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Which goal for fluid therapy during colorectal surgery is followed by the best outcome: near-maximal stroke volume or zero fluid balance?

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Editor's key points

- Optimal fluid therapy during major surgery is the subject of current interest.
- In this trial, goal-directed therapy is compared with zero-balance strategy in a multicentre setting.
- Postoperative mortality and many secondary outcomes were studied.
- Importantly, goal-directed therapy offered no advantage or harm over zero-balance strategy.

Background. We aimed to investigate whether fluid therapy with a goal of near-maximal stroke volume (SV) guided by oesophageal Doppler (ED) monitoring result in a better outcome than that with a goal of maintaining bodyweight (BW) and zero fluid balance in patients undergoing colorectal surgery.

Methods. In a double-blinded clinical multicentre trial, 150 patients undergoing elective colorectal surgery were randomized to receive fluid therapy after either the goal of near-maximal SV guided by ED (Doppler, D group) or the goal of zero balance and normal BW (Zero balance, Z group). Stratification for laparoscopic and open surgery was performed. The postoperative fluid therapy was similar in the two groups. The primary endpoint was postoperative complications defined and divided into subgroups by protocol. Analysis was performed by intention-to-treat. The follow-up was 30 days. The trial had 85% power to show a difference between the groups.

Results. The number of patients undergoing laparoscopic or open surgery and the patient characteristics were similar between the groups. No significant differences between the groups were found for overall, major, minor, cardiopulmonary, or tissue-healing complications (*P*-values: 0.79; 0.62; 0.97; 0.48; and 0.48, respectively). One patient died in each group. No significant difference was found for the length of hospital stay [median (range) Z: 5.00 (1–61) *vs* D: 5.00 (2–41); $P=0.206$].

Conclusions. Goal-directed fluid therapy to near-maximal SV guided by ED adds no extra value to the fluid therapy using zero balance and normal BW in patients undergoing elective colorectal surgery.

Keywords: colorectal surgery; fluid therapy; postoperative complications; surgery

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Hypovolaemia may cause postoperative complications, circulatory collapse, and death. To avoid this, i.v. fluids are given to patients undergoing surgery, and often in amounts greater than the measured fluid losses. However, recent studies have shown that excess fluid causes postoperative complications and increased risk of death after surgery.[1–7] It is therefore important to give the right amount of fluid, but how the right amount is determined is a subject of much controversy.

At present, there are three schools for fluid therapy during major surgery: 'The standard approach', recommends the replacement of fluid losses, including the so-called loss-to-third-space. This is the approach recommended in many text books, and results in a postoperative bodyweight (BW) increase of 3–6 kg.[8 9] Another approach is 'the goal-directed', where fluid boluses are given to reach the near-maximal stroke volume (SV), measured with a Doppler in the oesophagus. This brings the heart to work near the top of the Sarnoff curve (illustrating the Starling relation),[10] and the theoretical benefit is to avoid hypovolaemia and improve oxygen delivery to the tissues.[11–15] This approach may cause an increase in BW, but its magnitude has not been measured in the published trials. Finally is 'the restricted approach', where all measured fluid losses are replaced with a goal of zero fluid balance without the

replacement of the loss-to-third-space. This approach is based on the hypothesis that excess fluid causes interstitial oedema harmful for tissue healing and cardiac and pulmonary function.[1–7]

The standard fluid therapy was developed in the 1960s as a response to circulatory collapse after haemorrhagic shock;[16 17] however, the evidence supporting the very existence of a loss-to-third-space during surgery or shock does not hold for a modern critical analysis.[18] Without a loss-to-third-space, the restricted fluid therapy is not restricted but a zero-balance regimen, and we wish to abandon the term 'restricted' as it has caused much confusion in the literature.[19 20]

Both 'the zero-balance approach' and the 'goal-directed approach' have proven superior to 'the standard approach' in randomized clinical trials; however, the latter two have not previously been tested against each other.[20 21]

The aim of this trial was to test the goal of zero fluid balance against the goal of near-maximal SV measured with a Doppler in the oesophagus on postoperative outcome, that is, the former 'restricted' approach[22] *vs* the current recommendations of Great Britain.[23]

Two hypotheses were tested in subgroup analyses: both hypovolaemia (zero-balance group) and fluid overload (Doppler group) may cause: cardiopulmonary complications due to low oxygen delivery (hypovolaemia), pulmonal/cardiac congestion (overload), compromised wound healing and infection due to low oxygen delivery (hypovolaemia), or interstitial oedema (overload).

Methods

We included 150 patients undergoing elective colorectal surgery in five Danish hospitals in a double-blinded clinical randomized multicentre trial from March 2008 to July 2009. Patients were eligible if they were planned for colorectal resection, could give informed consent, were ASA I–III, and did not have disseminated cancer disease. We excluded the patients who drank more than 5 drinks a day, pregnant or lactating women, or patients who had contraindications for the use of hydroxylethyl starch (HES, Voluven®). The presence of both the investigating anaesthetist and surgeon was mandatory for inclusion, and patients were not screened for eligibility in the absence of any of them. Patients were informed by the surgeon or the anaesthetist before operation and gave both oral and written consent for participation. The trial was approved by the ethical committees of all participating hospitals (ref. no. H-C-2007-0030).

Patients were randomized to either zero-balance (Z group) or Doppler-guided fluid therapy (D group) in the operating theatre by the anaesthetist, so the surgeons and the patients were kept blinded. Block randomization with six patients in each block was performed to ensure an equal number of patients in the two groups from each centre. The randomization sequence was made by Fresenius Kabi and delivered in sealed, opaque consecutively numbered envelopes. The number of patients in each block was kept secret for all the investigators until the concealment was broken at the end of the trial. Stratification was performed for open *vs* laparoscopic surgery, and this simultaneously ensured stratification for the use of epidural analgesia, because epidurals were used only during open surgery.

The blinding of the surgeon was assured by letting the two fluid regimens to appear the same: all patients had a Doppler placed in the oesophagus and was monitored with the CardioQ-ODM™, and all patients had Voluven® and saline/acetated Ringer's solution hanging from the drip.

The anaesthesia and monitoring

The patients were premedicated according to departmental routine. General anaesthesia was induced with thiopental or propofol and fentanyl; rocuronium was used for neuromuscular block. The anaesthesia was maintained with sevoflurane and fentanyl or propofol and remifentanil (Ultiva®). If the patient underwent open surgery, epidural analgesia was used. The epidural catheter was placed at Th8–10, tested with 3–5 ml of bupivacaine or lidocaine, and continuous infusion of bupivacaine 0.5% was given for sufficient block. If the surgery was converted from laparoscopic to open surgery, an epidural was placed after operation. The patients were monitored with ECG, arterial pressure (AP), heart rate (HR), Sp_{O_2}, CO_2, temperature, diuresis, and neuromuscular block.

Immediately after the induction of anaesthesia, all patients had a Doppler placed in the oesophagus for the measurement of the flow in the aorta and the calculation of the SV.

Measurements in the D group were performed every 15 min on demand, and fluid therapy was given as described below. In the Z group, the SV was measured four times during surgery, described later. To avoid bias of the anaesthetist, if SV became low, the CardioQ-ODM-display was covered by carton and the SV were noted by a nurse.

To ensure comparable haemodynamic values in patients receiving open and laparoscopic surgery, the SV was noted at four key time points: after the induction of anaesthesia, at the beginning of surgery, at the removal of the preparation, and at the closing of the abdomen. At these time points, the patients were placed in the horizontal position with the abdomen desufflated, thus avoiding any possible influence of the positioning and the positive abdominal pressure during laparoscopic surgery.

The patients did not receive preoperative oral gut irrigation.

The fluid therapy

All patients were allowed to drink clear fluids until 2 h before surgery.[23 24] The fluid intake was registered from midnight and if $<$500 ml, saline was given during surgery (no specific rate).

In the zero-balance group, a slow infusion of Voluven® was commenced to replace lost blood volume for volume. An extra 500 ml was allowed to maintain the mean AP above 60 mm Hg. Erythrocytes were given to keep the

haematocrit between 25 and 35 depending on age and the presence of cardiac disease. If the blood loss was large, plasma and thrombocytes were added.

In the case of hypotension with suspicion of hypovolaemia, the effect of 200 ml of Voluven® could be tested on AP, HR, and (if needed) central venous pressure. If the hypotension was not caused by hypovolaemia, ephedrine or phenylephrine was given. In case the pressor substances were required for a longer period of time, dopamine was given as continuous infusion.

In the Doppler group, the basic fluid therapy was as above, but in addition 200 ml boluses of Voluven® were given until the increase in SV was $<$10% (Fig. 1). The optimization was done after induction of anaesthesia, and the obtained SV was intended to be maintained throughout the operation.

During laparoscopic surgery, the patient could change the position. To avoid fluid overload during anti-Trendelenburg position, the SV after the change was measured and intended maintained until the patient returned to the horizontal position.

In the case of hypotension despite Doppler-guided volume therapy, pressor substances were given as above.

Prophylactic antibiotics were given to all patients: four centres used metronidazol and cefuroxim, and one centre used metronidazol and gentamicin.

All patients entered a multimodal fast-track programme with early mobilization and feeding.

Postoperative fluid therapy was the same in the two groups: oral intake (both fluid and nutrition) was encouraged when the patient could swallow safely. Was oral fluid intake insufficient ($<$2 litre day^{-1}), i.v. fluid was given to supplement the daily needs for water, glucose, potassium, and sodium. Any pathological fluid losses were replaced with fluid containing electrolytes resembling the loss. Parenteral nutrition was commenced if the patient did not eat sufficiently for 2–3 days and the condition seemed to continue.

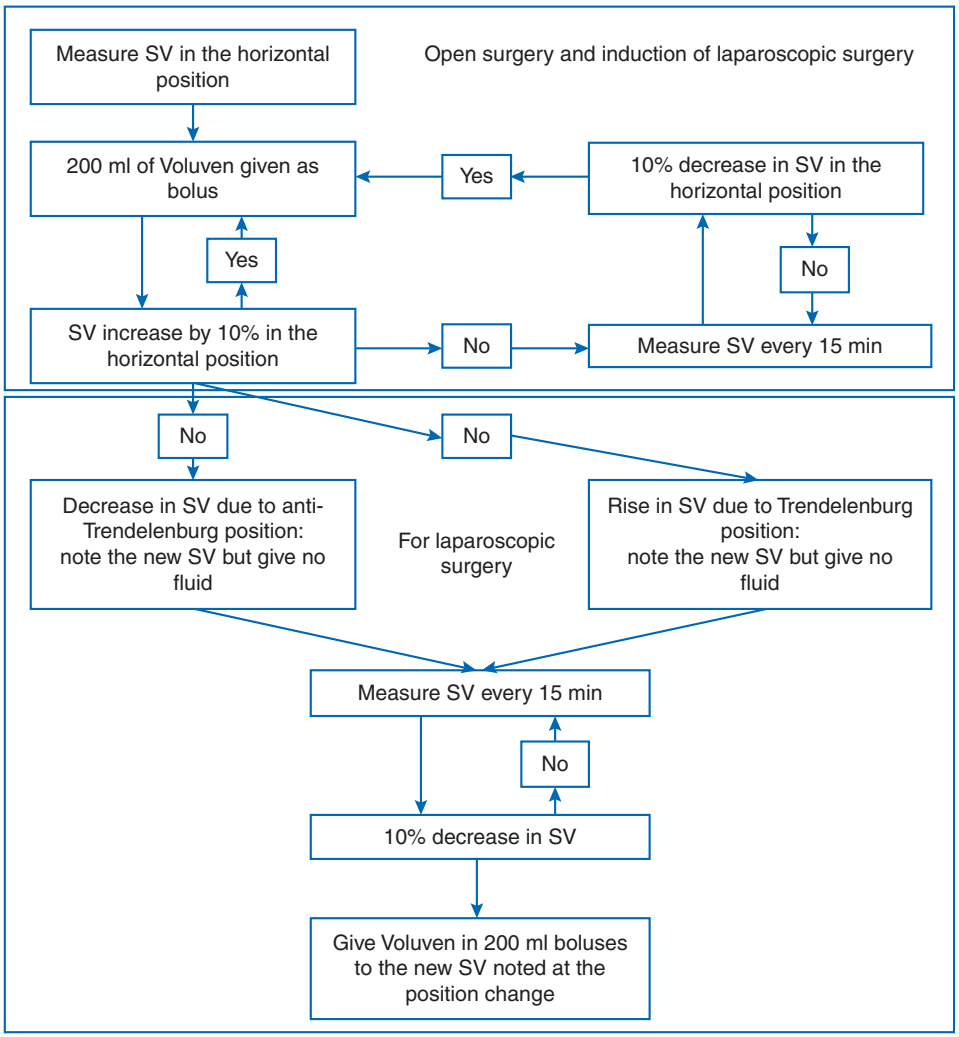

Fig 1 Diagram of the optimization with colloid in the Doppler group.

Diuresis was intended >0.5 ml kg^{-1} h^{-1}, and any case of low diuresis or hypotension led to the examination of the patient. Hypovolaemia was treated with fluid and in case of doubt, the effect of a fluid-bolus was tested. Vasodilatation (due to epidural analgesia or antihypertensive medication) was treated with adjustment of the dose given or in the recovery room with ephedrine. Low diuresis without hypotension or hypovolaemia was treated with furosemide.

BW was measured every morning, and more than 2 kg increase initiated the examination of the patient. Fluid overload was treated with furosemide and additional i.v. fluid was discontinued; intestinal paralysis was treated with a gastric tube or with medicine.

Pain after open surgery was treated with epidural analgesia for a maximum of 4 days, and supplemented with paracetamol, non-steroidal anti-inflammatory drug, or morphine as needed. Nausea was treated with ondansetron, metoclopramide, cisapride, or DHB.

Primary outcome measures were postoperative complications and mortality combined. As per protocol, a complication was recorded if clinical treatment was necessary and given diagnostic criteria were fulfilled (Table 3). The complications included in subgroup analyses are shown in Table 3. Major complications were defined as the life-threatening complications, including reoperations or transfer to the intensive care unit (ICU).

Secondary outcome parameters were the length of hospital stay (LOS), the need for antiemetic or diuretic treatment, and physiological changes [SV, cardiac output (CO), HR, AP, and the need for pressor substances].

The patients were seen by the surgeon every day and any complication was documented and treated.

The patient was contacted by telephone or seen in the outpatient clinic 30 days after surgery. The telephone interview was sufficient because the demanded documentation for a complication required contact with a hospital.

The number of patients included in the trial was calculated to show a 20% difference in complications between the groups, at a significance level of 0.05 and a power of 0.85. The overall complication frequency used for calculation was 30%. The analysis was by intention-to-treat. Frequencies were analysed by Fisher's exact test, if the number was $\leq$8; larger numbers were analysed by the χ^2 test. The physiological data were analysed by the *t*-test for independent and paired samples, if continuous and normally distributed and with the Mann–Whitney *U*-test, if discontinuous or not normally distributed. To avoid mass significance, the order of the analysis was determined to be: mortality, overall complications, complication subgroup analysis, and the physiological data. All *P*-values reported are two-tailed, and SPSS 8.0 software was used.

Results

One-hundred and seventy-three patients fulfilled the inclusion criteria, and 151 were randomized (Fig. 2). One patient was randomized to the Doppler group, but became unstable during the induction of anaesthesia, and the planned surgery was cancelled. He died of cardiac disease 2 weeks later without having the planned surgery. The decision of excluding this patient from analysis was made before the concealment was broken.[25 26] No patient withdrew their consent.

No differences between the groups were found for basic data (Table 1), diagnosis, or surgical data (Supplementary Table S1). The stratification towards open *vs* laparoscopic surgery worked well (Supplementary Table S1).

No significant differences in outcome were found between the groups (Tables 2 and 3). One patient died in each group. Two of the three cardiopulmonary complications in the Z group and three of the five in the D group occurred after a second surgical procedure.

The ASA score predicted the risk of complications, but the Doppler optimization did not improve the outcome for the ASA III risk patients (Supplementary Table S2). The surgical method and hence the use of epidurals did not influence the result (Supplementary Table S3).

No significant difference in LOS was found between the groups:

Ready for discharge [median (range) Z: 5.00 (1–61) *vs* D: 5.00 (2–41); $P=0.206$; mean (SD) Z: 6.72 (8.0) *vs* D: 8.04 (7.3); $P=0.293$].

Actually discharged [median (range) Z: 6.0 (2–61) *vs* D: 5.00 (2–42); $P=0.620$; mean (SD) Z: 7.66 (8.2) *vs* D 8.45 (7.5); $P=0.539$].

Significantly more fluid was given to the patients in the D group during surgery due to the extra Voluven® given for optimization (Supplementary Table S3). No significant differences were found for preoperative oral intake or preoperative i.v. fluid, or after operation in the recovery room, on the surgical ward, or on postoperative days 1–5 for i.v. fluid, but the patients in the Doppler group drank less on postoperative day 5.

The BW in the D group increased significantly from preoperative to postoperative days 1–4 ($P=0.006$; 0.001; 0.027; and 0.032, respectively), while the only significant BW increase in the Z group was on postoperative day 3 ($P=0.004$) (Supplementary Fig. S1). The mean BW increase was in the Z group <1 kg at all times, while it was 1.1 kg in the D group on the third postoperative day. There was no significant difference in BW between the groups.

The SV increased significantly from the induction of anaesthesia to the beginning of surgery in the D group ($P<0.0005$) and stayed significantly higher throughout surgery (Supplementary Fig. S2). After the optimization, the SV was significantly higher in the D group compared with the Z group ($P=0.042$). The SV did not change significantly in the Z group.

The HR decreased temporarily in both groups from the induction of anaesthesia to the incision of the skin but returned to normal, causing the CO to increase significantly at all measure points in the D group. Thus, the CO stayed high throughout surgery in the D group, while it decreased non-significantly in the Z group (Supplementary Fig. S2).

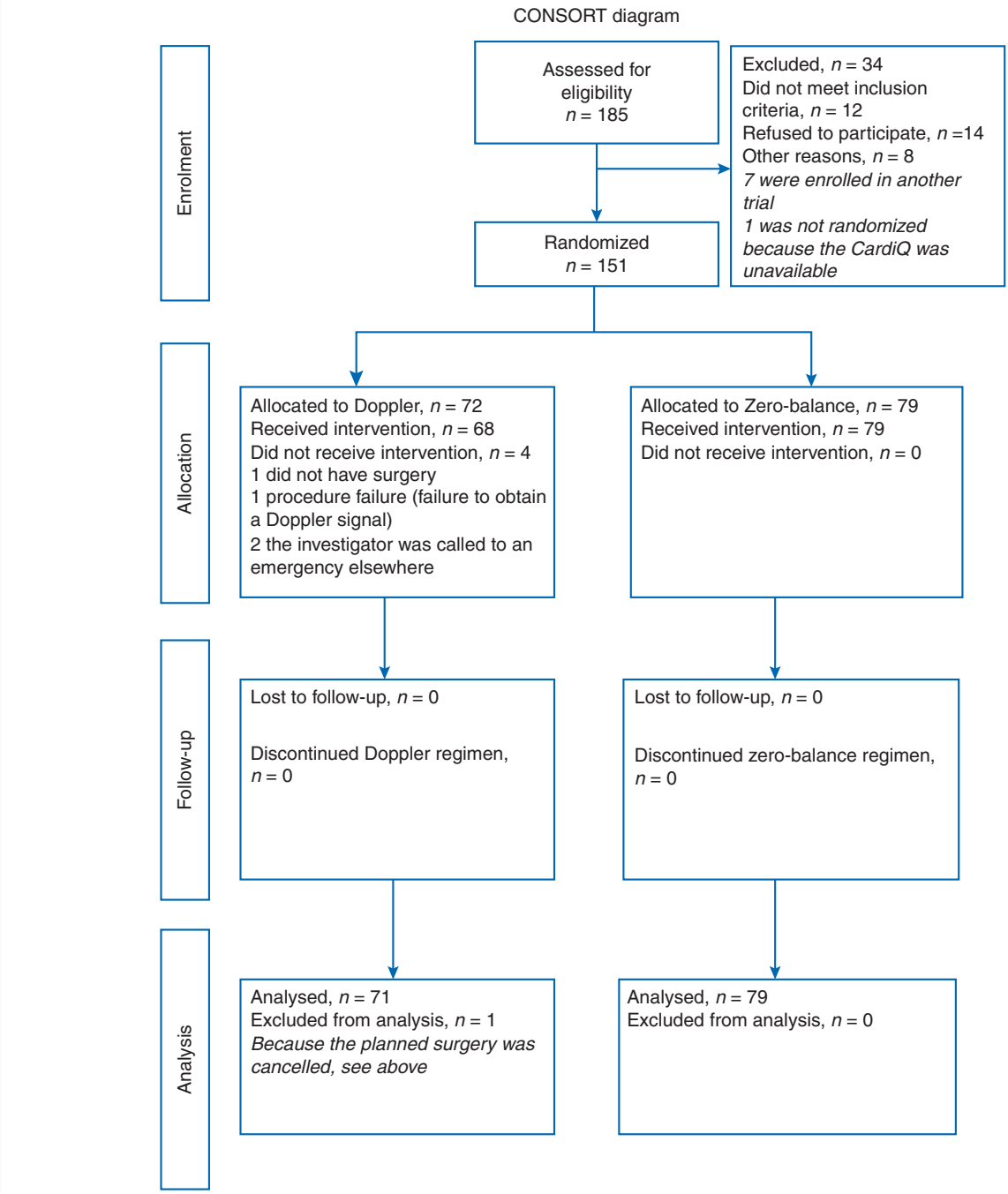

Fig 2 The CONSORT trial profile.

No significant differences were found for AP or for the need of pressor substances between the groups (data not shown).

No significant differences were found for the need for antiemetic drugs or diuretic treatment between the groups (data not shown).

Discussion

This is the first time that the effect of fluid optimization with a Doppler in the oesophagus is tested against a zero-balance regimen (restricted fluid regimen) on postoperative morbidity, and the first time this has been done in a multicentre double-blinded trial, making the results more applicable to the daily clinical practice. The trial was designed to show a difference in complications with per-protocol defined diagnostic criteria for postoperative occurrences accepted as complications. Such definitions have not been applied in any of the previous trials of the effect of Doppler optimization nor have hypotheses been tested with per-protocol planned analysis of subgroups of complications.[11–15 22]Another

Table 1 Patient characteristics

	Zero-balance group ($n=79$)	Doppler group ($n=71$)	*P*-value
Gender (n) (male)	47 (59%)	39 (55%)	0.573
Age [mean (SD)] (yr)	68.1 (14.9)	66.9 (14.9%)	0.787
ASA			
I	20 (25%)	26 (37%)	0.134
II	43 (54%)	37 (52%)	0.776
III	16 (20%)	8 (11%)	0.181
BMI [mean (SD)] (mean)	25.6 (4.3)	24.8 (4.3)	0.286
Smokers (n)	12 (15%)	15 (21%)	0.358
Alcohol habits [mean (SD)] (Drinks week^{-1})	5.2 (7.7)	5.9 (7.8)	0.600
Co-existing diseases			
None	30 (38%)	30 (42%)	0.708
Cardiovascular	50 (62%)	41 (58%)	0.488
Heart valve disease	3 (4%)	0 (0%)	0.247
Congestive heart failure	3 (4%)	1 (1%)	0.622
Ischaemic heart disease	8 (10%)	4 (6%)	0.376
Atrial fibrillation	3 (4%)	7 (10%)	0.193
Other heart diseases	1 (1%)	2 (3%)	0.603
Hypertension	32 (41%)	24 (34%)	0.397
Intermittent claudication	0 (0%)	2 (3%)	0.222
Previous DVT	0 (0%)	1 (1%)	0.473
CNS	5 (6%)	7 (10%)	0.550
Stroke	2 (3%)	3 (4%)	0.668
Other CNS diseases	3 (4%)	4 (6%)	0.708
Pulmonary	12 (15%)	5 (7%)	0.130
Cold	5 (6%)	4 (6%)	1.000
Asthma	7 (9%)	1 (1%)	0.066
Endocrine	14 (18%)	7 (10%)	0.239
NIDDM	7 (9%)	3 (4%)	0.334
IDDM	1 (1%)	2 (3%)	0.603
Other endocrine diseases	6 (8%)	2 (3%)	0.281
Renal diseases	3 (4%)	2 (3%)	1.000
Hepatic diseases	1 (1%)	0 (0%)	1.000
Rheumatic	3 (4%)	0 (0%)	0.247
Rheumatoid arthritis	1 (1%)	0 (0%)	1.000
Rheumatic polymyalgi	2 (3%)	0 (0%)	0.498

Table 2 Clinical outcome

	Zero-balance group ($n=79$)	Doppler group ($n=71$)	*P*-value
Mortality (n)	1 (1%)	1 (1%)	1.000
Patients with complications (n)	24 (30%)	23 (32%)	0.791
Patients with major complications (n)	8 (10%)	10 (14%)	0.616
Patients with minor complications (n)	22 (28%)	20 (28%)	0.965
Patients with cardiopulmonary complications (n)	3 (4%)	5 (7%)	0.477
Patients with tissue-healing complications (n)	13 (16%)	8 (11%)	0.481

strength of this trial was that the control group was well defined and described (the goal of zero fluid balance), and not a standard fluid regimen where fluid was given at the discretion of the anaesthesiologist, making it very hard to judge what the Doppler actually has been tested up against.[11–15 22] Perhaps the most important strength of this trial was the control of the fluid therapy not only intraoperatively, but also in the recovery room and on the surgical ward, preventing poor postoperative fluid therapy to jeopardize a possible beneficial effect of the intraoperative fluid optimization on an outcome registered after 30 days. Yet, we could not find any significant differences in outcome between the groups.

This trial also has weaknesses: first, a selection bias may occur, because the presence of both the anaesthetist and the surgeon was mandatory for inclusion of the patients and hence not a strictly consecutive patient inclusion. Secondly, the intention-to-treat analysis could blur the results because of patients belonging to the D group who did not actually receive the fluid optimization treatment. Only three patients were, however, included in the D group without receiving the therapy (Fig. 2).

In the Z group, procedure failure was not a problem, because no special equipment was required and it was routine therapy during colorectal surgery in Denmark. Another weakness may be differences in treatments other than fluid therapy between the participating hospitals. This was counteracted by the stratification of randomization towards each centre.

During the last 50 yr, it has been believed that surgical trauma caused an internal shift in body fluids, causing hypovolaemia if several litres of fluid were not given.[8 9 27] However, recently we have shown, however, that not only was this loss-to-third-space not evidence-based,[18] but postoperative outcome could be improved considerably if replacement fluid for third-spacing was abandoned.[1–7 21 22]

Anaesthetic drugs cause vasodilatation and a shift in blood volume from the central parts of the circulation to the peripheral parts. To counteract this central hypovolaemia, it has been argued that excess fluid during surgery was needed to increase the preload of the heart and thus increase the SV and CO. It was therefore somewhat

Table 3 Per-protocol defined diagnostic criteria for common complications and total number of complications registered. Besides these complications, one patient had spinal headache requiring a blood patch, and two patients had renal insufficiency[3] requiring dialysis in the zero-balance group. This occurred after reoperations and sepsis. In the Doppler group, one patient had an ulcer in the ventricle requiring endoscopic treatment, and one had a stroke[3] with clinical symptoms and CT changes. Some patients had more than one complication. *Per-protocol defined as tissue-healing complications. †Major complications. ‡Per-protocol defined as cardiopulmonary complications

Complication	Diagnostic criteria	Z group	D group	*P*-value
Superficial wound infection*	Surgical or conservative treatment of dermal/ subcutaneous wound defects with emptying of pus	9	6	0.596
Superficial wound rupture*	Surgical or conservative treatment of dermal/ subcutaneous wound defects without emptying of pus	3	3	1.000
Superficial wound haematoma*	Surgical or conservative treatment of dermal/ subcutaneous wound defects with emptying of haematoma	0	0	-
Dehiscence with or without infection*,†	Spontaneous dehiscence of the fascia with or without emptying of pus	2	1	1.000
Anastomotic leakage*,†	Symptomatic leakage requiring reoperation	3	1	0.622
Separation of the stoma*	Surgical or conservative treatment	1	0	1.000
Sepsis†	Clinical signs and positive blood culture	2	1	1.000
Peritonitis†	Pus in the abdomen needing antibiotic treatment and drainage or reoperation	2	3	0.668
Intra abdominal abscess†	Symptomatic and need for drainage	1	1	1.000
Cardiac arrhythmia, ventricular‡,†	New arrhythmia, symptomatic, and ECG changes	1	1	1.000
Cardiac arrhythmia, atrial‡	New arrhythmia, symptomatic, and ECG changes	1	2	0.603
Pulmonal congestion‡	Clinical and stethoscope findings, X-ray verified, and clinical improvement by diuretic treatment	0	0	—
Pleural exudation‡	Symptomatic, X-ray verified, and requiring treatment	0	0	—
Pulmonary oedema and ARDS†,‡	Requiring transfer to the intensive care unit	0	0	—
Pneumonia‡	Clinical and stethoscope findings (fewer, leucocyte increase, coughing, crepetition) and X-ray verified	0	2	0.222
Myocardial infarction‡,†	Acute changes in the ECG and significant cardiac enzyme increase	0	1	0.473
Pulmonary or other central thrombosis/ emboli†	Verified by scintegraphic examination, CT or another sufficient modality	0	1	0.473
Deep vein thrombosis	Clinical symptoms verified by ultrasound or phlebography	0	0	-
Reoperation pro haemostasis†	Requiring reoperation	1	1	1.000
Cystitis	Positive nitrite or clinical significant culture	7	4	0.540
Ileus, mechanical†	Clinical signs and reoperation	2	1	1.000
Ileus, paralysis	Minimum 5 days without flatus or faeces	3	6	0.309
Delirium/ psychosis	Requiring medical treatment	0	0	-

unexpected to find that the SV and the CO did not decrease significantly in the Z group. This supports the point of view that the zero-balance therapy was actually a normovolaemic therapy and not fluid restriction. Moreover, the lack of

improvement in outcome in the Doppler group was not explained by failure in adherence to the protocol, as the SV and the CO increased significantly in response to the fluid optimization in the D group.

For the patients undergoing open surgery, our Doppler regimen was similar to regimens used in previous trials,[15] but in the previous trials, laparoscopic surgical procedures were not included. Few trials have examined the effect of different fluid volumes on outcome after laparoscopic surgery: in gynaecological surgery, one trial found fluid to reduce dizziness and drowsiness,[28] another found fluid to reduce nausea and vomiting but not dizziness,[29] and the third found no difference between the groups.[30] One trial testing fluid volumes on patients undergoing laparoscopic cholecystectomy found that fluid reduced nausea, dizziness, and drowsiness, increased performance on a trade-mill, pulmonary function, and shortened LOS.[31] This trial was, however, biased by the fact that the patients in the low fluid group received significantly greater doses of opiates after operation. The combination of pain and opiates may be responsible for all the above-mentioned differences between the groups. One trial testing different fluid strategies in laparoscopic colectomy found no clinical relevant difference in outcome between the groups.[32] In our opinion, no evidence exists that patients undergoing laparoscopic surgery should be treated differently from those undergoing open surgery, and we could not show a benefit of the Doppler optimization as performed in this trial for the patients undergoing laparoscopic surgery.

With laparoscopic surgery being the surgery of the future, we included laparoscopic colorectal surgery to avoid the trial from being outdated before it was even begun.

The pressor substances needed to keep an acceptable AP were not changed by the fluid optimization. These findings are in accordance with the results of the trials of volume preloading of epidural analgesia,[11 33–37] all showing that volume does not effectively treat the decrease in AP caused by the epidural vasodilatation, that is, flow can be increased by fluid therapy, but AP must be controlled with pressor substances and is not influenced by fluid therapy in normovolaemic patients.

This trial had a power of 85% to show a difference in complications between the groups, leaving a 15% risk that the negative result may be due to a type 2 error (overlooking a difference that is actually there). The number of patients with complications in the two groups did not, however, show even a trend indicating that this should be the case. The optimization regimen resulted in a very small fluid volume difference between the two groups compared. However, in contrast to the previous published trials of Doppler optimization, the fluid volumes in our trial reached statistical significance. As we have previously argued, it may be understandable that such a small amount of a colloid may not cause a great difference in outcome.[22] Against this point of view is that the fluid was given individually to the patients needing it, and that looking at mean amounts of fluid may provide a wrong picture. On the other hand, the fluid optimization programme was not causing harm, and may therefore be useful for the anaesthesiologist treating patients with great fluid and blood losses, for example, during acute surgery or in the ICU; the latter calling for new clinical randomized trials.

In conclusion, we could not show any benefit nor harm for ED-guided goal-directed fluid therapy to near-maximal SV compared with goal-directed fluid therapy to zero fluid balance in patients undergoing elective colorectal surgery.

Supplementary material

Supplementary material is available at *British Journal of Anaesthesia* online.

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Declaration of interest

None declared.

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