6 h after operation	8.7 (5.2–8.0)	6.2 (5.4–8.6)	0.34
Haemoglobin 24 h after operation	6.4 (5.3–7.9)	6.4 (5.5–7.9)	0.89
Mobilized (walking) day 1 (no)	13	15	0.6
Mobilized (walking) day 2 (no)	16	16	
3 min walk before operation (m)	202 (203–285)	188 (80–283)	0.67
3 min walk 24 h after operation (m)	0 (0–231)	80 (0–210)	0.34
3 min walk 48 h after operation (m)	111 (0-260)	124 (0–250)	0.81
Exercise capacity before operation (W)	14 (1–75)	14 (1–75)	0.54
Exercise capacity 48 h after operation (W)	4 (0–75)	3 (0–75)	0.75
Diuresis (end op.–24 h after operation)	850 (240–1800)	975 (230–4900)	0.36
Intra-abdominal pressure 6 h postop. (mm Hg)	7 (1–14)	8 (3–20)	0.51
Intra-abdominal pressure 24 h postop. (mm Hg)	7 (2–12)	8 (3–16)	0.21
Flatus (day)	1 (0–5)	1 (0–3)	0.62
Bowel movement (day)	2 (1–5)	2 (1–3)	0.30
Gastrointestinal transit score	210 (100–386)	250 (100–465)	0.32

Pulmonary function did not differ between the groups after operation. There was a significant decrease in FVC and FEV_1 6 h after operation in Group 2 compared with Group 1 (Fig. 1). There was no difference in peak flow (Fig. 1) at any time point between the groups. No differences in exercise capacity (3 min walk and treadmill test) were seen before or after operation between the groups (Table 4).

No differences were seen on pulse oximetry before operation, but, on the second postoperative night, patients

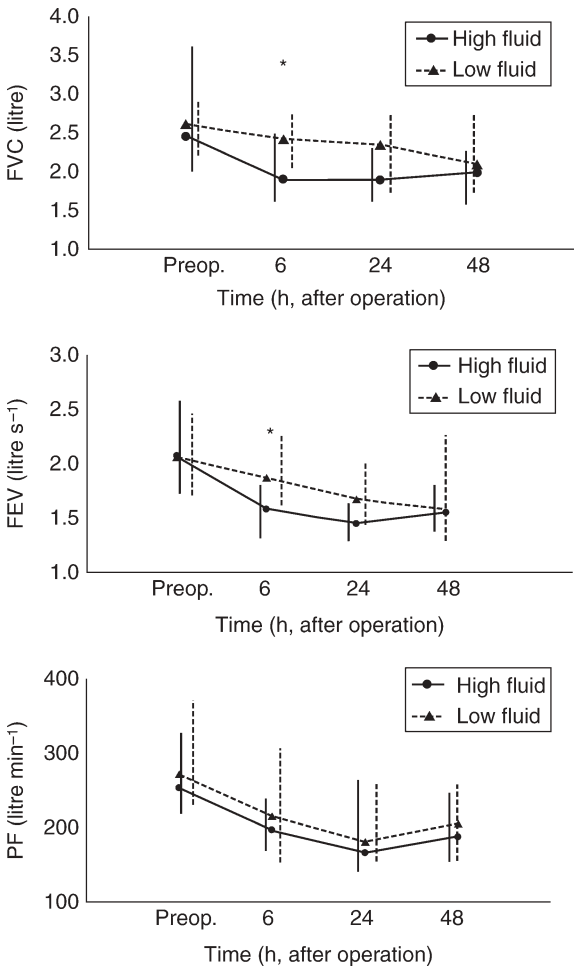

Fig 1 Effect of liberal *vs* restrictive fluid administration on pulmonary function after colonic surgery. FVC, forced vital capacity; FEV_1, forced expiratory volume in 1 s; PF, peak flow. *$P<0.05$, between-group differences from baseline (Mann–Whitney). Median values are presented. Vertical bars represent the 25th–75th quartiles.

in Group 2 had significantly lower Sp_{O_2}, more desaturations, lower minimum oxygen saturation, and longer time spent with a $Sp_{O_2}<90\%$ than patients in Group 1 compared with before operation (Fig. 2). Heart rate did not differ between the groups. No difference in orthostatic tolerance was found between the groups either before or after operation.

The duration of postoperative ileus did not differ between the groups determined either by the radio-opaque markers or by time to defaecation (median 2 days in both groups, Table 4). No difference in intra-abdominal pressure was found between the groups at either 6 or 24 h after operation (Table 4).

There were no significant differences between the plasma concentrations of any of the measured hormones before operation. The significant increase in plasma renin, aldosterone, and angiotensin II in response to surgery in Group 1 was suppressed in Group 2 (Fig. 3), whereas the ANP response was higher (NS) in Group 2 (Fig. 3).

Preoperative balance function did not differ between the groups. Balance function deteriorated significantly at both 24 h (all 15 measurements) and 48 h (11 measurements) after operation, but with no difference between the groups. We found no differences between the groups in pain, nausea, vomiting, appetite, general well-being, thirst, headache, dizziness, drowsiness, or fatigue either before or after operation. Patients were discharged at median day 3 (2–34 in Group 1) *vs* 2.5 (2–9) in Group 2 (NS). There were no differences in the numbers of re-admissions, but total hospital stay was significantly longer in Group 1 *vs* Group 2 [4 (2–39) *vs* 2.5 (2–9) days] ($P=0.03$). Six patients developed a total of 18 complications in Group 1 compared with one patient in Group 2 (Table 5) ($P=0.08$ for patients with complications, $P<0.01$ for total complications).

Discussion

In summary, we found that restrictive (median 1640 ml) compared with liberal fluid administration (median 5050 ml) led to improvements in pulmonary function and postoperative hypoxaemia, whereas no differences in ileus, exercise capacity, or other recovery measures were found. We found a significantly reduced stress response (aldosterone, renin, and angiotensin II) with liberal fluid administration. Our hypothesis was that intraoperative fluid administration leading to perioperative fluid excess (i.e. in excess of normohydration) may adversely affect perioperative organ functions and delay recovery,[2–4 7] and that restriction of intraoperative fluid administration may improve these measures. This hypothesis was not confirmed by our results. We deliberately chose our fluid regimens in order to reflect clinical practice for fluid administration in colonic surgical procedures which varies

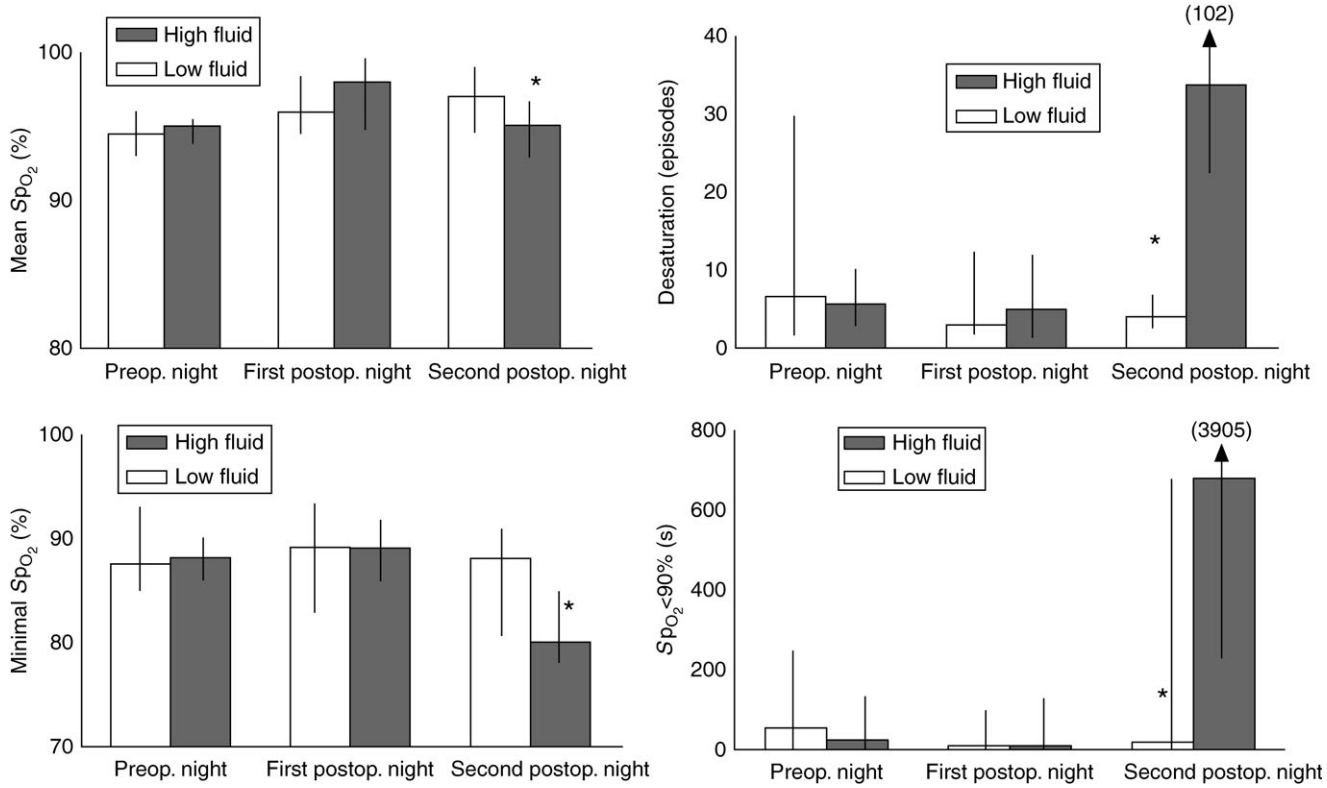

Fig 2 Effect of liberal *vs* restrictive fluid administration on nightly postoperative hypoxaemia after colonic surgery. *$P<0.05$ between the groups, compared with that of the night before operation. Median values are presented. Vertical bars represent the 25th–75th quartiles.

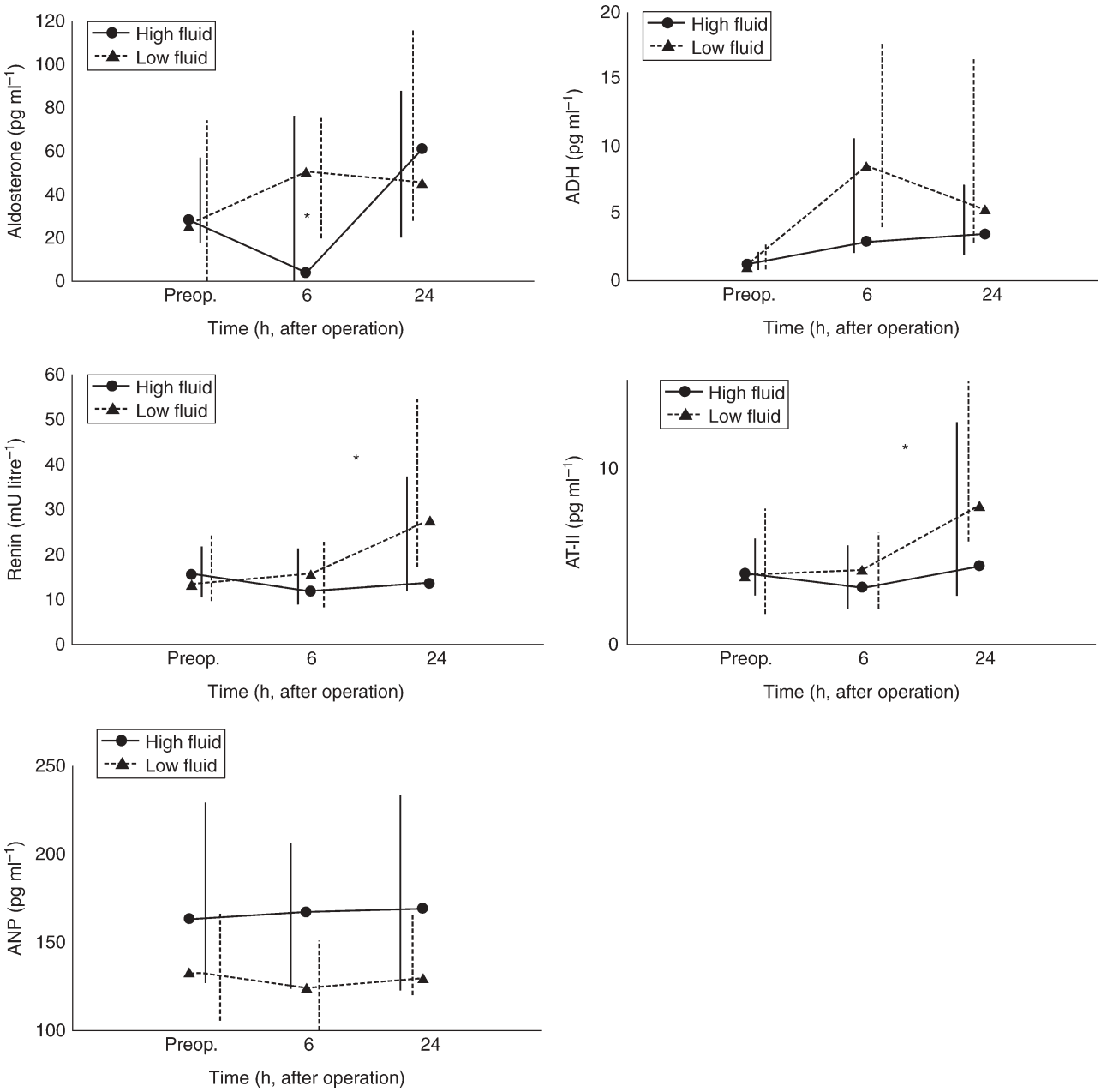

Fig 3 Effect of liberal *vs* restrictive fluid administration on hormonal responses after colonic surgery. *Significant difference ($P<0.05$) between the groups with Friedman's ANOVA. Median values are presented. Vertical bars represent the 25th–75th quartiles.

from 1.5 to 8 litre perioperatively.[3 4 6] In the present smaller study, liberal fluid administration only affected a few organ functions compared with restrictive therapy. Thus, the improvement in pulmonary function with restrictive fluid administration may not be of clinical importance, since it occurs only at 6 h after operation and with no difference between the groups at 24 h. In order to provide a bedside assessment of pulmonary function, we used hand-held spirometry. However, it should be noted that other factors, such as pain, drowsiness, and well-being, may have an effect on the spirometry results and a previous meta-analysis found that pulmonary function testing with spirometry values may not predict postoperative pulmonary complications.[27] The increase in late postoperative hypoxaemia observed in the liberal fluid administration group may not be readily explained since it did not relate to pulmonary function. As described earlier, postoperative nocturnal hypoxaemia is multifactorial,[20] depending on factors such as sleep disturbances and diurnal rhythms, and more detailed evaluation in relation to fluid administration is needed. The trend to more anastomotic leakages [3 *vs* 0 in the restrictive *vs* liberal fluid group (NS)] may question restrictive fluid administration strategies in surgery involving intestinal anastomosis and therefore call

Table 5 Postoperative data: clinical data. LOS, length of stay

	Restrictive fluid	Liberal fluid	*P*-value
Primary LOS (days)	3 (2–34)	2.5 (2–9)	0.52
Number of re-admissions	6	2	0.13
Re-admission (days hospital stay)	0 (0–36)	0 (0–4)	0.20
LOS including re-admission	4 (2–39)	2.5 (2–9)	0.03
Complications			
Cardiovascular			
Arrhythmia	3	0	
Cardiac failure	2	0	
Respiratory			
Respiratory failure	2	0	
Pneumonia	2	1	
Pulmonary oedema	1	0	
Infectious			
Anastomotic leakage	3	0	
Wound dehiscence	1	0	
Wound infection	1	0	
Thromboembolic			
Bleeding	1	0	
Renal failure	2	0	
Total complications	18	1	<0.01
Patients with complications	6	1	0.08

for further studies. Healing of colonic anastomoses has previously been found to be influenced by intestinal tissue oxygen tension,[28] which may decrease with administration of large amounts of crystalloid.[2] However, dehydration, as shown in experimental studies,[29] has adverse effects on anastomotic healing. The trend towards lower systolic pressure in the PACU with restrictive fluid in this study may indicate a lower peripheral perfusion and thus propensity for organ failure. The two incidents of acute renal failure occurred in the patients with anastomotic leakage and may be attributed to the septic condition of these patients. It must be emphasized, however, that the present study was powered to assess organ function and not to assess effects on clinical outcomes such as complications and hospital stay. Thus, the observed trends in increase in total complications need evaluation in larger trials. Furthermore, it must be emphasized that regimens appropriate in major elective surgery may not be transferred to intensive care settings in patients with multi-organ failure.

Our results are similar to those reported recently[30] but with a smaller range between restricted and standard fluid regimen (2 *vs* 3 litre of water and 72 *vs* 154 mmol sodium after operation), although that study did not include a fast-track regimen and only had bowel function and hospital stay as outcomes. What may be the explanations for apparent discrepancies compared with other recent randomized, clinical trials[3 4 6 7] on fluid administration? First, perioperative management and type of surgery were standardized, preoperative fluid status was standardized, the same amounts of colloids were administered, and diuretics were not used. These are all factors that may influence outcome, in particular when fluid administration supposedly is the main intervention. It should be noted that the role of colloids in general (large amounts) for outcome/risk is highly debatable[31–33] and is beyond the scope of our study and therefore not further commented on. Secondly, preoperative dehydration caused by fasting or bowel preparation may lead to functional hypovolaemia but has not been mentioned/standardized in most available studies. Thirdly, recent data have demonstrated that a multimodal revision of principles for postoperative care may improve outcome after major surgical procedures (e.g. fast-track surgery),[14–16] findings which may also have implications for fluid management practices, but not considered in previous fluid studies. It is imperative that perioperative management is standardized in order to determine the 'true' effect of fluid administration. Finally, there is an overlap between fluid volumes administered in the 'high' *vs* 'low' regimen in most of these studies, hindering detailed interpretation.

The major limitation in this study is the relatively small number of patients studied, which may have precluded demonstration of differences in the measured outcomes. The primary outcome was pulmonary function but without major changes, despite improvement with 'restrictive fluid' 6 h after operation. Furthermore, the standardized amounts of fluid administered to both study groups may not be ideal, since some patients may receive too much and other patients too little fluid. It may therefore be more appropriate to individualize fluid administration, preferably guided by flow-oriented as opposed to static measurements of intravascular pressure.[8–12 34]

In summary, we found that despite improvements in pulmonary function and oxygen saturation with a restrictive fluid regimen, overall functional recovery was not dependent on the amount of fluid administered in the fast-track colonic surgery. Since morbidity tended to be increased with the 'restrictive' fluid regimen, future studies should focus on the effect of individualized 'goal-directed' fluid administration strategies rather than fixed fluid amounts on postoperative outcome.

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